European Society of Pathology

Abstracts

37th European Congress of Pathology

Tradition Meets Future

6–10 September 2025

Vienna, Austria

Virchows Archiv
https://doi.org/10.1007/s00428-025-04179-2

ABSTRACTS

37th European Congress of Pathology - Abstracts

Oral Free Paper Sessions

OFP-01 Oral Free Paper Session Gynaecological Pathology & Cytopathology

OFP-01-001
p16/Ki67 dual staining as an additional special circumstance recommendation for p16 immunohistochemistry in the diagnosis of HPV-associated lesions in cervical biopsy specimens: results from a 7-year study

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Background & Objectives: p16 immunohistochemistry in diagnosing HPV-associated squamous lesions of the cervix follows the Lower Anogenital Squamous Terminology (LAST) criteria, which recommend its use in ≤IN1 surgical specimens with a high-risk for missed high-grade disease, defined as abnormal screening results (HSIL, ASC-H, ASC-US/HPV16+, AGC-NOS). p16/Ki67 dual staining (DS) has emerged as a promising HSIL/CIN2+ biomarker in secondary cervical cancer screening. This study evaluates whether DS-positive (DS+) status can serve as an equivalent diagnostic criterion to HSIL, ASC-H, and ASC-US/HPV16+ for p16 immunohistochemistry application in clinical practice.
Methods: A retrospective analysis included 28,525 cervical cancer screening tests and 602 histology results retrieved between 2015 and 2022. Among them, 314 patients had HR-HPV testing, liquid-based cytology, DS, histology diagnosis from colposcopy with biopsy, and p16 immunohistochemistry results. DS+ status was compared with HSIL, ASC-H, and ASC-US/HPV16+ regarding HSIL/CIN2+ results. Statistical methods included chi-square test, logistic regression, and ROC/AUC analysis. Machine learning models (Random Forest, XGBoost) were applied to explore the predictive potential of DS+. AGC-NOS cases (n=1) were excluded due to insufficient sample size.
Results: Among 314 patients, 227 were DS+, 19 had HSIL, 23 ASC-H, and 51 ASC-US/HPV16+. Chi-square test demonstrated the strongest association between DS+ and HSIL/CIN2+ (X^2=28.315, p<0.001), with higher values compared to HSIL, ASC-H, and ASC-US/HPV16+. Logistic regression confirmed DS+ as a significant HSIL/CIN2+ predictor (OR=2.14, p<0.001). ROC analysis revealed a higher AUC for DS+ (0.651) compared to HSIL (0.556), ASC-H (0.524), and ASC-US/HPV16+ (0.476), suggesting superior diagnostic performance.
Conclusion: The 7-year screening findings indicate that p16/Ki67+ is at least as strongly associated with HSIL/CIN2+ as the current LAST standardization criteria. Given its predictive value and higher AUC, DS+ may serve as a valuable additional criterion for p16 immunohistochemistry in HPV-associated squamous lesions of the cervix, alongside existing additional special circumstance recommendations.

OFP-01-002
WHO classification system in soft tissue cytopathology: diagnostic accuracy and malignancy risk assessment

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Background & Objectives: Diagnosing soft tissue tumours, which are intricate neoplasms, often necessitates precise identification through fine-needle aspiration (FNA). The World Health Organization (WHO) classification system seeks to standardize the cytopathological evaluation and assess the risk of malignancy (ROM) in these tumours. This manuscript aims to classify soft tissue FNA samples based on the recently proposed WHO classification for reporting soft tissue cytopathology and to assess this system's sensitivity, specificity, and diagnostic accuracy in diagnosing malignancies.
Methods: This retrospective analysis encompassed cytological specimens collected between January 2022 and June 2023. Specimens were classified into six categories following the WHO system: non-diagnostic (ND), benign, atypical, soft tissue neoplasm of uncertain malignant potential (STNUMP), suspicious for malignancy (SFM), and malignant. Histopathological comparisons were conducted, and the ROM, along with sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy, were determined.
Results: The study analysed 203 samples, with findings showing 62.5% benign, 13.8% SFM, and 9.9% malignant cases. The ROMs were calculated as 33.3% for ND, 1.2% for benign, 40% for atypical, 25% for STNUMP, 80% for SFM, and 100% for malignant. Histopathological correlation was available for 117 cases. The highest sensitivity and diagnostic accuracy (77.3% and 93.9%, respectively) were observed when SFM and malignant categories were grouped as indicative of malignancy. Specificity peaked at 100% when only the malignant cases were classified as positive. The interobserver agreement was moderate, with a Cohen's kappa of 0.45.
Conclusion: The WHO classification system for soft tissue cytopathology enhances diagnostic accuracy and standardizes reporting. It serves as an effective tool for categorizing soft tissue tumours and guiding clinical management, though further refinements are necessary for its widespread application.

Published online: 22 August 2025

OFP-01-003

DICER1 mutations are mutually exclusive with the _BRAF_^{V600E} mutation: a retrospective study with 510 cases of Bethesda III nodules

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Background & Objectives: This study aimed to investigate the prevalence and cytological features of *DICER1*-mutant fine-needle aspiration (FNA) specimens in Bethesda III thyroid nodules and to explore the relationship between *DICER1* and *BRAF*^{V600E} mutations.
Methods: We collected 510 consecutive FNA cases diagnosed as Bethesda III from a single medical centre over one year. Mutations in *DICER1* (exons 24 and 25), *BRAF*^{V600E}, and *TERT* promoter were detected using Sanger sequencing. The association between DICER1 mutations and cytopathological features was also analysed.
Results: *DICER1* mutations were identified in 25 patients (4.9%, 25/510), while the *BRAF* ^{V600E}mutation was detected in 76 patients (14.9%, 76/510). The two mutations were mutually exclusive. No cases exhibited *TERT* promoter mutations. All *DICER1*-mutant cases were classified as AUS-other in this cohort. We found that the *DICER1*-mutant FNAs exhibited *RAS*-like nuclear features. Patients with *DICER1* mutations were younger than those in the wild-type group, and their tumours were significantly larger. However, *DICER1* mutation status was not associated with serum thyroid hormone levels.
Conclusion: Our findings suggest that *DICER1*-mutant Bethesda III nodules are unlikely to be *BRAF*-mutant carcinomas. Further study of the molecular characteristics of *DICER1*-mutant FNAs will contribute to more accurate cytological diagnosis.

Funding: Taishan Scholar Program (No. tsqn202211376), National Natural Science Foundation of China (No. 82172616), Natural Science Foundation of Shandong Province (No. ZR2021MH097)

OFP-01-004

A predictive mutation to identify endometrial carcinomas with better prognosis: *CCNB3*

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Background & Objectives: Endometrial carcinoma, the most common gynaecologic malignancy in developed countries, has undergone molecular classification. *POLE* mutant (*POLE*mut) subtype shows the highest survival rates, and its presence influences treatment decisions. These mutations cause disordered proofreading activity. Consequently, errors in replication cannot be rectified, and the accumulation of mutations contributes to clinicopathological features. To better understand the *POLE*mut subtype and develop a more targeted genomic approach, we performed an in-silico analysis of Cyclin B3 (*CCNB3*), a gene responsible for cell cycle control frequently mutated in *POLE*mut patients.
Methods: Data regarding *CCNB3* alterations in The Cancer Genome Atlas Pancancer Atlas dataset was acquired from cBioPortal. 507 cases with precise molecular subtyping were included in the study. Clinicopathologic analyses were conducted using cBioPortal.
Results: *CCNB3* mutant cases included 45 *POLE*mut, 12 MSI, 1 copy number-low, and 2 copy number-high subtype cases with a high frequency of *POLE*mut subtype ($p<10^{-10}$, $q<10^{-10}$). Mutation count (mean: 6695.63 vs 304.16) and tumour mutation burden (mean: 229.98 vs 10.28) were higher in *CCNB3* mutant cases compared to wild-type cases ($p<10^{-10}$, $q<10^{-10}$). *CCNB3* mutant cases had 95.20% overall, 90.50% progression-free, while *CCNB3* wild-type cases had 51.67% overall (p=3.132e-3, q=6.264e-3, HR: 6.295 [95% CI: 3.348-11.838]) and 59.01% progression-free (p=1.386e-3, q=5.543e-3, HR: 4.408 [95% CI: 2.588-7.509]) survival. *POLE*mut subtype had 73.3%, 91.75, and *POLE*wt group had 56.30%, and 59.13% overall (p=4.473e-3, q=8.945e-3, HR: 0.169 [95% CI: 0.088-0.321]) and progression-free (p=1.211e-3, q=4.845e-3, HR: 0.186 [95% CI: 0.107-0.323]) survival, respectively.
Conclusion: *CCNB3* mutant group included 45 out of 49 from *POLE*mut subtype and distinguished 15 *POLE*wt cases. Even with the addition of 15 cases from subtypes with worse prognoses, a slightly lower progression-free survival but a significantly improved overall survival were observed compared to the *POLE*mut subtype. Utilizing *CCNB3* evaluation can be valuable in selecting cases from heterogeneous subtypes, leading to more comprehensive and effective molecular classification.

OFP-01-005

Correlation between p53 immunohistochemical staining and *TP53* molecular testing in endometrial carcinomas: a detailed assessment of discrepant cases with implications for patient management

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Background & Objectives: The TCGA molecular classification of endometrial carcinomas (ECs) has prognostic and predictive value. This study evaluates the concordance between p53 immunohistochemistry and *TP53* molecular testing in a consecutive cohort of ECs from a population-based setting.
Methods: A study was conducted on 386 consecutive ECs using NGS (83 genes, including *POLE* and *TP53* and microsatellite instability analysis) and immunohistochemistry for p53, hormone receptors, and MMR proteins. Cases with discrepancies between molecular and immunohistochemical p53 results were studied.
Results: Of the 386 carcinomas, 8% were *POLE*mut, 24.9% MMRd, 21.5% p53abn, and 45.6% NSMP. A total of 7% were multiple classifiers. The initial concordance between p53 immunohistochemistry and *TP53* NGS was 88.6% (44/386), increasing to 93.5% after reviewing the p53 stained slides of discordant cases. Among the 44 discordant cases, after review 19 were reclassified from p53 wild-type staining to mutation-type, including 13 with a subclonal p53 pattern of mutation-type immunoreactivity. Twenty-two cases (5.7%) with a subclonal pattern of mutation-type p53 immunoreactivity but with *TP53* mutations on NGS were identified, mostly low-grade endometrioid carcinomas (15/22;68.1%). Overall *TP53* mutations were detected in 9.6% of low-grade endometrioid carcinomas (25/260): 12 were of p53abn molecular type, all being low-risk carcinomas (Stage I).
Conclusion: The integrated use of NGS and immunohistochemistry enhances the accuracy of TCGA molecular classification. High concordance supports p53 immunohistochemistry as a *TP53* mutation surrogate, although the correlation is not perfect. Recognizing subclonal p53 immunohistochemical patterns is important for TCGA classification when molecular testing is not undertaken. Uncertainty persists regarding the classification and management of low-risk (low-grade and low-stage) endometrioid carcinomas in the p53abn subgroup.

OFP-01-006

Six-pattern-based p53 interpretation in 1284 vulvar squamous cell carcinomas: inter-pathologist variation, pattern distribution, and classification with incorporation of p16 and high-risk HPV

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Background & Objectives: The classification of vulvar squamous cell carcinoma (VSCC) distinguishes between human papillomavirus (HPV)-associated and HPV-independent types based on p16, a surrogate marker for high-risk HPV (hrHPV). p53 immunohistochemistry also has a key role, though its interpretation has varied over time. Recent studies, however, have identified six distinct p53 patterns. Using a large, unselected cohort of 1285 VSCC cases, we aimed to explore the robustness of this six-pattern p53 classification by evaluating inter-pathologist variation, map the pattern distribution and classify the cases by incorporating p16 and hrHPV DNA status.
Methods: In the Danish Pathology Data Bank, we identified 1285 women diagnosed with primary VSCC (1990–2017) and retrieved formalin-fixed paraffin-embedded tumour blocks. Eight gynaecological pathologists evaluated p53 immunohistochemistry, classifying cases as wild-type (scattered or mid-epithelial) or abnormal (basal overexpression, parabasal/diffuse overexpression, absent, or cytoplasmic). p16 had previously been scored, and p53 scoring was conducted with the corresponding p16 slide available for reference.
Results: Concordance across the six p53 immunohistochemical patterns was 66.6% (856/1285), increasing to 86.9% (1117/1285) when categorized as p53 wild-type or abnormal. Most discordances (313/429) involved cases where one pathologist assigned the 'scattered' pattern, while another classified it differently. Stratified by p16 status, concordance was 62.9% in p16-positive and 68.6% in p16-negative cases but increased to 94.5% and 82.8%, respectively, when categorized as wild-type or abnormal. A third evaluation of discordant pairs is ongoing.
Conclusion: This study represents the largest investigation to date on the robustness of the six-pattern-based p53 classification in VSCC. The overall concordance in scoring across the six patterns was 66.6%, increasing to 86.9% when simplified into abnormal versus wild-type categories. Concordance (wild-type/abnormal) was higher in p16-positive cases compared to p16-negative cases. The final distribution of p53 patterns and cohort classification, incorporating p16 and hrHPV DNA status, will be presented at the conference.

OFP-01-007

HPV-Independent CIN-lesions of the uterine cervix - a new concept cervix

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Background & Objectives: There is increasing evidence about HPV-independent (HPVI) squamous cell carcinomas of the uterine cervix (CSCC). While HPV-associated CSCC precursor lesions (i.e. high-grade squamous intraepithelial lesion, HSIL) are well characterised, features of HPVI-precursors are limited.
Methods: Histopathological and immunohistochemical evaluation (p16, p53) as well as mutational analysis by next generation sequencing performed on HPV high-risk DNA negative (HPVI) squamous precursor lesions.
Results: Six cases were available with a mean age of 74.5 years of age (range 64 to 83 years). Five precursors represented dVIN-like morphology, associated with aberrant p53-immunoepression (parabasal/diffuse overexpression), non-block-like p16 staining and pathogenic TP53-mutation, seen in patients with uterine prolapse. One case not associated with prolapsed uterus represented features similar to HPV-associated HSIL, no p16-overexpression but p53-wildtype staining pattern. On molecular level pathogentic *TERT* promotor mutation and a possible pathogenic mutation of *HRAS* occurred.
Conclusion: HPVI squamous precursor lesion of the uterine cervix are exceedingly rare and represent a range of morphologic findings. Some lesions represent features seen in differentiated vulvar intraepithelial neoplasia (dVIN-like) and others features similar to HPV high-risk associated HSIL. Molecular alterations are variable with *TP53*-mutation (dVIN-like HPVI precursors) and *TERT*- as well as *HRAS*-alteration (HSIL-like HPVI precursor).

OFP-01-008

Spatial Cancer-Immune Phenotypes in NSMP Endometrial Carcinomas: transcriptomic profiling reveals distinct pathways of immune evasion

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Background & Objectives: The classification of the tumour immune microenvironment into spatial cancer-immune phenotypes (SCIs)—inflamed, excluded, and desert—is gaining recognition as a key determinant of immune response and prognosis in solid tumours. NSMP endometrial carcinomas (ECs), which lack a defining molecular alteration, represent a heterogeneous group with limited predictive biomarkers. The aim of this study was to define the immune transcriptomic landscape of SCIs within NSMP ECs to uncover immune-related mechanisms associated with prognosis.

Methods: 47 NSMP ECs, previously classified by molecular subtype and SCI using digital pathology and immunohistochemistry (CD3, CD8, CD68, CD20, PD-L1), were profiled using the NanoString PanCancer Immune panel. Gene expression data were analysed to identify differentially expressed genes across the three SCI groups.
Results: Nanostring profiling revealed distinct transcriptional signatures across SCI groups:

- Inflamed tumours showed broad activation of the immune response, with significant upregulation of genes involved in antigen presentation (HLA genes), T and NK cell cytotoxicity (PRF1, IL15), interferon signalling, and immune checkpoints (PDCD1, CTLA4).
- Excluded tumours exhibited partial immune activation, but with concurrent downregulation of MHC-related genes and components of the antigen processing machinery, indicating functional immune exclusion despite immune cell presence (HLA genes down; CDH1, MAGEA4 up).
- Desert tumours were characterized by overall immune silence and upregulation of genes associated with cell cycle progression and immune escape (TTK, ILF3, TNFRSF11A).

Pathway analysis confirmed a progressive loss of immune-related functions from inflamed to excluded to desert, with excluded tumours showing selective suppression of antigen presentation as a hallmark of immune evasion.
Conclusion: Transcriptomic profiling reveals that SCI subtypes in NSMP ECs represent biologically distinct immune states. The immune-excluded phenotype, in particular, is defined by a paradox of immune infiltration with silenced antigen presentation. These findings support the incorporation of SCI into molecular risk stratification and suggest new opportunities for targeted immune modulation.

Funding: The research leading to these results has received funding from AIRC under MFAG 2021 – ID. 26319 project – P.I. De Leo Antonio

OFP-01-009

Transcriptomic dysregulation of the epithelial-to-mesenchymal pathway defines a novel HPV-independent subset of vulvar squamous cell carcinoma with worse disease specific survival

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Background & Objectives: Vulvar squamous cell carcinoma (VSCC) is a rare malignancy with two distinct pathways: human papillomavirus-associated (HPV-A) and HPV-independent (HPV-I), with HPV-I tumours having impaired prognosis. We investigated the transcriptional networks differentially activated in VSCC tumours, to improve risk stratification and identify therapeutic targets.
Methods: Retrospective analysis of 73 primary VSCC (19 HPV-A, 54 HPV-I) surgically treated from 1996 to 2023 at the Hospital Clínic of Barcelona. Whole transcriptomic analysis (HTG Edge-Seq) in a clinically annotated series was performed on formalin-fixed, paraffin-embedded samples.
Results: The study of the top differential transcriptional pathways activated in HPV-I samples revealed three distinct molecular clusters: clusters 1 and 2 composed mainly of HPV-I VSCC, and cluster 3 composed mainly of HPV-A tumours. Cluster 1 exhibited epithelial features (CDH1 overexpression) and metabolic pathways (mTOR). Cluster 2 exhibited an epithelial-mesenchymal (EMT) signature (TWIST1/SNAI2/ZEB1 upregulation) with angiogenesis activation (VEGFC/MMPs). Cluster 3 showed an enrichment in IFN-gamma response pathway. Patients with EMT signature (cluster 2 tumours) showed worse disease-specific survival (DSS, p=0.044) and a trend toward reduced recurrence-free survival (RFS; p = 0.056). A simple H&E classifier based on the invasion patterns was established, including two categories, closed/ finger and spray patterns. Spray pattern predicted tumours with EMT signature (cluster 2) with a sensitivity of 84.4% and a specificity of 71.4%. This H&E-based classifier also correlated with survival, with tumours showing spray pattern having worse DSS than those having closed/finger pattern (p=0.0052).
Conclusion: Our study provides a complete overview of the transcriptional networks supporting HPV-I VSCC cases, identifying a subset of patients with high EMT expression signature correlating with poorer DSS. We have successfully translated these molecular findings into a practical H&E-based classification system using the invasion pattern, which correlates with DSS. The H&E-based classifier offers a globally accessible tool to identify tumours with EMT signature, addressing unmet needs in resource-limited settings.

Funding: Project 'PI23/00494; funded by Instituto de Salud Carlos III and co-funded by the European Union 'A way to make Europe'

OFP-01-010

Update on the interpretation of somatic *POLE* mutations in endometrial carcinomas

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Background & Objectives: *POLE* mutation testing is essential for endometrial carcinomas (EC) molecular classification. Eleven hotspot mutations are considered canonical. While the POLE-score aids in evaluating rare variants, its use varies with testing methods. We present our interpretation of *POLE* and *POLD1* pathogenic mutations in a large, clinically and molecularly annotated EC cohort.
Methods: We analysed a cohort of EC cases previously sequenced using extended cancer gene panels (368–505 genes), assessing *POLE* and *POLD1* variants, tumour mutational burden (TMB), and microsatellite instability (MSI). Immunohistochemistry for p53 and MMR proteins completed the molecular profiling. Statistical analysis was used to correlate molecular and clinicopathological features.
Results: We surveyed a cohort of 2533 EC and identified 152 tumours with *POLE* variants involving the exonuclease domain of the gene (exons 9-14; 6%) and 16 cases with *POLD1* pathogenic variants (0.6%), among the *POLE* variants 84% were regarded as canonical. Within EC with canonical *POLE* variants, the median TMB was 52.7 mutations per megabase (m/mb) while for cases with non-canonical *POLE* exonuclease mutation the median TMB was 119 (m/mb) and for *POLD1* mutated cases it was 106 (m/mb; p=0.21). Among the cases with pathogenic *POLE* mutations, 5% had concurrent DNA mismatch repair deficiency (MMRd), while among the *POLD1* and non-canonical *POLE* mutated cases 80% and 47% had MMRd (p<0.001). No differences in histomorphologic features was identified. Survival analysis showed that the cases with non-canonical *POLE* had worse progression free and overall survival outcomes (log rank p<0.01).
Conclusion: Our analysis identified non-canonical *POLE* exonuclease domain and *POLD1* variants that show an ultramutated phenotype. They were more likely to be double classifiers (MMRd/*POLE* or

POLD1) and there may be clinical differences between their outcomes compared to canonical *POLE* mutated cases. These findings have implications for the testing methodology implemented in endometrial carcinoma molecular classification, as well as decisions regarding treatment de-escalation.

Funding: Fonds de Recherche du Québec - Santé (FRQS), Marathon of Hope Cancer Centres Network (MOH-CCN)

OFP-01-011

Endometrial and colorectal cancers: concordance between NGS-MSI and IHC-MMR

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Background & Objectives: Assessing mismatch repair (MMR) status is crucial for prognostic and predictive purposes, including Lynch syndrome screening. International guidelines recommend evaluating MMR status in newly diagnosed colorectal (CRC) and endometrial cancer (EC) patients. While immunohistochemistry (IHC) is the most commonly used method for MMR status assessment, other molecular tools, such NGS, can also be employed.
Methods: The aim of this study was to evaluate the concordance between NGS-MSI and IHC-MMR in a prospective cohort of CRC and EC patients from a large referral centre. We performed a detailed genomic and pathological analysis of discordant cases to explore reasons for discrepancies between methods.
Results: 520 patients were enrolled, 352 EC and 168 CRC. The overall concordance between IHC-MMR and NGS-MSI was 90% (CI: 87%-92%). Sensitivity was 62%, specificity 99%, with a positive predictive value of 98% and a negative predictive value of 88%. EC cases showed lower concordance rate (85%) compared to CRC cases (99%), largely due to microsatellite stable (MSS) status in MMR-deficient samples. Discordant CRC cases had poor responses to immunotherapy. In EC, 28% of discordant cases were linked to POLE mutations (10%), atypical IHC-MMR patterns (6%), MSH6 protein loss (18%). Around 60% of discordant EC cases involved Lynch syndrome (12%), MMR somatic variants (4%), MLH1 hypermethylation (37%). Differences in unstable loci among MMR phenotypes ($p = 0.003$) contributed to reduced MSI scores in cases with MLH1/PMS2 loss, accounting for 56% of discordant EC cases. Adjusting the MSI score threshold to 6.1 improved the AUC to 0.9 for predicting MMR status in EC.
Conclusion: The concordance between NGS-MSI and IHC-MMR was 90%, with a lower concordance in EC compared to CRC. Microsatellite instability assessed by NGS showed varying levels of concordance with MMR deficiency by IHC in CRC and EC patients. Tumour-specific thresholds may help reduce false negative cases and improve therapeutic decision-making.

OFP-01-012

KDM2B is a highly sensitive marker in high-grade endometrial stromal sarcoma

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Background & Objectives: KDM2B plays an important role in recruiting the polycomb repressive complex 1.1 (PRC1.1) to CpG islands, facilitating transcriptional repression. Recent studies have shown KDM2B to be highly expressed in soft tissue tumours harbouring alterations in *BCOR,* which is a core component of PRC1.1. The aim of this study was to evaluate the diagnostic value of KDM2B immunohistochemistry in the differential diagnosis of endometrial stromal neoplasms, including tumours with PRC1.1-associated alterations.
Methods: Formalin-fixed and paraffin-embedded (FFPE) tissue of endometrial stromal tumours of various genotypes was retrieved and a tissue microarray (TMA) constructed. A FFPE tissue section was stained on a Leica BOND RX stainer using a FBXL10 (KDM2B) antibody (clone D3T8J, Cell Signaling Technology) at 1:50 dilution. Only nuclear staining was evaluated, and the staining was quantified using an H-score.
Results: The series included 3 endometrial stromal nodules, 58 low-grade endometrial stromal sarcomas including tumours with confirmed *JAZF1::SUZ12* (n=9) and *EPC1::PHF1* (n=1) gene fusions, 11 high-grade endometrial stromal sarcomas including tumours with confirmed *ZC3H7B::BCOR/BCOR::LPP* (n=4) and *YWHAE::NUTM2* (n=5) gene fusions, 1 uterine tumour resembling ovarian sex cord tumour (UTROSCT) with an *ESR1::NCOA3*fusion, and 13 undifferentiated uterine sarcomas. An optimal cut-off value of H-score 10 was defined for KDM2B positivity. All endometrial stromal nodules, UTROSCT, and undifferentiated uterine sarcomas were negative for KDM2B. All but one low-grade endometrial stromal sarcomas were also negative. In contrast, all high-grade endometrial stromal sarcoma samples were positive for KDM2B (H-score range: 50 – 290).
Conclusion: In conclusion, our study shows that KDM2B is a highly sensitive and specific marker for high-grade endometrial stromal sarcoma, harbouring *ZC3H7B::BCOR* and *YWHAE::NUTM2* gene fusions. Future studies will aim to validate our findings and investigate additional molecular subtypes of uterine mesenchymal neoplasms to further confirm the specificity of KDM2B for HGESS.

OFP-01-013

Molecular profiling and tumour microenvironment in HPV-associated anogenital squamous cell carcinomas: detailed transcriptomic insights

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Background & Objectives: Human papillomavirus (HPV) infection plays a pivotal role in the pathogenesis of various anogenital squamous cell carcinomas (SCCs), including cervical, vulvar, and anal

cancers. Understanding the distinct molecular landscapes and immune microenvironments across these tumour sites may refine diagnostic accuracy and therapeutic approaches. We investigated transcriptomic profiles associated with tumour location and HPV genotypes to understand molecular distinctions and characterized the tumour immmune microenviroment.

Methods: We analysed 50 patients with HPV-associated SCC from cervix (n=19), vulva (n=16), and anal canal (n=15). HPV association was confirmed via p16 immunohistochemistry, high-risk HPV *in situ* hybridization, and PCR genotyping. Immune cell infiltration was assessed using multiplex immunohistochemistry (IRF1/CD20/CD3/CD68). Gene expression profiling employed Nanostring nCounter technology with the PanCancer Pathways panel covering 770 cancer-related genes.

Results: HPV16 was predominant across sites, while no HPV18 was detected. Transcriptomic profiling revealed two primary clusters distinguishing cervical from anal canal carcinomas, with vulvar cases distributed across both clusters. Cervical SCCs showed increased expression in inflammation, DNA repair, and FGF signalling. Anal canal tumours had elevated expression in epigenetic modulation and PI3K signalling. Vulvar tumours demonstrated mixed molecular features. GSEA further delineated HPV16-specific molecular characteristics. HPV16-driven SCCs exhibited suppressed DNA repair networks, senescence, and immune response pathways (CD8+ T-cell memory, activated CD4+ T cells), alongside activated extracellular matrix remodelling pathways. Cell cycle regulation was significantly altered, suggesting distinct proliferative dynamics compared to other HPV genotypes. The immune microenvironment showed higher intratumoral CD3+ T lymphocytes in cervical SCCs (p=0.028) and increased peri-tumoral CD68+ macrophages in vulvar carcinomas (p=0.012).

Conclusion: Distinct molecular signatures and immune profiles characterize HPV-associated anogenital SCCs according to tumour site and HPV genotype. Our transcriptomic analyses reveal molecular heterogeneity in HPV-associated anogenital SCCs based on location and HPV genotype. HPV16-driven tumours uniquely suppress DNA repair, immune responses, and cell cycle regulation while activating extracellular matrix remodelling.

OFP-01-014

YWHAE::NUTM2B-rearranged endometrial stromal sarcomas with pure low-grade morphology: a case series expanding the histologic spectrum

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Background & Objectives: The 2020 WHO classification categorizes endometrial stromal sarcomas (ESS) with YWHAE rearrangements as high-grade (HGESS). However, increased use of molecular diagnostics has expanded the recognized morphologic spectrum of YWHAE-rearranged ESS. Recent reports have described low-grade morphologies in these tumours. We present an additional case series highlighting unusual morphologic features in ESS harbouring YWHAE::NUTM2B fusions.

Methods: Cases with YWHAE gene fusions were identified from the institutional Sarcoma Targeted Gene Fusion Panel database. Pathology reports, and H&E slides were reviewed when available. Tumours with purely low-grade ESS (LGESS) morphology were selected. Detailed histologic features from one biopsy and five hysterectomy specimens were analysed, along with available clinical follow-up.

Results: Six patients with YWHAE::NUTM2B fusions were identified (median age: 43.5 years; range: 29–71). Tumour size ranged from 1.7 to 12.5 cm (median: 8.5 cm). All cases exhibited mild to moderate cytologic atypia with fibrous or fibromyxoid stroma, absent necrosis, and 1–3 mitoses per 10 high-power fields. Notably, three cases displayed pseudoangiomatoid features with dense hyalinized stroma lined by monolayer of cells, reminiscent of Masson's tumour. Immunohistochemically, cyclin D1 was positive in all cases (6/6); CD10 in 2/4; ER and PR in 4/4. Clinical follow-up was available for five patients (mean: 29 months). Two developed pulmonary metastases—one at diagnosis and one at 15 months—both alive at last follow-up. The remaining three showed no evidence of disease.

Conclusion: We describe a cohort of 6 ESS cases with YWHAE::NUTM2B fusions displaying purely low-grade morphology, including pseudoangiomatoid features and cyclin D1 co-expression with hormone receptors. CD10 expression was variable. These findings underscore the importance of molecular testing in morphologically low-grade ESS, as YWHAE rearrangement may not always correlate with high-grade histology but still carries metastatic potential.

OFP-02 Oral Free Paper Session Other Topics

OFP-02-001

The impact of congenital heart disease on hypoxic-ischemic encephalopathy: a comparative analysis

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Background & Objectives: Cardiorespiratory abnormalities, such as congenital heart disease (CHD), have been associated with significant disruptions in white matter. However, in recent years, grey matter involvement has also been analysed, including neuronal necrosis and gliosis, and degeneration of the posterior columns. The aim of this study is to review acute neuronal necrosis in CHD patients and compare it to findings in non-CHD.

Methods: The anatomopathological reports of foetal clinical autopsies (from week 22), perinatal and infant from 2000 to 2019 inclusive were reviewed. Subsequently, all cases with selective acute neuronal necrosis (SANN) in more than one vascular territory were selected. A total of 205 cases were identified, including 28 patients with CHD and 177 patients without CHD. An expansion of sample size including autopsies from 1992 to 2024 was made, resulting on the identification of 47 CHD cases more. Therefore, we compared the SANN cases of 75 cases of CHD (between 1992 to 2024) and the 177 non-CHD (between 2000 to 2019).

Results: CHD patients presented a greater involvement of cerebral neocortex in grey matter lesions, including both SANN and grey gliosis, compared to non-CHD individuals (SANN: p-value<0.001, chi-square=12.085; Grey gliosis: p-value<0.001, chi-square=13.76).
However, non-CHD showed a larger involvement of the thalamus, including SANN and grey gliosis (SANN: p-value=0.014, chi-square=6.096; Grey gliosis: p-value=0.018, chi-square=5.64). Additionally, non-CHD presented a higher involvement of SANN in pons (p-value<0.001, chi-square=32.012).
Furthermore, cerebral neocortex and midbrain involvement was more pronounced in individuals older than 37 weeks (cerebral neocortex: p-value<0.001, t=-3.600; midbrain: 0.035, t=-2.121).

Conclusion: CHD were found to be associated with both white matter and grey matter lesions. Our study aligns with previous authors who have identified the cerebral neocortex as a region of higher lesion frequency in CHD individuals. However, our findings contrast with

the classical perspective, which posits a greater involvement of the thalamus and pons.

OFP-02-002

Post-mortem toxicology analysis in a young Sudden cardiac death cohort – an Irish perspective

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Background & Objectives: Sudden cardiac death (SCD) is one of the leading causes of death worldwide, accounting for 10-15% of all deaths. SCD can be caused by acquired heart disease in older adults, and in younger adults it is more likely caused by a genetically acquired defect or by ingestion of illicit substances. In cases of SCD, toxicological analysis at post-mortem is crucial to elucidate the cause of death and detect the presence of substances causing drug-induced arrhythmias.
Methods: We aimed to assess post-mortem forensic toxicology in young sudden cardiac deaths over a 5-year period. A retrospective analysis was performed of completed autopsy reports in our institution from 2019 to 2023, aged from 16 to 49 years old.
Results: 2975 autopsy reports were reviewed and 277 cases (9.3%) of SCD with toxicological analysis performed were identified, all of which were coroner's cases. Mean age was 38 (SD 7.8). Toxicology was positive in 83.8% of cases (n=232) and negative in 16.2% (n=45). Drug overdose causing SCD accounted for 45.8% of cases (n=127), alcohol overdose 7.9% of cases (N=22), cardiac disease 30% of cases (n=83), SADS/SUDEP accounted for 5.8% each (n= 16 & n=16) and other (respiratory/DKA) 4.7% (n=13). Average heart weight was 420g (range 160g-985g). Polypharmacy (the presence of 2 or more substances on toxicology) was identified in 82.3% (n=191). The average number of substances identified on toxicology in each case was 4.9 (range 1-15). History of drug & alcohol misuse was significantly more common among cases with a positive toxicology profile (n=132, 56.9% vs n=4, 8.9%, P<0.001).
Conclusion: Toxicology plays a critical role in assessing the underlying cause of death in SCD cases. In our cohort, toxicology was positive in 83.8%, which is higher than previously published European data (57%). The overwhelming majority displayed polypharmacy (82.3%). 5.8% of cases were SADS (sudden arrhythmic cardiac death).

OFP-02-003

Modernising pathology education: enhancing medical students' exposure through simulated multidisciplinary team meetings

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Background & Objectives: Pathology, as a laboratory-based discipline, has traditionally been taught via didactic lectures and anatomy tutorials. While the growing emphasis on case-based learning and simulation in medical education fosters critical thinking and prepares students to contribute to multidisciplinary teams (MDTs) as junior doctors, this shift may reduce students' exposure to pathology, potentially influencing their interest in pursuing pathology as a career.
To increase medical students' exposure to pathology, while enhancing their readiness to contribute to MDTs as junior doctors, through the delivery of a simulated infectious diseases MDT meeting teaching session.
Methods: Four simulated cases were designed with an emphasis on teamwork and collaborative learning rather than solely on reaching the correct diagnosis. Students were divided into groups and assigned roles- clinician, pathologist and radiologist. Each group received a slide set relevant to their role and after a preparation period presented their findings in a simulated MDT meeting. Feedback on the session was obtained via a modified Readiness for Interprofessional Learning Scale (RIPLS), a validated questionnaire, to assess the students' readiness for interprofessional collaboration.
Results: Seventy-six medical students took part in the session. Of those who provided feedback, 97% agreed or strongly agreed that the event improved their understanding of the pathologist's role. Additional strengths included the team-based approach, with 91.2% of respondents stating that this helped them integrate clinical, pathological and radiological findings. 91.7% agreed or strongly agreed that the event would positively impact their approach to collaboration and diagnosis in future clinical practice.
Conclusion: This event was designed to enhance medical students' communication and teamwork skills, in keeping with current trends in medical education, while increasing their exposure to pathology. This approach aligns with the 37th European Congress of Pathology's theme, 'Tradition Meets Future' and offers a model to increase pathology exposure within the modern medical curriculum.

OFP-02-004

The Tumour Tissue Bank of the German National Cohort (NAKO): pilot of a centralized epidemiologically based biobanking

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Background & Objectives: The NAKO Health Study is a nationwide, long-term, population-based study. It contains 200,000 participants recruited by 18 study centres since 2014 and has the aim to gain knowledge of how widespread diseases develop, to improve prevention, early detection, and treatment. The centralized Tumour Tissue Bank (TTB) collects, characterizes, validates, and stores pseudonymized cancer tissue samples from participants of NAKO for future research. It's an integral infrastructure of NAKO, attached to the NCT tissue bank and the BioMaterialBank Heidelberg (BMBH) and represents a worldwide unique approach, combining structured epidemiological data with decentralized clinico-diagnostic tissue acquisition and expert-driven, quality-assured tissue biobanking.
Methods: Representative FFPE tumour tissues obtained in clinical context from NAKO participants are requested from the pathologies via NAKO study centres. To test the workflow and resulting tissue acquisition, a pilot project was carried out in December 2022 in cooperation with the Leipzig Cancer Registry and the Saxony State Cancer Registry.
Results: The successful pilot demonstrated correct data transfer from Leipzig Cancer Registry to TTB and enabled the implementation of all relevant processes. The consent rate from participants to tumour sample request was 42%, the response rate of requested cases was 50%. This resulted in 27 cases being acquired, processed, and validated in TTB, consisting of one tumour and one normal tissue sample. In addition, histopathological quality assessment as well as virtual microscopy was performed. The most frequently included tumour entity was breast cancer (52%).
Conclusion: The successfully implemented processes of TGB show the feasibility and potential of joining quality assured tissue biobanking with high-dimensional epidemiological studies. On the other side, regulatory issues pose significant challenges to efficient probe acquisition. A higher compliance from study participants as well as pathologies is aspired. This approach allows comprehensive analyses to multiple research issues due to the connection of structured epidemiologic data with high-quality tissue biobanking.

Funding: The NAKO is funded by the Federal Ministry of Education and Research (BMBF) [project funding reference numbers: 01ER1301A/B/C, 01ER1511D, 01ER1801A/B/C/D and 01ER2301A/B/C], federal states of Germany and the Helmholtz Association, the participating universities and the institutes of the Leibniz Association

OFP-02-005

The aromatic amino acids inhibit proteasome translocation and suppress tumour growth via selective mTOR activation

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Background & Objectives: The proteasome, the catalytic arm of the ubiquitin system, undergoes translocation from the nucleus to the cytosol under stress. This adaptive response is regulated by newly identified mTOR-agonistic amino acids—tyrosine, tryptophan, and phenylalanine (YWF)—promoting proteasomal functions crucial for cell survival, including amino acid recycling and clearance of misfolded proteins. YWF-induced mTOR activation results in nuclear proteasome sequestration and subsequent cell death, positioning this pathway as a key stress-coping mechanism. Our objective was to investigate the role of YWF-mediated proteasome dynamics in vivo and explore its potential clinical relevance.
Methods: We analysed proteasome subcellular localization in tumours versus adjacent normal tissues using xenograft, endogenous, and metastatic tumour models. The effect of YWF on proteasome dynamics and tumour progression were evaluated across multiple cancer types. Human breast and uterine cervix xenografts, along with endogenous murine models of colorectal and urinary bladder carcinoma, sarcoma, and metastatic triple-negative breast cancer were employed. Proteasome localization and tumour response were assessed following YWF administration, either orally or subcutaneously to the tumour bed.
Results: Across all tumour models—sarcoma, breast, cervix, colorectal, and bladder—the proteasome predominantly localized to the cytosol, in stark contrast to adjacent non-neoplastic tissues. YWF administration triggered nuclear sequestration of the proteasome in tumour cells, leading to extensive apoptosis and marked tumour regression (sarcoma: 84.6% reduction, $p = 3.76\times10^{-5}$; breast: 81.2%, $p = 1\times10^{-7}$; cervix: 74.8%, $p = 1\times10^{-4}$; colorectal: 86.7%, $p = 0.006$; bladder: 87.8%, $p = 0.01$), as well as a significant decrease in metastatic burden (51.1% reduction, $p = 0.001$).
Conclusion: Our findings identify proteasome dynamics as a core mechanism of tumorigenesis and cellular stress tolerance. Modulating proteasome subcellular localization—particularly via nutrient-sensing pathways—emerges as a novel therapeutic strategy, effectively reprogramming the tumour cell's "satiety centre" and undermining its survival advantage under stress.

Funding: Foulkes Fellowship, Rappaport Research Program for Early Career Clinician-Scientists, Atidim-Rambam Fellowship

OFP-02-006

Contactless Traceability Automation in the Pathology Laboratory

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Background & Objectives: Pathology laboratories are dealing with a constant increase in their workflow due to the shortage of dedicated professional figures and the overwhelming amount of data required in the era of personalized medicine. In this setting, automation, defined as the employment of devices meant to supplement or replace human efforts in a process, is pivotal.
Methods: In this work, we present a project for an automatic contactless traceability identification solution based on high-frequency alternating current electromagnetic wave technologies with real-time localization integrated with a dedicated dissection hood.
Results: The system depends on Tag/chip micro-transponders and 2.45 GHz RTLS-UWB labels, which can be interfaced through "pairing" between the tag and the receiver connected to the LIS. The tags may be implanted, among others, on fresh operator samples with a metallic "micro-tag" marker, slides, bio-cassettes, operator containers, and Eppendorf tubes. The whole system relies on contactless identification with a database that stores clinical records, IHC, FISH, and WSI results. This traceability system is integrated into an anatomical dissection hood capable of detecting the presence of biological tissue on the work surface and providing unique identification using next-generation transmitter modules with RTLS-UWB radio frequency signal reception functions coupled with GPS tracking hidden under the work surface. When the sample passes over the hood's workbench, it will be detected and identified via a touch monitor, displaying its complete related information. The subsequently created bio-cassettes will then be coded and placed in a basket inside an integrated compartment in the hood, constantly tracked through the coded tags in the block structure. The software will then perform a verification of the acquired images/data and, upon operator confirmation, transfer the information to the LIS.
Conclusion: The solutions proposed by the present project carry a disruptive potential to enhance sample management, lessen human-based mistakes, and increase timesaving and productivity of operators.

OFP-02-007

Beyond the microscope: introducing high school students to the medical world through pathology "Ege University Pathology Summer School Experience"

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Background & Objectives: Historically, physicians have been predominantly associated with treatment, while branches focused on disease mechanisms and diagnosis, such as pathology, remain less understood by the public. Modern medicine requires a multidisciplinary approach, and recognizing all branches as an integrated whole shapes the public's perception of the healthcare system, potentially preventing future issues. High school students are at a critical stage in career selection, and it is crucial that their foundational knowledge in medicine is shaped early and accurately. Moreover, this age group is most receptive to experimental learning.
Methods: We initiated a nonprofit one-day workshop to introduce high school students to the importance of pathology within the medical field. The theoretical section covered disease mechanisms, including neoplastic, infectious, and degenerative diseases, as well as their effects on tissues. Students also learned about materials examined and methods used in pathology. The practical section provided hands-on experience in some macroscopic examinations, tissue sectioning, preparing their

own mouth mucosal cytological preparations and staining, as well as examining common diseases under the microscope.
Results: A total of 126 students participated in the workshops (including 32 students in 2022, 50 in 2023, 44 in 2024). Pretests and posttests were performed and written informed consent was taken from the parents. Initially most students were unfamiliar with the role and outline of pathology. However, after the workshop, they reported gaining a deeper understanding of pathological processes, laboratory workflows, and diagnostic procedures, while also expressing enjoyment from their hands-on experiences.
Conclusion: Our study demonstrates that pathology, positioned at the intersection of clinical, surgical, laboratory, and basic medical sciences, serves as an excellent entry point for introducing high school students to medicine. Our three-year observation indicates that the program is sustainable, functional, and adaptable, suggesting it could be successfully repeated annually as part of a "Summer School" initiatives in collaboration with relevant institutions.

OFP-02-009

Exploring the spatial heterogeneity of antibody-mediated heart allograft injury through transcriptomic profiling

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Background & Objectives: Antibody-mediated rejection (AMR) remains a major challenge to the long-term success of heart transplantation. Microvascular inflammation (MVI) and complement deposition are hallmark features of AMR, yet their spatial distribution is often heterogeneous. The molecular mechanisms underlying this heterogeneity remain poorly understood. We aimed to investigate the transcriptional basis of AMR heterogeneity through spatial transcriptomics, to better understand its pathophysiology and uncover potential therapeutic targets.
Methods: We analysed an explanted human heart diagnosed with AMR using histology, C4d immunostaining, immunofluorescence, and spatial transcriptomics (10X Genomics Visium). Regions with MVI and/or C4d deposition were annotated and correlated with spatially resolved gene expression patterns.
Results: MVI^+C4d^+ regions aligned with a distinct transcriptomic cluster, supporting a strong biological specificity of this injury pattern at the mRNA level. MVI^+C4d^- and MVI^-C4d^+ areas lacked unique clustering, suggesting more heterogeneous or transitional transcriptional states. These findings highlight the limitations of histology alone in capturing molecular complexity. MVI+C4d+ regions showed upregulation of genes associated with antigen presentation (*CD74*, *HLA-DQA1)*, classical complement activation (*C1QB*, *C1QC*), and interferon signalling (*GBP5*, *CXCL11*). Immunofluorescence showed local expression of C1q by $CD45^+$ leukocytes. MVI+C4d- areas were enriched in transcripts linked to T-cell activation (*IL7R*, *CD69*), lymphocyte chemotaxis (*CCL21*) and dendritic cell regulation (*WDFY4*). MVI-C4d+ regions showed a distinct profile with increased expression of genes associated with vascular injury (*PLAT*), matrix remodelling (*MMP9*), and myeloid cell activation (*SLAMF8*), indicating that complement deposition in these zones may reflect underlying vascular activation.
Conclusion: AMR is a spatially complex and transcriptionally diverse phenomenon. MVI^+C4d^+ regions aligned with a distinct molecular identity, while other histological patterns lacked clear transcriptomic boundaries. These findings redefine our understanding of AMR as a mosaic of immune processes and highlight the potential of spatial transcriptomics to uncover clinically relevant biological processes.

OFP-02-010

Histopathological features of different types of cardiac amyloidosis

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Background & Objectives: Cardiac amyloidosis (CA) poses diagnostic challenges due to the non-specific nature of early symptoms and its rarity. The objective of this study is to identify histopathological characteristics of CA that influence outcomes, compare the percentage of the most common types of amyloidosis revealed by ante- and post-mortem examination, and to estimate the frequency of clinically underdiagnosed heart involvement in patients with amyloidosis.
Methods: The study describes the results of 46 endomyocardial biopsies and 56 autopsies in patients with CA. All tissue sections were stained with haematoxylin-eosin and Congo red and observed under a polarized light. A broad panel of antibodies against different types of amyloidosis was used for immunohistochemical (IHC) typing of amyloid.
Results: The study included 54 male and 48 female patients (mean age 76 years). Based on IHC typing, AL amyloidosis was detected in 40 cases (39%), ATTR in 45 (44%), and AA in 17 cases (17%). In most cases of AL amyloidosis, reticular or pericellular patterns of amyloid deposition were observed. Commonly, ATTR amyloidosis was characterized by multifocal interstitial amyloid deposits that may not cause early clinical symptoms. Patients with AA amyloidosis usually had intravascular amyloid deposition. This finding can explain why cardiac symptoms were not observed in such cases.
Conclusion: This study has demonstrated that AL amyloidosis can be accompanied by the diffuse intravascular and pericellular patterns of amyloid deposition with cardiomyocyte atrophy. Such patients may develop a rapid progression of CA leading to heart failure. Both in biopsy and autopsy specimens, the most extensive amyloid deposits were found in AL kappa amyloidosis. They caused an aggressive and rapidly progressing CA and a poorer outcome for these patients. The assessme nt of autopsy cases revealed that ATTRwt amyloidosis was frequently detected only at the post-mortem examination suggesting that it is a common underdiagnosed cause of heart failure in elderly patients.

Funding: This work was supported by the Russian Science Foundation, grant No 23-15-00138

OFP-02-011

Autophagy related proteins' immunohistochemical expression and their potential role as biomarkers in thymic epithelial tumours

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Background & Objectives: Thymic Epithelial Tumours (TETs) constitute the most frequent neoplasms in the anterior mediastinum exhibiting clinicopathological and molecular heterogeneity. Autophagy, a self-destructive cellular mechanism with a paradoxical nature, plays a part in both tumour suppression and induction by either providing cancer cells with metabolic substrates and nutrients as well as activating oncogenes and inhibiting tumour suppressor genes, resulting in cell proliferation and survival. The aim of the present study is to investigate the clinical significance of four autophagy pathway components (LC3b,

ATG3, BECLIN, p62) in pathogenetic mechanisms of TETs with possible prognostic importance.
Methods: Archival formalin-fixed and paraffin-embedded tissue from 99 patients with TETs resected between 2009 and 2020 at Evangelismos Hospital, were retrieved and immunohistochemical staining for LC3b, ATG3, BECLIN, p62 was performed. The possible correlations between the expression of the examined autophagy pathway components and patients' clinicopathological parameters, such as WHO histological subtype, Masaoka-Koga stage, overall survival and presence of relapse was examined.
Results: Higher cytoplasmic BECLIN and p62 expression was associated with male gender (p=0.027 and p=0.014, respectively). B3 thymomas and thymic carcinomas (TC) displayed higher cytoplasmic p62 expression (p=0.019), while cytoplasmic LC3b expression was marginally more often observed in non B3/TC TETs (p=0.098). A positive correlation between higher cytoplasmic BECLIN expression and advanced Masaoka-Koga stage was also observed (p=0.009). ATG3 was not associated with any of the investigated clinicopathological parameters (p>0.05). There was also no significant correlation between any of the four examined molecules and overall survival or relapse.
Conclusion: Our findings reveal definite associations between autophagy and clinicopathological aspects in TETs indicating autophagy activation in B3/TC and advanced Masaoka- Koga stage cases. Further studies are needed to explore the role of autophagy in TETs and its blockage as a potential therapy.

OFP-02-012
Clinicopathological analysis of thymoma: a 12-year retrospective study from a single institution
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Background & Objectives: Thymoma is a rare mediastinal tumour with diverse histopathological subtypes and variable clinical behaviours. A comprehensive understanding of its epidemiological and pathological characteristics is crucial for improving diagnosis and management. This study retrospectively analyzes 59 thymoma cases diagnosed at Istanbul Haydarpasa Numune Training and Research Hospital between 2013 and 2024. The objective is to evaluate patient demographics, histopathological and clinical findings (including paraneoplastic syndromes), and survival outcomes to identify potential prognostic factors.
Methods: A retrospective review was conducted on 59 thymoma cases, documenting patient age, sex, histologic type, tumour size, T stage, presence of paraneoplastic syndromes, and survival outcomes. Histopathological classification followed WHO criteria, and T staging was based on the TNM system. Immunohistochemical analysis was performed in 55 cases. Diagnosis was made through biopsy in 7 patients and surgical resection in 52 cases. Statistical analyses, including survival analysis and correlation tests, were performed to explore associations between these clinicopathological variables.
Results: The cohort included 36 males and 23 females, with a median age of 55 years (mean: 53.2). Tumour size was recorded in 49 cases (median: 6 cm, mean: 6.58 cm). Histologic subtypes included 7 type A, 6 type AB, 6 type B1, 18 type B2, 13 type B3, 5 thymic carcinoma, 3 microscopic thymoma, and 1 micronodular thymoma with lymphoid stroma. Among 46 cases with documented T stage; 35 were pT1a, 4 pT2, 6 pT3, and 1 pT4b. Myasthenia gravis was observed in 15 patients (25.42%). Survival analysis showed that 42 patients remain alive, while 17 succumbed within 1 to 10 years post-diagnosis.
Conclusion: This study provides a detailed analysis of thymoma cases over 12 years, emphasizing variations in tumour characteristics, paraneoplastic manifestations, and survival outcomes. Further statistical assessment will refine our understanding of key prognostic factors and support evidence-based clinical management strategies for thymoma patients.

OFP-02-013
Gallstones in the mummies of a monastic community in central Italy (17^{th}-18^{th} century)
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Background & Objectives: Gallstones were described in mummified/skeletal remains of 22 subjects from Egypt, Sweden, Greece, Italy, Sicily, Spain, China, Ohio, Chile, and Colombia, dating back from 2000 b. C. to 18^{th} century A. D. The age at death was comprised between 25 and 60 years old, with female predominance, and a 3:1 ratio of cholesterol:pigmented stones. The mummified bodies of the Poor Clares Hermits monastic community in Fara in Sabina belonged to Franciscan nuns who followed the first Rule of Saint Clare combined with strict seclusion and absolute loyalty to ecclesiastical hierarchies. Most of them came from wealthy Roman families.
Methods: The bodies were investigated by external examination and computed tomography (CT) scanning. 3D rendering and densitometry allowed to reconstruct the exact stone morphology and establish chemical composition. Written sources hosted in the current monastery library were examined to find information about the sisters who lived there.
Results: Cholesterol-based gallstones were found in 3 individuals (17.5%) and were probably linked to dietary factors and genetic predisposition. The age at death of the subjects ranged from 40 to >50 years. The Book of the Dead allowed to recognize 2 nuns with symptoms ascribed to cholelithiasis (Maria Francesca Romana, who died in 1730 at 75; Maria Giovanna Romana, who died in 1718 at 82) and 1 sister affected by sudden fever and an undefined deep lateral chest pain (Maria Isabella, who died in 1698 at 50).
Conclusion: In conclusion, gallstones may be easily recognized in natural mummies through CT scanning, whereas densitometry helps to establish their chemical composition. As its modern counterpart, ancient cholelithiasis was most frequently due to cholesterol-based stones and may thus represent a good bioanthropological marker of high social class. The presence of gallstones may also be a valid clue for the identification of the subject, when information recorded in textual sources are available.

OFP-02-014
Development of a virtual, on-line pathology curriculum for residency training in pathology: the OPEN experience to lower barriers for the developing world
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Background & Objectives: Current training models in pathology are poorly scalable in the developing world when compared to projected increases in demand for pathology services. The Open

Pathology Education Network (OPEN) was launched in 2022 as a means to address the global workforce shortage in pathology by lowering barriers to access. The training model consists of self-paced on-line materials sourced from largely extant materials, coupled with intermittent on-line live mentoring sessions. This study assesses the process of developing OPEN modules to date.
Methods: Teams of subject matter experts were recruited to curate and develop content for use on the OPEN learning management system (LMS). Each team consisted of six-eight individuals and included senior, junior and some trainee volunteers. Support for development was provided by OPEN leadership and staff via regular check-ins. A survey of participant experiences was sent to the 30 volunteers to date. Usage data from the LMS was also collected.
Results: To date, modules have been developed and presented live on the OPEN LMS in gynaecologic pathology (3), urine cytology, breast pathology, MMR testing, Basics of Pathology, and gynaecologic cytology. Additional teams in head and neck pathology, paediatric pathology, lung pathology, CNS pathology, dermatopathology, histology basics, and endocrine pathology have been formed or are pending launch. Survey results showed participants found OPEN goals matched personal values. Learners in 89 countries have accessed the LMS for one or more courses.
Conclusion: The OPEN module development process has succeeded using volunteers, but often requires lengthy development. Teams with strong leadership, and some intra-institution collaboration are more effective. Many disciplines have sufficient open-source content for a curriculum, while some require significant further development, slowing the process. Developers show ready transition to on-going mentorship roles. Trainee response to developed content and live mentorship shows promising results in developing competency.

OFP-02-015

A survey of molecular testing availability in Arab countries

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Background & Objectives: Molecular diagnostic testing is essential for accurate cancer diagnosis and targeted therapy, and is widely integrated in the current series of WHO Classification of Tumours, yet its availability across Arab countries remains unclear.
Methods: A cross-sectional survey targeting the status of molecular testing in healthcare facilities in Arab countries to assess the availability of molecular diagnostics. Centers were identified through an index-pathologist selected in each country. The survey included questions on availability of various inhouse molecular testing modalities, and infrastructure.
Results: 68 centres responded to the survey, 58 of which offered oncology services. Centers were distributed across 14 Arab countries, with the highest representation from Egypt (n=13), Morocco (n=10), and Saudi Arabia (n=9). Of the responding centres, 44 (75.9%) were located in large cities (population > 1 million), 13 (22.4%) in medium cities (population 100,000–1 million), and 1 (1.7%) in a small city (population < 100,000).
44 (75.9%) centres have PCR, 28 (48.3%) FISH, 26 (44.8%) karyotyping, 19 (32.8%) NGS, 16 (27.6%) Sanger sequencing, 8 (13.8%) methylation profiling, and 6 (10.3%) MLPA. Thirty-two centres lacked inhouse capability for some or all tests and opted for outsourcing—most commonly FISH and NGS.
Among 39 centres lacking specific tests, 27 (69.2%) cited high cost and 12 (30.8%) cited limited expert personnel as key barriers. Of 31 centres with inhouse testing, 11 (35.5%) adopted molecular diagnostics to improve diagnostic accuracy and treatment planning.
Conclusion: In the era of precision medicine and molecular-based classification of tumours, the availability of molecular diagnostic testing is increasing across Arab countries. However, a significant proportion of oncology-health centres still lack in-house testing capabilities, primarily due to high costs and limited specialized personnel. Expanding training programs and investing in molecular-diagnostic molecular infrastructure are essential steps toward achieving equitable access to precise diagnostics and personalized cancer treatment across the region.

OFP-03 Oral Free Paper Session Dermatopathology

OFP-03-001

Prognostic relevance of worst pattern of invasion in cutaneous squamous cell carcinoma: an analysis of 151 cases

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Background & Objectives: The "Worst Pattern of Invasion" (WPOI) scoring system is widely used in head and neck squamous cell carcinomas (SCC) to assess prognosis. In this study, we investigated the applicability and prognostic significance of this scoring system in cutaneous SCCs (cSCCs).
Methods: We retrospectively reviewed 151 cases of cSCC diagnosed between 2019 and 2024, all followed by the dermatology department. WPOI scores were assigned independently by two pathologists (AS, BÖ) and classified into two groups based on WPOI status: low (WPOI 1–3) and high (WPOI 4–5). These scores were compared with clinicopathological features (tumour size, tumour thickness, histological differentiation, perineural invasion (PNI), lymphovascular invasion (LVI), nodal metastasis, recurrence, subcutaneous extension, stage, T and N classification, and histologic subtype and demographic data extracted from the hospital information system. Prognostic assessment was made according to 'BWH T classification system' recommended by the European Dermatology Association. Associations were evaluated using chi-square tests and t-tests, with a significance level set at $p < 0.05$.
Results: A total of 144 patients with a median age of 71 (9-97) years were included in our study. High WPOI was found to be significantly associated with various adverse pathological features such as between high WPOI and PNI ($p < 0.000001$), subcutaneous tissue invasion ($p < 0.000001$), increased tumour size ($p < 0.00001$), and greater tumour thickness ($p < 0.0001$), poor differentiation ($p = 0.0003$), advanced stage ($p < 0.000001$), and higher pT classification ($p < 0.000001$).
WPOI was not significantly associated with nodal metastasis, recurrence, LVI, multiple SCCs, age, sex, or histological subtype.
Conclusion: Our findings suggest that the WPOI is a valuable histopathological marker in cutaneous SCC and could provide helpful insight into tumour behaviour. This may assist in identifying high-risk patients, treatment planning and long-term follow-up.

OFP-03-002

Diagnosing urticarial vasculitis and chronic urticaria: a critical evaluation of a histopathological algorithm and scoring system

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Background & Objectives: Urticarial vasculitis (UV) and chronic urticaria (CU) share clinical and histopathological features, complicating their distinction. Puhl et al. proposed a histopathological algorithm and UV score (UVS) based on leukocytoclasia, erythrocyte extravasation, and fibrin deposition (FD) in blood vessels to aid the diagnosis. This study applied and critically evaluated the proposed algorithm in archival cases.
Methods: Archival cases from 2016–2024 with a referral diagnosis of UV (n=141), CU (n=32), or both (n=34) were analysed. Biopsy specimens were scored for leukocytoclasia (3 points), erythrocyte extravasation (2 points), and FD based on the number of affected fields of view (FOV) (1–3 points). The UVS was calculated based on the proposed formula, and a cut-off of 2.75 was applied to classify cases as CU or UV. Histopathological features were assessed in detail for diagnostic value.
Results: The algorithm classified 49.8% of cases as CU and 50.2% as UV, with 46.1% of clinically suspected UV cases reclassified as CU. Leukocytoclasia, erythrocyte extravasation, and FD were significantly more frequent in UV (76%, 45.2%, and 97.1%, respectively) than in CU (6.8%, 9.7%, and 1.9%, respectively; $p<0.001$). FD was extensive (≥3 FOV) in 83.7% of UV cases, but in CU, it was mild (affecting <3 FOV) and rare (1.9%). While eosinophils were more common in CU ($p=0.036$), their presence did not exclude UV, nor did neutrophils rule out CU ($p=0.175$). Intravascular neutrophils/eosinophils were frequent in UV ($p<0.001$). Perivascular lymphocytes with leukocytoclasia and/or FD were characteristic of UV (31.7% and 29.8%, respectively). Exclusion of other skin diseases was needed in cases with a sole presence of lymphocytes, even though they were classified as CU.
Conclusion: Fibrin deposits in blood vessels are the most reliable marker for UV diagnosis. While the proposed algorithm aids classification, its clinical applicability in cases without fibrin deposits requires prospective validation.

Funding: This research was supported by the Ministry of Science, Technological Development and Innovation of the Republic of Serbia and the Faculty of Medicine, University of Belgrade, project No. 451-03-66/2024-03/200110

OFP-03-003

Cutaneous metastasis: an 18-year retrospective study in a tertiary hospital

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Background & Objectives: Cutaneous metastases account for approximately 2% of all skin tumours, affecting between 0.7% and 9% of patients with malignant neoplasms. Typically, there is a prolonged interval between the diagnosis of the primary tumour and the identification of cutaneous metastases. However, in some cases, such metastases may be the initial manifestation of occult primary malignancies.
Methods: A descriptive, retrospective study was conducted on patients diagnosed with cutaneous metastases between January 2007 and January 2025, whose histopathological examination was performed at Unidade Local de Saúde de Braga. Clinical and histopathological data were collected from electronic medical records.
Results: Seventy cases of cutaneous metastases were identified, which corresponds to 1% of all cutaneous neoplasias. Most patients were female (65.7%, n=24), and the mean age at diagnosis was 67.5 ± 13.8 years. Clinically, 88.6% (n=62) of the skin lesions presented as a nodule and 51.4% (n=36) had multiple skin lesions at the time of diagnosis. In our series, 38.6% (n=27) of cases were metastasis of primary breast carcinomas, 15.7% (n=11) of primary lung carcinomas, and 12.9% (n=9) of primary colorectal carcinomas. The most common site of cutaneous metastasis was the chest (n=25), followed by the abdomen (n=19). The mean time between the diagnosis of the primary tumour and cutaneous metastasis was 55.5 months. In seven cases, the diagnosis of metastases was synchronous with that of the primary tumour, and in nine patients, the primary tumour was diagnosed through histopathological/cytological examination of the skin lesions. Currently, only seven patients are alive, and the median survival after the diagnosis of cutaneous metastasis was 14.4 months.
Conclusion: Overall, the prognosis for patients with cutaneous metastases remains poor, as these are associated with the aggressiveness of the primary tumour. Understanding their clinical features and maintaining a low threshold for performing biopsies may be useful in such cases.

OFP-03-004

Skin neoplastic lesions in the "very old" Portuguese population: a retrospective study in a two-year period

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Background & Objectives: Non-melanocytic skin tumours rank as the 5th most common cancer worldwide, while melanoma is less frequent. Due to an increase in life expectancy, the WHO defines individuals aged 85 and older as "very old". This study aimed to characterise skin tumours in this understudied segment of the Portuguese population.
Methods: We analysed anatomopathological reports of skin lesions received in our department from January 2023 to December 2024, from patients with 85 years or older. Specimens were collected in different institutions across Portugal. The data collection included age, gender, anatomical site, histopathological diagnosis (by WHO Classification of skin tumours, 5th ed.) and personal history.
Results: A total of 668 reports from 520 patients were reviewed. The median age was 89.2 years (85-103), with a sight female predominance (M/F ratio= 0.93). Malignant tumours constituted 63.17% of cases (n=422), mainly corresponding to epithelial tumours (n=390; 92.4%), with the most frequent being basal cell carcinoma. Melanocytic malignancies were less common (n=17; 4.03%), followed by sarcomas (n=8;1.90%), adnexal carcinomas (n=6;1.42%) and lymphoproliferative disorders (n=1; 0.24%).
Among the benign lesions/ precursor lesions (n=246; 36.83%), the most common were epithelial tumours (n=209; 85.00%), followed by melanocytic lesions (n=18; 7.32%) – 5 (27.78%) corresponding to blue nevi and 4 (22.22%) had dysplastic features; followed by mesenchymal lesions (n=13; 5.28%) and adnexal tumours (n=6; 2.44%).
Multiple reports were available in 22.16% of patients in this time period, with only 13 patients having the biopsy and excision of the same lesion. The remaining patients (n=102) had at least two different skin lesions submitted to analysis.
Conclusion: Skin tumours are prevalent in the "very old" group, yet remain understudied. Our findings corroborate the predominance of non-melanocytic malignancies. The higher incidence of blue nevi might be justified by the nature of the institution (private), yet further study is needed.

OFP-03-005

Histological melanoma findings in *POT1* germline carriers in a Swedish familial melanoma cohort

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Background & Objectives: About 7 to 15% of cutaneous melanomas (CM) are familial melanoma (FM) cases. High-risk genes include *CDKN2A* (up to 40% of cases), *CDK4, BAP1* and the more recently identified telomerase maintenance genes (TMG) which are *POT1, TERF2IP, TERT* and *ACD*. Spitzoid morphology is commonly observed in patients with germline variants in TMG. This Swedish study represents the first report in the Nordic countries on the prevalence and pathogenicity of *POT1* variants along with the histopathology of melanoma cases in the identified carriers.
Methods: Since 2021, all the CM families in Stockholm have undergone *POT1* testing as an implementation of the routine panel. The SweGen Dataset and the gnomAD database were used to assess the frequency of pathogenic variants (PV). The melanoma cases were reviewed.
Results: Among 150 melanoma families negative for *CDKN2A, CDK4,* and *BAP1*, only one likely *POT1* PV (c.676C>A, p.His226Asn) was detected (0.7%). Population data confirmed its rarity. Three carriers were identified. Carrier 1 had two invasive melanomas in early 20s. One, in the head and neck area, showed 100% of spitzoid morphology, BRAF+, classified as a spitzoid melanoma, Breslow 0,6 mm, growing adjacent to a nevus, suggesting that the melanoma had arisen from a precursor lesion. The other on the leg was a superficial spreading melanoma with 90% of spitzoid cells, Breslow 1,2 mm, BRAF+. Carrier 2 was diagnosed on the leg with a melanoma in situ without spitzoid features, BRAF+. Carrier 3 was diagnosed on the leg with a superficial spreading melanoma without spitzoid features, Breslow 0,6 mm, NRAS mutated (p.Gln61Arg). There were several other tumours in the pedigree, including brain and soft tissue tumours.
Conclusion: *POT1* testing should be offered in high-risk FM cases, especially when negative for *CDKN2A, CDK4* and *BAP1,* with an early onset of melanoma exhibiting spitzoid features, and other tumours in the pedigree.

Funding: This work was supported by grants from the Swedish Cancer Society (20 0156 F, 21 1486 Pj and 24 3826 Pj), ALF grant from Region Stockholm (grant number FoUI-975235 and FoUI-1023897) and the Cancer Research Funds of Radiumhemmet (grants numbers 194092 and 2240233 (HH) and 174172 and 194103 (VH))

OFP-03-006

Gene expression profile comparison of atypical fibroxanthoma and undifferentiated pleomorphic sarcoma

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Background & Objectives: Atypical fibroxanthoma is a dermal neoplasm of uncertain histogenesis with a relatively low-grade behaviour. However, AFX exists in a clinical and histopathologic spectrum and can show a more aggressive lesion as undifferentiated pleomorphic sarcoma/ pleomorphic dermal sarcoma. Recent literature has confirmed the overlap of AFX and UPS also at the molecular level, however, little is known about the gene expression profiles of these tumours.
Methods: We applied gene expression profiling through RNA sequencing of TruSight RNA Pan-Cancer Panel Kit (Illumina) to 9 cases of AFX and 3 cases of UPS.
Results: Unsupervised cluster analysis revealed a clear molecular distinction between AFX and PDS, despite both tumours sharing common DNA mutation profiles and a TP53 UV radiation signature. RNA sequencing identified unique gene expression patterns that help differentiate the two, particularly involving apoptosis and cell adhesion pathways. Receptor tyrosine kinases, such as FLT3, also showed differential expression between the groups. In AFX, both apoptosis and adhesion pathways were consistently upregulated across multiple platforms—BioPlanet2019, KEGG2019Human, and WikiPathways2019Human and these findings align with AFX's clinical behaviour, as increased apoptosis limits cellular survival, and enhanced adhesion restricts migration—traits that contribute to its less aggressive nature. Among these, apoptosis was the most frequently upregulated function, followed closely by adhesion. Additionally, three signalling pathways—PI3K-Akt, B-cell receptor/activation, and Ras—were found to be commonly altered in both tumour types, according to KEGG and WikiPathways analyses. These pathways are typically associated with cell proliferation and survival, and their downregulation in AFX further supports its limited growth potential.
Conclusion: Overall, while AFX and PDS share mutational similarities, their distinct transcriptomic profiles, especially in apoptosis and adhesion-related processes, suggest that RNA-based analysis may aid in distinguishing these closely related tumours.

OFP-03-007

Melanocytic lesions – correlation between margin status and residual pathology of wider excisions

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Background & Objectives: Dermatological excisions are frequently performed for melanocytic lesions, where achieving clear histological margins is critical to reduce risk of recurrence. This retrospective study evaluates margin status and diagnostic changes in patients with melanocytic lesions discussed in a skin cancer multidisciplinary team (MDT) setting over a one-year period ('24-25).
Methods: 301 patients were discussed at the MDT. Of these, 191 patients with melanocytic pathology were included in analysis. Patients were categorized based on number of excisions of the same lesion: single excision (n=191), two excisions (n=146), and three or more excisions (n=25). Margin status and diagnostic alterations were assessed for each excision event.
Results: Mean age was 65 years (range 17-93). The most common diagnosis was in situ melanoma (n=118), followed by invasive melanoma (n=46). Frequently affected sites included upper limb (n=51), face (n=40), and back (n=28). Positive margins were observed in 90 patients following first biopsy/excision, 25 patients following a second and 4 after a third excision. The mean negative margin after each excision was 1.8mm, 3.25mm and 2.4mm respectively. Of the 90 patients with positive margins after initial excision,

75 proceeded to further surgery—12 (16%) had no residual disease. In contrast, among 101 patients with initially negative margins, 71 underwent further excision, and 14 (19.7%) were found to have residual melanocytic pathology. Thirteen patients (9%) had their diagnosis upgraded on subsequent excision (e.g., from benign to in situ, or in situ to invasive melanoma). Notably, the average clear margin in those with residual versus no residual disease differed by only 0.1 mm.

Conclusion: Some evidence exists correlating histological margins and residual disease in melanocytic lesions. However, this study underscores the sometimes paradoxical relationship, particularly in excisions that are <5mm. These insights reinforce the critical role of MDTs in optimizing patient outcomes, particularly when pathology and clinical context may not align.

OFP-03-008

A whole-lesion morphometric analysis in melanoma: towards a prognostic role for image analysis

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Background & Objectives: Previous morphometric studies in melanoma have proven useful in differentiating between melanoma and nevi. Correlations have been established between cell nuclear area, circularity, and optical density (OD), and p53 and Bcl-2 expression, mitotic index and tumour stage. In this study, we determined for the first time on whole-slide image (WSI) the prognostic significance of morphometric nuclear features in melanoma.

Methods: We evaluated 9 malignant melanomas, 4 metastatic(mM), with a mean progression-free survival (PFS) of 629 days, and 5 non-metastatic (nmM) with mean follow-up of 1637 days. All clinical and histopathological variables were collected.

We analysed the most representative slide for each case: following the digital slide acquisition by Aperio Scan Leica system, we selected all invasive tumour cells from the sections with the highest cell density and analysed 19 nuclear variables using the QuPath software analysis tools (ver. 0.5.1).

Results: In total, we extracted 782.793 cells(mean 86997/case, range 16967-236224/case). Mean nuclear area, nuclear perimeter, nuclear maximum and minimum caliper were positively correlated with melanoma diameter and Breslow thickness (all $p<0.05$); minimum nuclear calliper also correlated with the number of mitosis/mm^2 ($p=0.015$) and ulceration ($p=0.024$).

When the 503.788 cells from mM were compared with the 279.005 cells from nmM, many variables showed significant differences ($p<0.001$): nuclear max and min caliper, mean/sum/range of Haematoxylin OD, among others.

Conclusion: Our results strengthen the correlation of nuclear morphometric features (studied for the first time on WSI) and the prognostic variables in melanoma: mitotic index, tumour dimensions, ulceration, and Breslow thickness (the latter for the first time, to the best of our knowledge). Furthermore, our cell analysis revealed a correlation between the Haematoxylin OD features and metastatic potential, akin to cervix non-keratinising squamous cell carcinoma. While these findings necessitate a larger case series to establish PFS, they suggest that image analysis not only distinguishes nevi from malignant melanomas but also differentiates metastatic from non-metastatic cases.

OFP-03-010

Carcinoid-like pattern in basal cell carcinoma: a large series of 40 cases with detailed clinicopathological and immunohistochemical characterization

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Background & Objectives: Basal cell carcinoma (BCC) is histologically diverse, yet carcinoid-like architecture remains an extremely rare and under-recognized variant. This growth pattern may mimic sebaceous, neuroendocrine, or even melanocytic neoplasms, leading to potential diagnostic pitfalls. Our objective was to systematically characterize the largest known series of BCCs with carcinoid-like pattern, defining their clinicopathological spectrum and immunophenotypic profile.

Methods: We retrospectively reviewed 1373 BCC cases diagnosed between 2018 and 2025. Forty tumours (2.9%) demonstrated a carcinoid-like arrangement, characterized by branching and anastomosing trabeculae within fibrovascular stroma. Clinical parameters, histologic patterns, and ancillary features (ulceration, perineural invasion, recurrence) were evaluated. Immunohistochemistry (IHC) for BerEP4, EMA, CK20, synaptophysin, chromogranin, and vimentin was performed to delineate lineage and rule out mimics.

Results: The cohort comprised 21 females and 19 males (median age: 74, range: 40–103). Tumour size ranged from 4 to 65 mm. The majority (92.5%) were located on the head and neck region. Carcinoid-like pattern involved 5–90% of the tumour area, frequently coexisting with nodular and/or infiltrative components. Ulceration was present in 50% of cases. Perineural invasion and local recurrence were observed in only one case each. IHC revealed strong diffuse BerEP4 positivity in all tumours; CK20, EMA, synaptophysin, chromogranin, and vimentin were consistently negative.

Conclusion: Carcinoid-like BCC is a rare but distinct and recognizable histologic variant with characteristic morphology and a consistent immunoprofile. Awareness of this pattern is critical to prevent misclassification as adnexal, neuroendocrine, or melanocytic tumours. Our findings expand the histologic spectrum of BCC and reinforce the diagnostic utility of BerEP4 in challenging cases.

OFP-03-011

Evaluation of PRAME expression in dysplastic nevi: a comparative analysis of low- and high-grade lesions

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Background & Objectives: PRAME (PReferentially expressed Antigen in Melanoma) antibody is a crucial biomarker for differentiating melanoma from benign lesions. Although useful, its diagnostic value in dysplastic nevi (DN) remains controversial. This study investigates its diagnostic potential and clinicopathological correlations.

Methods: PRAME was immunohistochemically assessed in 115 low-grade dysplastic nevi (LG-DN) and 18 high-grade dysplastic nevi (HG-DN). Staining was scored from 0 (no staining) to 4+ (75% or more). The relationship of PRAME expression with age, gender, localization, and histological grade was examined.

Results: We analysed 133 DNs from 107 patients. Of these, 49.5% were female and 50.5% were male. The mean age was 36.6 years (range: 7-91). Lesions in females were observed to appear at an earlier age than males (mean: 31.7 vs 40.6, $p<0.001$). Histological grade increased with advancing age ($p=0.017$). Most lesions were located on the trunk (51.9% back, 27.1% chest) followed by the head and neck (7.5%). 27.8% of lesions were junctional, while 72.2% were compound.

PRAME was immunohistochemically assessed using a five-tiered system (0 to 4+). Among LG-DN 84.3% presented score 0, 5.2% score 1+, 0.9% score 2+, 2.6% score 3+, 7% score 4+. Among HG-DN 77.8% presented score 0, 5.6% score 1+, 0% score 2+, 5.6% score 3+, 11.2% score 4+. Although PRAME expression showed an increasing trend from LG-DN to HG-DN, the difference was not statistically significant. No correlation was found between PRAME expression and age, sex, localization, nevus subtype.
Conclusion: The findings indicate that PRAME expression is not associated with histological grade or clinical and histological parameters in DN, suggesting that this marker may have limited prognostic or diagnostic value in these lesions. These results need to be supported by larger sample-sized and comparative studies.

OFP-03-012
Comparative histological description between breast and abdominal skin territories with a special focus on erogenous sensation
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Background & Objectives: Sensory recovery constitutes an essential outcome of breast plastic surgery, either aesthetic or reconstructive. Abdominal wall-based flaps remain the gold standard for autologous breast reconstruction in most centres, and flap neurotization is increasingly popular since it has been shown to provide quicker and better postoperative sensation. Previous research shows that even with the neurotization of the flaps, full sensory recovery remains inconsistent. This study aims to address this issue by describing and comparing neurohistologically the skin of the breast and the infraumbilical abdominal wall.
Methods: An observational cross-sectional study was performed on 100 hemi-bodies from 35 mommy makeover patients (submitted to abdominoplasty + mastopexy/breast reduction) at the LMR – Plastic Surgery Clinic and 15 formalin-preserved adult cadavers at the Institute of Anatomy, Lisbon Faculty of Medicine, Portugal. From each hemi-body, 10x5mm full thickness skin biopsies have been collected: four from the infra-umbilical lower abdomen and five from each breast quadrant and from the areola. Samples were histologically prepared including staining with haematoxylin and eosin and immunohistochemistry using antibodies specific to neuronal markers S100, Peripherin (sympathetic nerve fibres), Annexin V (sensory nerve fibres), and PIEZO2 (erogenous sensation receptors). Microscopic analysis was focused on the comparisons between breast and abdomen skin histologic features, with a special focus on the skin layers, nerve endings and cutaneous sensory receptors, including the ones related to sexual function.
Results: Although skin thickness and epithelial layers are grossly similar, significant differences between these two anatomical regions were found in terms of nerve fibre distribution and density, especially concerning the PIEZO2 ion channel.
Conclusion: A comprehensive understanding of the skin neurohistology of the mammary and abdominal region can significantly influence surgical decisions, particularly in prioritizing flap areas with greater similarity to the breast. This understanding can potentially lead to improved sensory recovery, including erogenicity, and ultimately enhance patient outcomes in breast reconstruction.

Funding: The authors declare that they received a grant from GAPIC (Gabinete de Apoio à Investigação Científica, Tecnológica e Inovação) of Lisbon School of Medicine

OFP-04 Oral Free Paper Session Neuropathology & Ophthalmic Pathology & Paediatric and Perinatal Pathology

OFP-04-001
The prognostic value of ATRX and TERT promoter status in the context of histopathological findings in conjunctival melanoma
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Background & Objectives: Conjunctival Melanoma (CM) are rare melanocyte-derived malignancies with only partial overlap concerning biological background and clinical course compared to their cutaneous counterpart. While the recurrent and metastatic tendencies of CM call for literature-driven unified treatment and follow-up protocols, CM scarcity impedes reliable determination of regimen-deciding prognostic markers. Previous studies associated several clinicohistopathological features and a mutated *TERT* promoter (*TERTp*) with an adverse clinical course. This study builds upon prior research aiming to determine the prognostic value of ATRX status in CM patients.
Methods: A retrospective single-centre cohort study of Radboudumc CM patients between 1985 and 2022 is conducted to analyse the value of ATRX immunohistochemistry in additional to *TERTp* status using Sanger sequencing, correlated to clinicohistopathological context.
Results: Preliminary data of 32 CM patients include 9/32 (28%) male and 23/32 (72%) female patients, with 12/32 (38%) showing recurrent disease and 7/32 (22%) exhibiting metastases. Currently, ATRX immunohistochemistry was performed on 31 CM, showing ATRX loss in 7/31 (23%) instances. Recurrences were found in 4/7 (57%) ATRX-loss cases compared to 8/24 (33%) in the ATRX wild-type population. Metastases occurred in 3/7 (43%) ATRX-loss cases compared to 4/24 (17%) in the ATRX wild-type cohort.
So far, prior routine diagnostic molecular analyses show 2 *TERTp* wild-type cases and 1 mutated sample. Remarkably, the *TERTp*-mutated case showed concomitant ATRX loss and multiple hotspot mutations.
Conclusion: These preliminary findings of higher percentages of recurrences and metastases in ATRX-loss CM cases align with previously reported findings. Furthermore, 1 case showed both a *TERTp* mutation and ATRX loss, bringing prior propositions of its mutual exclusive occurrence into question. In addition to incorporation of upcoming data concerning *TERTp* status and clinical parameters, collaborations with other centres to increase the examined population will be of utmost importance in identifying prognostic parameters aiding in adequate personalized treatment.

Funding: This study is currently completely covered by funds received from the Dutch government as part of the scientific part of my pathology residency

OFP-04-002
Conjunctival melanocytic lesions: does simplifying WHO grading improve reproducibility?
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Background & Objectives: Accurate grading of conjunctival melanocytic intraepithelial lesions is essential for predicting melanoma risk and guiding treatment. Three systems are commonly used: Primary Acquired Melanosis with atypia (PAM), Conjunctival Melanocytic Intraepithelial Neoplasia (C-MIN), and the 2022 World Health Organization (WHO) classification, which introduced the Conjunctival Melanocytic Intraepithelial Lesion (C-MIL) system. This study evaluated

interobserver agreement and correlations among these systems using real-life pathological cases.
Methods: Thirty-six conjunctival lesions diagnosed between March 2015 and January 2025 were reviewed independently by three experienced pathologists using PAM (0–3), C-MIN (quantitative score), and WHO 2022 C-MIL classifications. The C-MIL system was assessed in both its original format (four-tiered, including melanoma in situ as a separate category) and a simplified format (three-tiered, combining melanoma in situ with high-grade lesions). Fleiss' kappa was used to measure interobserver agreement, while Spearman correlation coefficients were used to assess relationships between the systems.
Results: Agreement was low for PAM ($\kappa = 0.270$) and C-MIL (four-tiered) ($\kappa = 0.272$), and moderate for the simplified three-tiered C-MIL ($\kappa = 0.467$). PAM and C-MIN showed higher agreement in "no atypia" and "severe atypia" categories, with lower consistency in intermediate grades. Among the original systems, C-MIN showed relatively higher agreement ($\kappa = 0.392$). The simplified WHO C-MIL format demonstrated the highest reproducibility. Correlation analysis revealed strong to very strong relationships across all systems (e.g., PAM vs C-MIN: $r = 0.819–0.854$; PAM vs C-MIL: $r = 0.908–0.947$; C-MIN vs C-MIL: $r = 0.824–1.000$; all $p < 0.001$).
Conclusion: The simplified WHO 2022 C-MIL classification improves diagnostic consistency while maintaining strong alignment with previous systems. Reducing the number of grading categories enhances reproducibility, especially in borderline lesions. These findings support the simplified C-MIL as a practical and standardized tool for routine reporting.

OFP-04-003
Integrating snRNAseq and Spatial Transcriptome (ST) shows diverse transcriptomic landscape for Tumour Microenvironment (TME) in intracranial germinomas
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Background & Objectives: The incidence of intracranial germ cell tumours is 5-8 times higher in East Asia and histologically, germinoma is well known to show intense lymphocytic infiltrates. The latter can be so marked that the malignant germ cells can be masked. However, there have only been a few studies on its tumour micro-environment (TME). The lack of studies is attributed to the unavailability of tumour specimens in western countries. There has been no study using the recent and comprehensive techniques of single nucleus sequencing or spatial transcriptomics to study its TME.
Methods: We studied snRNAseq (Chromium 10X) of FFPE tissues of 51 intracranial germinomas, and spatial transcriptoms (STs) (Visium Spatial) from fresh tissues from 12 matched cases.
Results: For the TME, in contrast to common belief, macrophages and fibroblasts were equally represented as T- and B-cells as immune cells. There was no correlation with proportion of tumour cells with either focal vs bifocal disease or clinical stage. Common gene modules (metaprograms) were epithelial-mesenchymal transition, cell cycle and immune cells. Cell interaction analysis showed strong interaction between germ cells and macrophages involving CXCL, MIF and MK pathways. By ligand-receptor analysis, MIF combined with CD74 might promote tumour development. For twelve cases, we studied STs with fresh tissues and integrated the results with snRNSeq, deconvoluting the spots for ST using snRNAseq cell types. Multimodal Intersection Analysis integrated significant genes based on snRNAseq and different regions' significant genes based on STs. Ligand and receptor was expressed in close proximity. There was correlation between the expression of the four gene modules for tumour and immune cells for cell neighbourhood. Multichannel immunofluorescence (Hyperion) confirmed spatial distribution of cell types and cell neighbourhood findings.
Conclusion: We showed in details the expression landscape of TME of germinomas.

OFP-04-004
***TERT* promoter mutations in medulloblastoma: clinicopathological and molecular correlation**
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Background & Objectives: *TERT* promoter(*TERT*p) mutation has emerged as one of the distinct marker of adult subtype of *SHH*-activated medulloblastoma(MB), which is associated with a better prognosis. The current study aims to evaluate the frequency of *TERT*p mutations and correlate it with various clinical, histoarchitectural and molecular features.
Methods: Cases of medulloblastoma diagnosed between 2021 and 2024, which were molecularly grouped by targeted gene expression profiling (GEP), and evaluated for *TERT*p mutation by Droplet digital PCR(DdPCR) were included
Results: Cohort of 142 cases; the age range was-0-3years: 21(14.8%), 4-6years: 36(25.4%), 7-18years: 58(40.8%), 19-25years: 13(9.2%), 26-39 years: 12(8.5%) and ≥40years: 2(1.4%).M:F ratio-2.2:1. The molecular grouping based on GEP and with additional p53 immunohistochemistry, the cases were molecularly grouped - 23(16.2%)*WNT*-activated, 44(30.9%)*SHH*-activated and *TP53* wildtype immunophenotype, 2(1.4%)*SHH*-activated and *TP53* mutant immunophenotype and 73(51.4%)non-*WNT*/non-*SHH* group [27(19%)group3, 35(24.6%) group4, 11(7.7%)unclassified]. Histologically, classic(n=97,68.3%) histoarchitecture was the most common followed by D/N (n=24,16.9%), LC/A(n=11,7.7%), with myogenic differentiation(NOS; n=6,4.2%) and MBEN(n=4, 2.8%) histoarchitecture. The overall frequency of *TERT*p mutation was 16.9% (n=24). 19 were of *C228T* and 5 were of *C250T* type of mutations. *TERT*p mutations were significantly seen in adults(≥19 years) and *SHH*-activated group($p<0.001$). The frequency of mutation was 4.3% (n=5) and 70.3% (n=19) in <19 years and ≥19 years age-group respectively. Of the 24 mutant cases, 22(91.6%) were *SHH*-activated (≥19 years:19, 86.4%; <19 years:3, 13.6%), 1(0.7%) was *WNT*-activated and 1(0.7%) was non-*WNT*/non-*SHH* group. 8(33.3%) were midline and 16(66.7%) were laterally localized.13(54.1%) cases showed classic and 11(45.8%) showed D/N histoarchitecture. None of the mutant cases showed *TP53*-mutant immunophenotype, monosomy 6, and *MYCN* amplification. The one-year OS for *TERT*p mutant cases (100%) was better than *TERT* promoter wild-type cases(94%).
Conclusion: *TERT*p mutations were highly frequent (86.4%) in adult *SHH*-activated MB patients, observed in classic and D/N histoarchitectural patterns, lateralized locations, absent in *MYCN*-amplified or *TP53*-mutated cases, and associated with better overall survival.

OFP-04-005
Real-life investigation of nanopore sequencing for rapid epigenomic classification of brain tumours
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Background & Objectives: DNA methylation profiling has been established as a crucial diagnostic biomarker for the classification of brain tumours. In the routine diagnostic workflow, traditional histopathology must be interpreted in synopsis with molecular pathology findings for precision diagnostics. However, conventional molecular assays, such as EPIC DNA methylation profiling and NGS require 2-4 weeks, delaying comprehensive tumour board decision and initiation of personalized therapy. This study explored the feasibility of nanopore sequencing as a rapid diagnostic approach capable of epigenetically classifying brain tumours within 24 hours.
Methods: We analysed 45 brain tumour specimens using Nanopore sequencing. Nineteen different common and rare tumour types were included. DNA was extracted, quantified, and sequenced using the MinION platform. Methylation-based classification was conducted in parallel using the NanoDx pipeline and the neural network classifier Sturgeon.
Results: Nanopore-based classification was obtained within a few hours of workflow initiation. NanoDx yielded a classifiable result in 31 (71 %) and Sturgeon in 39 (89 %) samples. The predicted class matched the integrated diagnosis obtained by histological and molecular pathological analyses in 29 cases (94 % of classifiables) for NanoDx and in 29 cases (74 % of classifiables) for Sturgeon. For non-classifiable cases, the prediction with the highest score matched the integrated diagnosis in 46 % of the cases for NanoDx and 20 % for Sturgeon. For 30 samples that were classifiable by both algorithms, NanoDx and Sturgeon yielded concordant results for 29 samples.
Conclusion: Nanopore sequencing substantially accelerates the diagnostic timeline for brain tumours, offering the potential to initiate personalized therapy within five days. Despite its promise, further refinement is necessary to improve classification accuracy, particularly for specimens with low tumour cell content. Ongoing investigations will assess whether earlier integrated diagnosis translates to improved clinical outcomes. Overall, these findings underscore the clinical benefits of nanopore sequencing for rapid integrated histopathological and molecular diagnostics.

OFP-04-006
Dissecting the methylomes of *CDKN2A/B* deleted glioblastoma
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Background & Objectives: Glioblastoma IDH wildtype is the most common brain tumour of adults in the western world. It is highly aggressive and shows a devastating outcome. Up to now, there is no targeted therapy available. A very interesting novel approach for individualized patient care is the tumour suppressor gene *cyclin dependent kinase inhibitor (CDKN) 2A/B* that is lost in a fraction of Glioblastomas.
Methods: In this study, we performed integrated epigenome-wide DNA-methylation analysis of 866,895 methylation specific sites in 100 glioblastoma IDH wildtype samples with known *CDKN2A/B* deletion status comparing the DNA methylome of deleted and retained glioblastomas.
Results: We found distinct significantly differentially methylated CpGs (DMCG) with $\Delta\beta \geq 0.1$ and p-value < 0.05 in *CDKN2A/B* deleted compared with *CDKN2A/B* retained. Of these DMCGs, we were able to allocate distinct loci with tiling, promoter, gene and CpG island locations. Interestingly, the list of differentially methylated genes allocated functionally relevant RNAs. Gene ontology (GO) analysis showed enrichment of distinct pathways in *CDKN2A/B* deleted glioblastomas.
Conclusion: In summary, dissecting the methylomes of *CDKN2A/B* deleted and retained glioblastomas revealed globally altered pathways that are associated with cellular proliferative activity.

OFP-04-007
Single-nucleus RNA sequencing and spatial transcriptomics reveal sustained microglial activation in Post COVID-19 condition
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Background & Objectives: Post COVID-19 condition (PCC) resembles chronic fatigue syndrome, with cognitive impairment and fatigue as common symptoms. However, the underlying pathomechanisms remain poorly understood, and therapeutic options are limited. We aimed to investigate the role of neuroinflammation and innate immune activation in PCC by analysing cerebrospinal fluid (CSF) and brain tissue from affected individuals.
Methods: We analysed CSF from PCC patients (n=20) presenting with neurological impairments one year post SARS-CoV-2 infection. To investigate long-term effects in the central nervous system, we performed single-nucleus RNA sequencing (snRNAseq; n=12) on postmortem brain tissue from donors who had died months after infection. To validate and spatially contextualize these findings, we applied StereoSeq, a spatial transcriptomics method, to fresh-frozen brainstem sections from the same individuals (n=8). Transcript mapping to individual nuclei was combined with computational label transfer using snRNAseq data to classify cell types. Lower-resolution binning was used to delineate tissue niches.
Results: We observed activation of the innate immune system in the CSF, indicative of marked microglial activation in PCC patients compared to non-infected controls. This activation persisted in postmortem brain tissue, as shown by snRNAseq. Harnessing spatial information confirmed these findings and revealed distinct localization patterns and transcriptional states of parenchymal versus perivascular microglia. We identified differentially expressed genes between microglial subtypes and quantified their local abundances in diseased versus control tissue. Niche analysis further revealed altered spatial interactions between microglia and their microenvironment in the context of systemic viral infection.
Conclusion: Our results provide hints for sustained neuroinflammation in PCC, driven by long-term microglial activation. Spatial and transcriptomic profiling highlights distinct microglial states, offering insights into the cellular basis of persistent neurological symptoms following SARS-CoV-2 infection.

OFP-04-008
Pathological findings of triplet placentas associated with assisted reproductive technology: a study of 98 triplet pregnancies
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Background & Objectives: Triplet pregnancies have increased over the past few decades due to an increase in assisted reproductive technology (ART) and are considered high-risk pregnancies. Generally, ART pregnancies are associated with poorer obstetric outcomes. Placental pathological findings of ART pregnancies are not well known. Our aim is to determine if triplet placentas conceived by ART present more placental abnormalities than those conceived in vivo.

Methods: This is a retrospective case-control study. It includes all triplet pregnancies followed up in a tertiary referral hospital between 2000 and 2024 whose placentas were analysed in a Pathology Department. The control group were the in vivo conceived triplet pregnancies (natural conceptions and artificial insemination) and the case group were the ART-conceived triplet pregnancies (in vitro fertilization and intracytoplasmic sperm injection). Univariate and multivariate statistical studies were performed.
Results: 98 triplet pregnancies were analysed: 33 triplet pregnancies in the in vivo conceptions group and 65 triplet pregnancies in the ART group. After multivariate analysis, the monochorionic triamniotic percentage was significantly higher (p=0.02) in the in vivo group and the dichorionic triamniotic (p=0.03) in the ART group. The percentage of primiparous women in the ART group was significantly higher (p=0.02). The ART group placentas presented less placental weight (p=0.03) and more marginal (p=0.01) and velamentous (p<0.01) insertion. Higher rates of chronic villitis (p=0.02), accelerated villous maturation (p=0.01), intervillous fibrin deposits (p=0.01) and chorangiomas (p=0.04) were found in the ART group and more oedema (p=0.01) and the presence of nucleated red blood cells (p=0.02) were detected in the in vivo group.
Conclusion: Gross and pathological placental evaluation is key to understand pregnancy outcomes. Further studies analysing the possible immunological and vascular mechanisms of these findings; and if these differences between groups are related to a higher rate of maternal, obstetric, foetal or neonatal complications are needed.

OFP-04-009

Leveraging artificial intelligence for grading chorioamnionitis: diagnostic precision in inflammatory cell localization and quantification

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Background & Objectives: Chorioamnionitis is an acute inflammation of the amniotic membranes, leading to severe maternal and foetal complications. Early diagnosis is essential but current clinical methods lack precision. This study developed an artificial intelligence (AI)-based algorithm for identifying chorioamnionitis at varying severity levels. The algorithm aims to identify the grade (GRADE) and stage (STAGE) of anatomical spread based on Amsterdam criteria using placental and umbilical cord tissue images. The study hypothesizes that AI can accurately identify these factors, measure inflammatory cells, and reveal connections between chorioamnionitis and foetal diseases.
Methods: A total of 102 placental patches were captured and amnion layer was manually segmented. A previously developed algorithm was used for nuclear segmentation. Statistical analysis compared cell counts across GRADE groups and the median distance of cells from the amnion layer between the algorithm and pathologist's STAGE groups.
Results: A strong correlation was found between GRADE ratings and the number of cells, with cell count increasing as severity rose: GRADE 0 had 21.6±14.73 cells, GRADE 1 had 29.46±11.56, and GRADE 2 had 56.19±38.41 (P<0.01). In STAGE 3, the distance between inflammatory cells and reference points significantly decreased to 123.78±73.13 pixels (P<0.01). However, an anomaly was found in STAGE 1, where the average distance (235.79±64.9 pixels) was lower than in STAGE 2 (269.66±92.3 pixels), warranting further investigation.
Conclusion: The algorithm successfully identified the severity grades of chorioamnionitis and stages, providing quantitative tools for measuring the quantity and distance of cells. The findings confirm the known associations between inflammation severity and cell count. The integration of artificial intelligence in pathology may improve diagnostic accuracy, reduce pathologist workload, and enhance medical intervention capabilities in cases of chorioamnionitis.

OFP-04-010

Comprehensive analysis of gene expression profiles in paediatric myofibroblastic neoplasms

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Background & Objectives: Myofibroblastic lesions in children are a group of soft tissue proliferations including a full spectrum of benign, intermediate, and malignant neoplasms. The aim of our study was to characterize the gene expression profiles of paediatric myofibroblastic neoplasms carrying tyrosine receptor kinases (TRK) fusions and classified as Inflammatory Myofibroblastic Tumours (IMT), Infantile Fibrosarcoma (IFS) or TRK-driven mesenchymal tumours according to Paediatric tumours WHO classification 2022, in order to define their differences and the pathways responsible for their clinical diversity.
Methods: We performed unbiased transcriptome-wide RNA-sequencing analysis on all the cases of myofibroblastic neoplasms arrived at our institution in the period 2000-2023. Paired-end sequencing was performed using a NextSeq550 Illumina platform. Gene Set Enrichment Analysis was performed on DESeq2-normalized counts. Analysis results were validated using bulk transcriptomic datasets.
Results: Our analysis was performed on 46 samples including 15 IFS (7 with prominent vascular pattern, all with *ETV6::NTRK3* fusion), 4 vascular lesions from 2 patients, arising in the site of previous IFS or at a distance, all carrying the *ETV6::NTRK3* fusion, 9 IFS-like lesions, 6 TRK rearranged paediatric mesenchymal tumours and 12 IMT. RNA-seq analysis demonstrated three main groups with distinct expression profiles: IFS, IFS with prominent vascular pattern (IFSv), and IMT. Hemangiomas formed an additional small sub-cluster. IFS-like tumours (i.e. IFS showing TRK rearrangement different from *ETV6::NTRK3)* and TRK-rearranged mesenchymal tumours formed 2 heterogeneous clusters, one closely related to IMT and the other one very close to IFS. Interestingly, 2 *ETV6::NTRK3* rearranged IMT clustered with *ALK*-rearranged IMT, and 2 IFS-like lesions with *ALK* rearrangement clustered with other IFS-like lesions.
Conclusion: These preliminary results demonstrate how the molecular profile of IFS and IMT reflects and confirms their classification based on morphology and also highlight a different molecular profile in IFSv. This study may pave the way to an evolution towards an integrated classification of myofibroblastic neoplasms.

OFP-04-011

From slides to capturing the whole picture: visualization of the downstream behaviour of twin-twin anastomoses in dye-injected placentae with 3D virtual histology using X-rays

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Background & Objectives: Twin to twin transfusion syndrome (TTTS) is a complication occurring in 10-15% of monochorionic

twin pregnancies and in case of unbalanced blood flow often resulting in foetal loss without treatment. It is characterized by a disproportionate blood flow between twins due to vascular anastomoses leading to severe complications. To validate ultrasound findings and identify missed or newly developed anastomoses after laser coagulation in TTTS, dye can be injected into the umbilical cord vessels. However, deep anastomoses can be missed since gross pathology identification often does not provide the identification of both superficial and deep anastomoses in TTTS placentae. Through 3D virtual histology using X-rays and following segmentation work we are able to visualize vessel trees of dye injected TTTS placentae in 3D showcasing anastomoses with actual intersections which are important for determining a change in behaviour of said vessels.
Methods: Placentae were prepared, injected with dye, and fixed with formalin according to Turowski [3]. The FFPE samples were scanned using a laboratory phase-contrast X-ray tomography setup by Histomography GmbH. The FFPE samples were cut into histological slides and compared to the segmented vessel trees after. Segmentation was performed using the open source 3D Slicer software, marking the dyed vessels based on thresholding of the measured intensities, followed by cleaning up artifacts with Gaussian smoothing.
Results: Downstream, anastomoses were identifiable in both histological slides and the unedited tomography scans. The vessel tree can be visualized based on grey levels with VG Studio Max. The segmentation performed with 3D Slicer can be used for further analysis like intervascular connectivity and blood flow simulations.
Conclusion: Using 3D virtual histology and segmentation, we can visualize placental vessel trees in 3D, highlighting intersections critical to understanding vessel behaviour. This method can enhance understanding of TTTS and contribute to more accurate diagnostics, staging, and future research on vascular structures.

OFP-04-012
A novel pattern-based histological approach to IBD-like colitis in children with PID
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Background & Objectives: Primary immunodeficiencies (PID) can present as very early-onset (VEO) IBD or monogenic disease (MD), associated with gene defects in mucosal immune response. We, hereby, present our PID case series using a novel pattern-based histological approach highlighting the IBD-like morphology in ileocolonic biopsies.
Methods: A total of 33(13 girls and 20 boys) PID cases with GI symptoms were retrospectively evaluated for inflammatory patterns categorized as UC-like, CD-like, enterocolitis-like, apoptotic, eosinophil-rich, IBD-unclassified (IBD-U), and mild colitis. Clinicopathological features including age at diagnosis, symptoms, genetic and survival data were assessed in correlation with histologic data.
Results: Mean age at diagnosis and symptom onset were 44 and 56.85 months, respectively. PID cases composed of 6 severe combined immunodeficiency(SCID), 4 chronic granulomatous disease, 3 common variable immunodeficiency(CVID), 2 IgA deficiency, 2 other Ig deficiencies, and 1 hyper-IgM syndrome while monogenic defects including 4 MEFV and 3 LRBA mutations, 1 IL10R deficiency, 1 IL21 deficiency, 1 DGAT mutation, 1 prolidase deficiency, 1 RIPK1 defect, 1 Bruton's tyrosine-kinase deficiency, and 2 DOCK8 deficiency were detected in the remaining 15 cases. MDs showed UC-like (n=2), CD-like (n=2), IBD-U (n=1), and 2 mixed (apoptotic+UC-like/CD-like), 1 apoptotic, 1 enterocolitis-like pattern and 2 mild colitis. Non-monogenic cases (50%) comprised of 3 UC-like, 4 CD-like, 1 IBD-U, 4 mild colitis, 2 mixed (apoptotic+IBD-U/eosinophilic), and 1 eosinophilic patterns. No significant difference was found between MD and non-MD cases for colitis patterns, age, and survival. MDs (12:3) showed a higher M/F ratio compared to non-MDs (8:10) (p=0,037). IBD-like patterns were significantly more common before the age of 6, compatible with a diagnosis of VEO-IBD (68,8%, p=0,024) which was associated with monogenic disease in 50% of the cases.
Conclusion: IBD-like colitis seems to be more common in young children with PID which emphasizes the need for a multidisciplinary approach for accurate diagnosis and treatment of monogenic disease.

OFP-05 Oral Free Paper Session Breast Pathology

OFP-05-001
Ki-67 and lymph node status as predictive biomarkers for chemotherapy decision-making in moderately differentiated breast cancer
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Background & Objectives: The decision to offer or withhold adjuvant chemotherapy (aCT) in patients with moderately differentiated (grade 2) luminal breast cancer, particularly those with a Ki-67 index between 5% and 30%, remains a clinical challenge. Although molecular tests can provide helpful information, they are costly and may not be accessible. On the other hand, immunohistochemistry is a more affordable and widely accessible option.
We aim to evaluate the ability of immunohistochemistry to correctly determine molecular subgroups in grade 2 breast cancer. We also assessed the predictive value of Ki-67 expression and lymph node status (pN) in determining the need for chemotherapy.
Methods: A retrospective analysis was performed on 59 patients with grade 2 breast carcinoma who underwent surgery followed by adjuvant therapy between January 2019 and December 2022. Logistic regression models were used to evaluate the relationship between Ki-67 expression, pN, and aCT. The optimal Ki-67 cutoff for selecting patients who would benefit from chemotherapy was determined using the receiver operating characteristic (ROC) curve.
Results: The median age of the cohort was 54.3±11.9years, with a median tumour size of 18.9±13.1mm. Most tumours (86.4%) were "no special type" carcinomas, and ductal carcinoma in situ was observed in 84.7% of cases. Metastatic involvement was found in 35.1% of sentinel lymph nodes. Immunohistochemical classification using a Ki-67 cutoff of 22% showed strong agreement with PAM50/Prosigna's molecular subtypes (Cramér's V=0.476,*p=0.001*). The ROC analysis for Ki-67>19.5% showed moderate predictive ability for the benefit of aCT (AUC=0.660). Logistic regression revealed that Ki-67>19.5% (OR=9.996,*p=0.005*) and pN (OR=14.015,*p=0.002*) were significant predictors of aCT benefit.
Conclusion: Immunohistochemistry-based molecular subtyping offers a cost-effective and reliable alternative to molecular testing. Regarding aCT, our findings suggest that Ki-67>19.5% and positive pN status could potentially serve as useful biomarkers for deciding whether a patient should undergo aCT, particularly when molecular testing is not available.

OFP-05-002
Breast carcinomas with low oestrogen receptor expression (1-10%): characteristics and therapeutic implications
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Background & Objectives: Invasive breast carcinomas with low oestrogen receptor (ER) expression (1-10%) represent a rare subgroup. The

2020 ASCO/CAP guidelines recommend reporting them separately, and the 2025 guidelines emphasize internal control assessment. This study characterizes these tumours and compares oestrogen receptor immunohistochemistry (IHC) between biopsy and surgical specimens.
Methods: We retrospectively analysed clinicopathological data of 3,851 primary invasive breast cancer biopsies at IPO Porto (July 2017–December 2024). Data included tumour size, histologic type, grade, HER2 status, hormonal receptor status, treatment modalities, and IHC reevaluation in surgical specimens.
Results: Fifty cases (1.30%) with ER 1-10% were identified in biopsy, all in females (29-92 years). Most tumours (88%) were ductal/non-special type (NST), all grade 2 and 3. Tumour size ranged from 0.6 to 7.5 cm (mean 4.1 cm). Thirty-three tumours were HER2-negative (0, 1+ and 2+ FISH negative). Posteriorly, surgical specimens from 39 patients were analysed (22 post-neoadjuvant chemotherapy [NAC], 8 with pathological complete response). Among NAC-treated patients with residual tumour, 5 lacked ER reevaluation, 2 retained ER 1-10%, 6 became ER-negative, and 1 had ER 75-100%. In the primary surgery group, 7 lacked reevaluation, 3 retained ER 1-10%, and 7 became ER-negative. Of the total 19 patients who repeated ER testing in the surgical specimen, only 5 (26.3%) retained ER 1-10%. Post-surgery, 25 patients received hormone therapy, 30 radiation therapy, and 15 anti-HER2 therapy. No local recurrence was observed; however, 11 developed distant metastases, and 7 died. In the case with ER 75-100% in the surgical specimen, biopsy was revised and internal controls were adequate, but fixation time exceeded 72 hours.
Conclusion: ER-low tumours were usually high grade and stage and significant IHC discordance between biopsy and surgical specimens was observed. Routine ER retesting in surgical specimens should be recommended to avoid losing true positive results, which could have treatment implications.

OFP-05-003
Clinicopathological and molecular features of Glycogen-Rich Breast Carcinomas
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Background & Objectives: Since its first description by Hull et al in 1981, several case series have described the clinicopathological features of glycogen-rich breast carcinoma (GRC); however, these studies often involved low number of cases, and no detailed genetic study has been performed. To enhance our understanding of this rare breast carcinoma, we conducted the largest molecular study to date with 10 GRCs to describe their genetic landscape.
Methods: 10 invasive GRCs were identified, diagnosed between 2001-2024. All were subjected to DNA sequencing using TruSight Oncology 500 panel (523 genes).
Results: All patients were female (ages: 32 to 74 years; median 51). Tumour size ranged from 0.7-3.8 cm (median 1.45). All GRCs showed relatively well-defined borders and its characteristic appearance with nests/cords formed by clear cells with glycogen accumulation in cytoplasm confirmed by PAS/PASD staining. Four were grade 2 and six were grade 3. Seven showed associated DCIS with glycogen-rich features. Lymph node metastasis was seen in 2. Eight were ER/PR+/HER2-, two were ER/PR/HER2-. Follow-up (available for 9/10) ranged from 6 to 186 months (median 38). Three patients had distant metastasis; six had no evidence of disease. DNA sequencing identified two major molecular subgroups: *GATA3*-mutant GRCs (5/10) with frequent *RPKSB1* copy number gain (4/5) and *TP53*-mutant GRCs (4/10) with a subset harbouring *BRCA1* alterations (2/4; one germline). *FGFR* family copy number gains were seen in 3/10. *TP53*-mutant GRCs were all grade 3, showed low/negative ER, and 3/4 patients showed distant metastasis while *GATA3*-mutant GRCs were mixed grade 2/3, all were ER+ without distant metastasis.
Conclusion: Two molecular subgroups of GRCs were identified: *GATA3*-mutant and *TP53*-mutant. The latter was associated with higher grade, ER-negativity and poor clinical outcome. Molecular studies or p53 immunohistochemistry as a surrogate could be helpful to identify this subgroup for closer follow-up and/or more aggressive treatment.

OFP-05-004
Integration of next-generation RNA sequencing-based MammaPrint and BluePrint analysis in clinical decision making: performance evaluation in the first 1278 cases
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Background & Objectives: MammaPrint and BluePrint can identify breast cancer patients with luminal disease who may forego adjuvant chemotherapy. We validated a decentralised Next-Generation RNA Sequencing-Based MammaPrint and BluePrint (RNA-seq MP/BP) using total RNA extracted from paraffin tissue. We aimed at evaluating the technical performance and feasibility of RNA-seq MP/BP in the context of a national multigene signatures (MGS) testing in Belgium.
Methods: Data on MP/BP RNA-seq tests conducted at University Hospitals Leuven (UHL) were obtained from December 2019 until December 2022. The collected metrics included failure rate, turnaround times, MP and BP indices.
Results: To date, 1278 MP/BP RNA-seq tests were analysed accounting for 40% (n=1278/3227) of total national MGS output during this period. The total test failure rate was 6.1% (n=78/1278), which was reduced to 3.8% (n=49/1278) after repetition of a failed test. The average turnaround time was 13 days [range: 9-27 days] in 2021. Tests requested by external breast clinics accounted for 73% (n=930/1278) while the remaining were requested in UHL (27%; n=348/1278). The MP/BP RNA-seq test was Low-risk/Luminal Type A in 57% (n=679/1200), High-risk/Luminal Type B in 42% (n=510/1200), High-risk/Basal type and High-risk/HER2-Type in 1% of the patients (respectively 9 and 2 cases). Further categorisation of the MP index showed MP High-risk 2 in 5.1% (n=61/1200), MP High-risk 1 in 38.3% (n=459/1200), MP Low-risk in 41.9% (n = 503/1200) and MP Ultra-low risk in 14.8% of patients (n=177/1200). Based on these results, 520/1200 patients (43.3%) would have been recommended adjuvant chemotherapy.
Conclusion: Decentralisation of the MP/BP RNA-seq test is feasible with low failure rates and acceptable turnaround time. Our results suggest that adjuvant chemotherapy could be omitted in nearly 57% of patients. Further analysis of the MP/BP RNA-seq test in clinical decision-making and clinical follow-up of patients is warranted.

OFP-05-005
PRAME expression in Triple Negative Breast Carcinomas
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Background & Objectives: Triple negative breast carcinoma (TNBC) represents a heterogenous group of neoplasms defined by the absence of hormone receptor expression and HER2 overexpression. Accurate diagnosis of TNBC can be challenging due to inconsistent expression of many breast-specific markers. PRAME has emerged as a useful diagnostic marker for melanoma, however recent studies have reported expression in breast carcinomas. Our study evaluates the expression of PRAME, in the context of other melanoma and breast-site specific markers in a large cohort of TNBCs.
Methods: Sections from tissue microarrays (TMAs) composed of 316 TNBC in triplicate 1 mm cores were immunostained for PRAME, pankeratin (AE1/AE3) (PANK), GATA3, K7, SOX10, S100, HMB45 and Melan-A using standardized protocols. PRAME was scored according to the proportion of tumour cells with positive expression. Staining intensity and the cellular compartment of staining were also assessed. Weak nuclear expression of PRAME in >25% of cells or moderate to strong nuclear expression in any portion of cells were classified as positive. The remaining markers were scored using a modified Allred method. Histologic tumour types were assigned according to the WHO classification.
Results: Over half (51.9%) of the TNBCs showed nuclear expression of PRAME. Of these, 77.4% expressed SOX10, 75.0% expressed S100, 3.7% expressed HMB45 and 1.2% expressed Melan-A. Only 1.2% of PRAME positive cases did not co-express PANK, K7, or GATA3. 11.1% of TNBCs expressed PRAME, but not SOX10, S100, HMB45 or Melan-A. Strong cytoplasmic PRAME expression was associated with apocrine carcinoma or tumours with apocrine features (specificity=98.9%, sensitivity=43.2%).
Conclusion: Nuclear expression of PRAME is common in TNBC, frequently occurring in cases co-expressing other melanoma markers and rarely in cases with no expression of PANK, CK7, or GATA3. The findings underscore the importance of utilizing a panel of markers in accurately distinguishing TNBC from melanoma.

OFP-05-006
Predicting therapy response in triple negative breast cancer by applying DNA methylation profiling
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Background & Objectives: Breast cancer (BC) is the most prevalent form of cancer among women. Therapy is contingent upon the biological profile underlying the specific type of breast cancer, including factors such as hormone receptor expression, Her2 status, and proliferative activity. Depending on the tumour subtypes, patients with BC receive individualized treatments. Triple-negative breast cancer (TNBC) is characterized by its highly aggressive tumour biology. The standard systemic treatment for TNBC is chemotherapy. In many cases, TNBC undergoes neoadjuvant therapy prior to surgical intervention with the aim of reducing tumour mass. However, only a subset of tumours show therapeutic response that is characterized by the residual cancer burden (RCB). The present study aims to predict therapy response in patients diagnosed with TNBC by applying DNA methylation profiling.
Methods: In this study, we performed epigenome-wide methylation analysis on 24 TNBCs, with 12 cancers demonstrating good therapy response (RCB 0) and 12 exhibiting poor therapy response (RCB 2). Utilizing the Illumina Infinium EPIC V2 bead chip array, we were able to interrogate more than 935,000 methylation-sensitive CpG sites in parallel. Subsequent computational analyses were then performed to identify differentially methylated genes. Gene ontology (GO) analyses were processed to reveal altered pathways.
Results: A computational analysis revealed that there were distinct epigenomic differences in the two TNBC subgroups of RCB 0 and RCB 2. Differential methylation analysis revealed distinct differences in the DNA-methylation landscape. GO analysis indicated that RNA processing emerged as the most significantly differentially methylated pathway.
Conclusion: In summary, our findings demonstrate that DNA methylation profiling serves as a valuable tool in breast cancer research. Our findings reveal substantial disparities in the DNA methylation signatures between TNBC of RCO 0 and RCB 2. These findings have the potential to serve as valuable predictors of therapy response status.

OFP-05-007
Multi-site study of an AI solution as clinical decision-support tool for the identification of microinvasive and T1a carcinomas of the breast
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Background & Objectives: Histologic identification of small foci of invasive breast cancer (BC) is challenging and time-consuming. We assessed the accuracy of pathologists supported by an artificial intelligence (AI) breast H&E solution vs. those not assisted in identifying microinvasive (MI) and T1a BC associated with DCIS.
Methods: This two-arm multi-reader study compared 4 pathologists' ("readers") performance in the evaluation of 200 digitized H&E slides of BC biopsies from two different US and EU centres, without and with a fully automated AI breast solution. Pathologists' accuracy in both arms compared to ground truth (GT) and review time were analysed. GT was established by 3 expert breast pathologists. Cases were enriched for DCIS with potential confounding features (e.g., stromal chronic inflammation, lobular involvement).
Results: The four pathologists evaluated each case twice, once in each study arm separated by a wash-out period of two weeks. Pathologists supported by AI showed significantly higher accuracy in identifying MI and invasive carcinoma or foci suspicious for invasive carcinoma compared to pathologists without AI (84.2% vs 78.8%, p=0.045). In addition, the use of AI reduced the time required to evaluate MI+pT1a cases from a mean of 92 seconds without AI to 79 seconds with AI.
Conclusion: The AI solution demonstrated significantly improved detection of MI and pT1a BC, despite coexistent DCIS enriched for potentially confounding alterations. In addition, the use of the AI solution reduced the time required for slide evaluation in MI and T1a cases by 14%. This approach holds promise for enhancing diagnostic accuracy and consistency in the detection of MI and T1a BC, enhancing pathologist workflow, and reducing the time spent identifying small foci of BC.

OFP-05-008
A model of sensitive tissue transfer for breast reconstruction - the rat neurotized epigastric flap
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Background & Objectives: Sensory recovery is a key outcome in breast reconstruction, with abdominal wall-based flaps being the gold standard for autologous tissue transfer. Although neurotization offers significant benefits, its technical complexity hinders widespread implementation. A precise histological understanding of these flaps is essential for optimizing sensory restoration. The rat epigastric flap is a widely used model due to its anatomical resemblance to humans, but its neurohistology remains poorly studied. This study aims to characterize the rat's neurotized epigastric flap, highlighting its sensory nerve components and relevance for surgical applications.
Methods: An observational cross-sectional study was conducted on twenty murine models. The caudal epigastric nerve and the 10th to 12th intercostal nerves as well as samples from the rats abdominal skin were dissected and histologically processed. Haematoxylin-eosin and Masson's trichrome staining were performed, along with immunohistochemistry using anti-neurofilament antibodies (neuronal identification), Peripherin (sympathetic fibres), Annexin V (sensory fibres), and anti-PIEZO2 (mechanoreceptors). Microscopic analysis focused on nerve fiber types and cutaneous receptor density, classification and distribution relative to the dermo-epidermal junction.
Results: Histological analysis enabled a detailed characterization of the neuronal structures within the flap skin, including nerve fiber density, type, and receptor distribution. Findings revealed significant similarities between the rat and human ventrolateral abdominal skin, supporting the validity of this model for sensate tissue transfer research.
Conclusion: The neurohistological features of the rat neurotized epigastric flap reinforce its relevance for studying sensory nerve restoration in reconstructive surgery. This detailed analysis enhances understanding of flap neuroanatomy, providing a foundation for optimizing neurotization techniques and enhancing microsurgical training.

OFP-05-009

Hypoxia-induced CAIX expression restricts CD8+ T-cell infiltration in breast cancer

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Background & Objectives: Hypoxia and necrosis are common features of invasive cancer. In solid tumours, including breast carcinoma, the dynamic upregulation of carbonic anhydrase IX (CAIX), induced by hypoxia-inducible factor 1 (HIF-1), supports cellular adaptation to hypoxia. CAIX activity contributes to extracellular acidosis and reshapes the tumour microenvironment, impacting tumour behaviour and prognosis. This study aimed to assess the mass and distribution of the immune infiltrate—specifically CD8+ effector T-cells—in relation to tumoral CAIX expression.
Methods: Formalin-fixed, paraffin-embedded breast carcinoma sections were analysed via double immunohistochemical staining for CAIX and CD8. Digital slides were evaluated using HistoQuant (3DHistech) image analysis software to quantify CD8+ signal within and outside CAIX-positive tumour areas. Statistical analysis was performed using GraphPad Prism.
Results: Among 34 breast carcinomas, 18 were partially CAIX-positive, and 16 were CAIX-negative controls. Necrotic foci were associated with CAIX overexpression, and tumours with necrosis showed significantly higher relative CAIX expression than those without (11.47 ± 5.51 vs. 3.77 ± 3.5; $P = 0.0216$). However, relative CD8+ lymphocyte counts did not differ significantly between necrotic and non-necrotic cases (134.7 ± 55.7 vs. 97.7 ± 57.25; $P = 0.1579$). Similarly, no significant difference was observed in overall CD8+ T-cell infiltration between CAIX-positive and -negative tumours (98.5 ± 37.3 vs. 96.0 ± 50; $P = 0.5928$). Notably, in CAIX-positive tumours, CD8+ T-cell distribution correlated with the extent of CAIX expression. Within individual tumours, CD8+ T-cell counts were significantly lower in CAIX-positive versus CAIX-negative areas (13.1 ± 9.4 vs. 135.6 ± 62.2; $P < 0.0001$).
Conclusion: These findings suggest that CAIX-expressing tumour regions may hinder CD8+ T-cell infiltration, and that the hypoxia-driven tumour microenvironment could limit the efficacy of immune and targeted therapies requiring intact T-cell responses.

OFP-05-010

Multi-centre NHS evaluation of artificial intelligence as a decision support solution for breast cancer diagnosis: accuracy and early efficiency results from the DEBORAH study

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Background & Objectives: This study investigates the performance of a commercial AI solution across a prospective consecutive patient cohort from five NHS hospitals (UK), while exploring its accuracy and contribution to enhancing diagnostic efficiency in the breast pathway.
Methods: The diagnostic performance of the AI solution was evaluated in an observational study involving over 3,000 consecutive patients undergoing breast biopsy. Initial diagnoses were made by pathologists following standard of care procedures, without AI support, within digital pathways. After issuing a preliminary report, pathologists reviewed the AI-generated findings and compared outcomes specifically in the classification of Benign, Cancer, Invasive Cancer, and DCIS. Efficiency metrics, including number of patients, turnaround time (TAT) and immunohistochemistry (IHCs) tests, were extracted from operational data in the Laboratory Information Management Systems (LIMS). The study is ongoing and will compare results from six months prior to AI deployment with six months after its integration into the workflow.
Results: When differentiating between cancerous and benign cases, the AI system demonstrated a sensitivity of 100%, specificity of 99.6%, positive predictive value (PPV) of 99.5%, and negative predictive value (NPV) of 100%. For invasive carcinoma detection, it showed a sensitivity of 99.5%, specificity of 99.8%, PPV of 99.5%, and NPV of 99.8%, while for DCIS diagnosis, the AI's sensitivity was 98.9%, specificity of 99.9%, PPV of 98.9%, and NPV of 99.9%. Early efficiency findings from one hospital indicate a 21% increase in productivity and a 73% reduction in diagnostic IHCs for benign cases, such as p63, CK7, and CK5/6. User feedback suggests that the IHC reduction is driven by increased pathologist confidence in signing off benign cases without additional tests.
Conclusion: The AI solution demonstrated high diagnostic accuracy and encouraging improvements in efficiency, including increased productivity and reduced IHC requests, suggesting its potential to enhance workflow in breast cancer pathology, leading to improved patient outcomes.

Funding: This project has received funding from the Artificial Intelligence (AI) in Health and Care Award, which is an NHS AI Lab programme run by the Accelerated Access Collaborative (AAC) in partnership with the National Institute for Health Research (NIHR)

OFP-05-011

Different HER2 immunoreactivity in biopsies compared to corresponding surgical specimens of invasive breast carcinomas with potential therapeutic implications

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Background & Objectives: HER2 analysis by immunohistochemistry and in situ hybridization (ISH) for immunoreactive score (IRS) 2+ is standard for invasive breast carcinomas (IBC) and performed on diagnostic biopsies. Recently, non-amplified HER2 was reclassified as HER2 low (IRS 1+ and IRS 2+/non-amplified) and HER2 ultralow (IRS 0 with <10% positivity), respectively, considering response to antibody-drug conjugates (ADC). We routinely repeat HER2 on the surgical specimen. The aim of this study was to compare HER2 expression between biopsies and surgical specimens with emphasis on HER2 low and ultralow categories.

Methods: We searched for breast biopsies and corresponding surgical specimens from 2024. The HER2 reports were retrieved and compared using 2023 ESMO guidelines. Discrepant cases were reviewed. In our lab, HER2 testing is highly standardized and regularly checked by robin round trials.

Results: For 158 patients corresponding biopsies and surgical specimens were available. In the biopsy group 6.9% were HER2 negative, 8.9% ultralow, 70.9% low and 13.3% positive whereas in the surgical group 12.6% were HER2 negative, 22.2% HER2 ultralow, 55.7% low and 9.5% positive. These differences were statistically significant (p=0.001; chi^2 test) with 51 cases (32.2%) discrepant cases: downgrade from biopsy to surgical in 44 cases, upgrade in 7 cases. Downgrade involved IRS 2+ (low) amplified to non-amplified (6; 3.8%), low to ultralow (26; 16.5%) and low to negative (8; 5%). Upgrades involved negative to ultralow (1.2%), negative to low (0.6%) and ultralow to low (2.4%). All IRS 3+ cases remained positive.

Conclusion: HER2 low and ultralow and low HER2 amplification is detected more frequently in IBC biopsies compared to surgical specimens, which may have therapeutic implications on adjuvant anti-HER2 and ADC therapy. These discrepancies may be influenced by preanalytical and analytical conditions and highlight the necessity of standardized companion testing. The use of artificial intelligence for HER2 assessment may be considered.

OFP-05-012

Can criteria from DCIS de-escalation trials be used to select for atypical ductal hyperplasia with low risk of upgrade to carcinoma?

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Background & Objectives: De-escalation of surgical treatment of low-risk DCIS is under active investigation. However, surgical excision remains the standard of care in the management of atypical ductal hyperplasia (ADH) diagnosed on core biopsy. This study examines the use of criteria from the DCIS de-escalation trials to identify ADH cases with low risk of upgrade to carcinoma.

Methods: A registry of ADH patients from 2004 to 2022 was reviewed for cases treated with surgical excision. Criteria from the COMET DCIS surgical de-escalation trial applicable for ADH including age, imaging findings and personal history of breast cancer were evaluated and rates of upgrade to carcinoma were compared in patients who would and would not meet these criteria.

Results: Of 362 ADH cases treated with surgical excision, 233 (64.4%) met trial criteria for de-escalation (Cohort 1) (patient age >40y, no mass lesions, no previous cancer in the ipsilateral breast within the last 5 years, and no concurrent cancer) and 129 (35.6%) did not meet these criteria (Cohort 2). The age at surgical excision, race, breast density or lesion size on imaging was not significantly different between two cohorts. Cohort 1 patients were more likely to have been diagnosed by mammography (94% vs 72%, $p<0.0001$) and more likely to present with calcifications (82% vs 30.2%, $p<0.0001$). While there was no significant difference in rate of ADH upgrade to DCIS between the two cohorts, there was a significantly lower rate of ADH upgrade to invasive disease in Cohort 1 (3.43%) compared to the cohort that did not meet the selected trial criteria for surgical de-escalation (10.85%) ($p<0.010$).

Conclusion: Our data show a very low rate of ADH upgrade to invasive disease in patients who meet criteria from trials of surgical de-escalation for DCIS, suggesting that such patients could also be considered a low-risk cohort for whom observation may be appropriate.

OFP-06 Oral Free Paper Session Soft Tissue and Bone Pathology

OFP-06-001

A clinicopathological analysis of 42 cases of paratesticular tumours in orchiectomies

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Background & Objectives: Due to their low incidence, paratesticular tumours pose a diagnostic challenge for many pathologists. Therefore, understanding the diagnostic spectrum is crucial. This study aims to showcase the cases retrieved from our archives and provide a detailed analysis of the clinicopathological characteristics of this rare group of tumours.

Methods: A retrospective analysis was conducted on orchiectomies from 2014 to 2025. Cases of paratesticular tumours were selected and reviewed in terms of clinical, morphological, and molecular characteristics.

Results: Paratesticular tumours comprised 42 of 567 (%0.07) orchiectomies. The mean age was 45.3 (5-89). Liposarcoma was the most common diagnosis (19 cases, 45%) followed by rhabdomyosarcoma (14 cases, 33%) and leiomyosarcoma (4 cases, 10%). Liposarcomas included dedifferentiated (11 cases), well-differentiated (7) and myxoid (1) subtypes. Rhabdomyosarcomas were mostly embryonal (11 cases), with spindle-cell (2) and pleomorphic (1) variants. Other diagnoses included mesothelioma (2), myeloid sarcoma (1), aggressive angiomyxoma (1), and cellular angiofibroma (1). Liposarcomas were more common in patients older than 50 (mean: 63), while rhabdomyosarcomas were commonly seen in younger patients (mean: 17). The average tumour size was 6.1 cm (26 cases). Surgical margins were positive in 12 cases (29%). In 7 cases, the diagnosis required a molecular test; RT-PCR for *PAX3/7::FOXO1A* or *MDM2* and *DDIT3* FISH. Follow-up data (n=29, median: 12.5 months) showed recurrence in 3 cases and metastases in 6 cases. Nine patients died of disease (3 rhabdomyosarcomas, 3 liposarcomas, 1 leiomyosarcoma, 1 mesothelioma, and 1 myeloid sarcoma).

Conclusion: Paratesticular tumours are rare comprising <1% of orchiectomies. In this large series, nearly 90% of the tumours are

liposarcomas, leiomyosarcomas, and rhabdomyosarcomas, depending on age. In selected cases, molecular support is helpful in differential diagnoses such as leiomyosarcoma versus liposarcoma, and subtypes of rhabdomyosarcomas and liposarcomas. Orchiectomy may not achieve clear surgical margins and prognosis is poor, with one-third of patients succumbing to disease.

OFP-06-002

Soft tissue and bone tumours in a sarcoma reference centre: a retrospective study of 4163 cases in its 8-year existence

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Background & Objectives: Soft tissue and bone tumours constitute a heterogeneous group with an often-overlapping morphology, making accurate diagnoses a challenge. This study aims to describe the caseload at our Sarcoma Reference Centre (SRC) and to assess the degree of agreement between biopsy and surgical specimens.
Methods: A retrospective analysis of soft tissue and bone tumours was performed at the ULSSM in Lisbon, Portugal, from 2017 until 2024, since becoming a SRC. Pathology reports with diagnoses currently listed in the WHO Soft tissue and bone tumour classification volume (5^{th} edition, 2020) were selected. For each case, patient demographics and tumour features (e.g. location, behaviour, histogenesis groups, entity, grade, immunohistochemistry - IHC - and molecular profiles) were analysed.
Results: During this timeframe, the exams performed at the SRC doubled. Among 3607 patients, 4163 diagnoses were made, of which 2947 were benign lesions, 855 malignant lesions, 305 showed intermediate behaviour; the remaining 56 cases were inadequate for diagnosis. Across all histogenesis groups listed in the WHO, benign adipocytic and vascular tumours were the most frequent. Of the 4163 diagnoses, 668 pertain to patients with over 1 exams/diagnosis, of which only 320 had matching biopsy-surgical specimen pairs reported at our SRC; of these, 97%, 86% and 86% were given matching behaviour, entity and grade, respectively. Of the 202 reviewed cases from other centres, 21 were different from the entity/differential diagnoses considered at our SRC.
Conclusion: The demographics and epidemiology reported in this study are similar to those documented in the literature for soft tissue and bone tumours. Most of these tumours can be diagnosed based on morphology alone, if evaluated by experienced soft tissue and bone tumour pathologists. Considering the increasing molecularly defined entities, access to IHC and molecular testing is often available only at SRC, enabling a more accurate and swift diagnosis, ultimately optimizing patient treatment and prognosis.

OFP-06-003

Giant Cell Granuloma of jaw: a study on demographics, aggressiveness, and recurrence of a benign hidden threat

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Background & Objectives: Giant cell (reparative) granuloma (GCG) is a benign but locally aggressive lesion primarily affecting the jawbones,with a risk of recurrence after treatment.
Methods: This study evaluates the clinicopathological characteristics of 302 cases analysed through 364 biopsies between 2010 and 2025 at a single pathology centre. Age, gender, localization, recurrence, and associated diseases were assessed using nonparametric statistical tests.
Results: Females constituted 59% (n=179) of cases, with a median age of 46±20.9 years (range: 3–95 years). The mandible was the most affected site (59.7%, n=92). Recurrence was observed in 55 cases (18.2%), with a higher frequency in females (70.9%, p=0.035, chi-square). The earliest recurrence occurred within one year, while the latest was ten years post-diagnosis. Six cases experienced multiple recurrences. Surgical management required mandibular resection (n=2) and maxillectomy (n=2). Parathyroid pathology was detected in seven recurring cases (five adenomas, one hyperplasia, one carcinoma). Two cases were initially misdiagnosed as pyogenic granuloma before a definitive GCG diagnosis. No significant correlation was found between recurrence and age or lesion localization.
Conclusion: Our findings align with previous literature regarding demographic distribution. The recurrence rate (18.2%) falls within the reported range of 5%–70.6%. Higher recurrence is often associated with incomplete excision, particularly in central GCGs. Cases with multiple recurrences should raise suspicion for hyperparathyroidism-related giant cell lesions, which histologically resemble GCG. Improved histological biomarkers and surgical techniques are needed to predict disease outcomes and reduce recurrence, as multiple recurrences complicate the clinical course.

OFP-06-004

Clinico-pathological analysis of 19 osteofibrous dysplasias and 25 adamantinomas with respect to the current WHO classification: a single institution experience over 12 years

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Background & Objectives: Osteofibrous dysplasia (OFD) and adamantinoma are rare bone tumours. The present study provides a detailed clinicopathological evaluation of these tumours.
Methods: OFDs and adamantinomas diagnosed from 2012 to 2024 were retrieved. Additionally, tumours diagnosed as fibrous dysplasia (FD) and intra-osseous synovial sarcoma of the tibia and the fibula were retrieved. Fifty-five tumours were reviewed. Finally, 19 OFDs and 25 adamantinomas were included. The initial diagnosis was revised in 12/55 (21.8%) tumours. In addition to the tibia and the fibula, a single adamantinoma occurred in the metatarsal bone.
Results: Among 25 adamantinomas, there was a single OFD-like adamantinoma and 24 classic adamantinomas with various morphological patterns, most frequently tubular and basaloid. OFD-like areas were noted in 6/24 (25%) classic adamantinomas. Pan keratin was positive in scattered cells in 18/19 (94.7%) OFDs and 16/17 (94%) adamantinomas. P40 (4/4,100%) and p63 (4/6,66.7%) were useful in diagnosing adamantinomas. None of the OFDs, on follow-up (n=16) progressed to an adamantinoma during a median follow-up duration of 51.15 months. Four patients harbouring adamantinomas developed recurrences (4/25,16%), and four developed metastasis (4/25,16%) to the lungs and regional lymph nodes.
Conclusion: This constitutes the largest series of OFDs and adamantinomas from our subcontinent as per the recent WHO classification. These tumours are associated with errors in interpretation. Testing FD, especially in the tibia/fibula for keratin, is useful to avoid missing an OFD. A cluster of 3 or more keratin-positive cells in a fibro-osseous neoplasm indicates an OFD-like adamantinoma, which is rare. Although a morphological continuum was seen between OFD and adamantinoma, no OFD progressed to an adamantinoma. Given treatment-related implications, it is crucial to distinguish an OFD, OFD-like adamantinoma, and classic adamantinoma, from their mimics, especially synovial sarcoma from spindle cell adamantinoma. The

risk factors for recurrence and metastasis in adamantinomas include an incomplete curettage and a spindle cell pattern.

OFP-06-005

RNA sequencing expands the molecular spectrum of chondromyxoid fibroma: a multicentric study within the ResOs french network

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Background & Objectives: Chondromyxoid fibroma (CMF) is a rare locally agressive bone tumour whose diagnosis could be difficult in small biopie samples. Previous studies have identified GRM1 overexpression as a hallmark of the tumour, which is associated with *GRM1* rearrangements in a subset of cases. However, the full spectrum of fusion partners remains only predicted. We aim to characterize the clinical, phenotypical, and molecular features of CMF, particularly focusing on identifying novel *GRM1* fusion partners.
Methods: We conducted a retrospective multicentric study including 95 CMF samples from 85 patients diagnosed in twelve centres. We analysed clinicopathological data and phenotypic features. Targeted RNA sequencing was performed using our in-house developed NGS assay, with validation through orthogonal molecular techniques (FISH) where applicable.
Results: Media age at diagnosis was 33 [IQR:20-43] with a female/male sex ratio of 0.85. Main localizations were long bones of lower limb (35%), feet bones (28%) and flat bones (22%). Median size at diagnosis was 28 mm [IQR:20-37.25]. Sensitivity of GRM1 immunohistochemistry was 95%.
RNA sequencing analysis was performed on 74 samples. We identified nineteen *GRM1* fusion partners in twenty-nine cases (39%) including previously reported *BCLAF* gene (five cases) and novel *AOPEP* gene fusion partner (five cases). 8/19 fusion partners (42%) were located on chromosome 6, same as *GRM1*. Eleven cases (15%) were wild-type (WT) and thirty-four cases (46%) were non-contributive due to decalcification process. Eight patients relapsed during follow-up, six out of them were WT. Additional molecular testing and validation using *GRM1* FISH, notably for WT cases, is ongoing.
Conclusion: Our study represents one of the largest CMF cohorts analysed to date and highlights the utility of GRM1 immunohistochemistry and RNA sequencing in aiding the differential diagnosis of CMF. Morevover, the identification of novel *GRM1* fusion partners expand the known molecular spectrum of CMF and may contribute to a deeper understanding of its pathogenesis.

OFP-06-006

A clinicopathologic and molecular characterization of 15 distinctive hyalinizing spindle cell neoplasms of soft tissue with MUC4 and beta-catenin co-expression and frequent biallelic inactivation of *APC*

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Background & Objectives: MUC4 and beta-catenin are two important immunohistochemical markers that have well established applications in the diagnosis of fibroblastic soft tissue tumours. The former is highly specific for the related entities low-grade fibromyxoid sarcoma and sclerosing epithelioid fibrosarcoma, while the latter is commonly positive in desmoid fibromatosis and Gardner fibroma. It is generally considered that expression of these markers is mutually exclusive. In this study, we describe the clinicopathologic and molecular features of a group of distinctive fibroblastic soft tissue neoplasms characterized by consistent co-expression of MUC4 and beta-catenin.
Methods: Fifteen hyalinized spindle cell neoplasms with MUC4 and beta-catenin co-expression were identified from our institutional archives. Targeted DNA sequencing was performed on 9 tumours. In a subset, FISH was performed to assess for *FUS* and/or *EWSR1* rearrangement.
Results: The cohort comprised 15 adult patients (6 female, 9 male) with a median age of 40 years (range 20–61). No patients had a known history of familial adenomatous polyposis. Tumours were located in the extremities (9), trunk (5), and retroperitoneum (1). The tumours consisted of a hypocellular proliferation of spindled-to-stellate fibroblastic cells in a variably hyalinized collagenous stroma. No atypia, fascicular growth, or myxoid stroma was present. Sequencing demonstrated biallelic *APC* inactivation in 7/8 (86%) tumours successfully assessed. Variant allele frequencies were consistent with somatic rather than germline events. No gene fusions were detected. None of the tumours assessed with FISH showed *FUS* (0/9) or *EWSR1* (0/8) rearrangement. Clinical follow-up data are pending.
Conclusion: We describe a novel fibroblastic neoplasm of soft tissue characterized by co-expression of MUC4 and beta-catenin and frequent underlying *APC* inactivation. Our findings support that this represents a distinct soft tissue tumour type that is important to distinguish from LGFMS/SEF, as well as desmoid fibromatosis and Gardner fibroma.

OFP-06-007

Tertiary lymphoid structures in soft tissue sarcomas: prognostic and molecular associations

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Background & Objectives: Tertiary lymphoid structures (TLSs) have been linked to improved outcomes in several cancers, but their role in soft tissue sarcomas is unclear. We integrated histopathological TLSs evaluation on H&E with RNA-seq data, correlating morphometric and spatial features with survival, molecular profiles, and a 12-chemokine TLSs gene signature.
Methods: We evaluated tertiary lymphoid structures (TLSs) in 191 soft tissue sarcoma (STS) samples from The Cancer Genome Atlas, integrating whole-slide imaging in QuPath for morphological assessment on H&E. TLSs density and area were calculated per tumour region (intra-, border-, extratumoral), along with overall TLSs score (number of TLSs inside+border). For transcriptional analysis, RNA-seq count files were obtained from the Genomic Data Commons. Patient stratification was based on the median score of a summed 12-chemokine genes generated signature score (*CCL2*, *-3*, *-4*, *-5*, *-8*, *-18*, *-19*, *-21*, *CXCL9*, *-10*, *-11*, *-13*). Spearman correlation, Kaplan–Meier, and Cox proportional-hazard models were performed with Python libraries (lifelines 0.30).

Results: TLSs were present in 74 of 191 (39%) STS samples. Median TLSs density reached 0.0215/mm² (range 0.0032–0.4957), with dedifferentiated liposarcoma showing the highest burden. Only 2 TLSs-positive cases (2.7%) displayed germinal centres. TLSs score correlated moderately with the 12-chemokine signature (Spearman r=0.428, p=6.38×10^{-10}). TLSs absence trended toward worse overall and recurrence-free survival in Kaplan–Meier analyses, while higher TLSs density suggested more favourable outcomes. However, univariate Cox models showed no statistical significance for TLSs parameters (p=0.732). By contrast, the 12-chemokine signature approached borderline significance (HR=0.891, 95% CI 0.779–1.019, p=0.092).
Conclusion: Though not definitively significant, the robust correlation between TLSs burden and the 12-chemokine signature underscores an immune-mediated advantage in STS. Larger, multicentre cohorts with deeper immunophenotyping are essential to further confirm TLSs prognostic utility and inform prospective immune-targeted therapeutic interventions.

OFP-06-008

Comprehensive analysis of m6A RNA methylation regulators in soft tissue leiomyosarcoma

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Background & Objectives: N6-methyladenosine (m6A) is a prevalent RNA modification involved in various biological processes, including carcinogenesis, tumour progression, and immune regulation. This study aimed to investigate the role of m6A regulatory genes—including METTL3, METTL14, WTAP, FTO, ALKBH5, and YTHDF1–3—and their associations with c-MYC and programmed death ligand 1 (PD-L1) expression in soft tissue leiomyosarcoma (LMS).
Methods: The expression levels of m6A regulators were analysed using next-generation sequencing data from 53 LMS cases obtained from a public database. We further examined the relationship between m6A regulators and c-MYC and PD-L1 expression in an LMS cell line. Immunohistochemical staining (IHC) was performed on 69 LMS tissue samples. Functional analyses included siRNA-mediated knockdown of selected m6A regulators in LMS cells.
Results: IHC revealed that high expression levels of METTL3, METTL14, ALKBH5, FTO, and WTAP were associated with elevated c-MYC expression, while high expression of ALKBH5, YTHDF2, and WTAP correlated with increased mitotic activity. Knockdown of METTL3, METTL14, and FTO led to reduced c-MYC target gene expression and decreased cell proliferation, underscoring the role of m6A modifications in c-MYC-driven oncogenesis. Furthermore, knockdown of YTHDF2 suppressed interferon-γ-induced PD-L1 expression, suggesting its involvement in immune evasion. Multivariate Cox regression analysis identified low YTHDF2 and high WTAP expression as independent poor prognostic factors.
Conclusion: Our findings highlight the oncogenic and immunoregulatory roles of m6A regulators in LMS. Targeting these molecules, especially in combination with immune checkpoint blockade, may offer novel therapeutic strategies. Further studies are warranted to clarify the mechanisms underlying m6A-mediated regulation of c-MYC and PD-L1 in LMS.

OFP-06-009

Multi-omics profiling identifies two epithelioid sarcoma molecular subtypes with distinct signalling and immune characteristics

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Background & Objectives: Epithelioid sarcoma (EpS) is an aggressive soft tissue sarcoma affecting young adults, characterized by SMARCB1 loss. Traditionnaly, EpS is classified into two histological subtypes (HS) — distal and proximal, which may co-exist ("hybrid" EpS) — with distinct clinical behaviours. Despite its phenotypic diversity, the molecular basis of EpS heterogeneity remains poorly understood. We aimed to build a molecular classification to improve our understanding of EpS biology and guide therapeutic decisions.
Methods: To establish an EpS molecular classification and uncover determinants of inter- and intra-patient heterogeneity in EpS, we used multi-omics profiling and integrated the genomic, transcriptional and methylome landscapes with single-cell RNA sequencing on fresh samples as well as spatial transcriptomics.
Results: We identified two molecular subtypes of EpS: "distal-like" and "proximal-like". Distal-like tumours (n = 20) include all distal HS, two proximal HS and four mixed HS. They express a specific molecular single-cell derived epithelial-to-mesenchymal transition signature, which associates with improved patient survival and includes Desmoglein 2 (DSG2), which we identify as a potential routine immunohistochemical biomarker to improve diagnosis. Distal-like EpS also display increased peri-tumoral CD8+ T cell infiltrates and specific tumour-immune cell interactions. Conversely, proximal-like EpS (n = 13) — comprising 12 proximal HS and one mixed HS — harbour a higher inter-tumoral molecular heterogeneity with some cases resembling other SMARCB1-deficient tumours by DNA methylation profiling, and increased intra-tumoral immunosuppresive macrophage infiltrates.
Conclusion: Our study introduces a novel molecular classification of EpS with prognostic value, potential diagnostic markers and distinct tumour immune microenvironments, that extends beyond traditional clinicopathological classification. These insights pave the way for more personalized and effective treatment strategies for patients with EpS.

OFP-06-010

Clinicopathologic features of clear cell sarcoma and the role of PRAME in differential diagnosis

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Background & Objectives: Clear cell sarcoma(CCS) of soft tissue is a rare, aggressive malignancy that primarily arises within the deep soft tissues of the extremities. The genetic alteration (EWSR1-ATF1 fusion), caused by the t(12;22)(q13;q12) translocation has not been found in melanoma, highlighting the crucial role of molecular diagnostics in ensuring precise differentiation. Due to its resemblance to histopathological similarity to melanoma, distinguishing between the two can pose substantial diagnostic difficulties especially with immunohistochemistry.
Methods: In this study, 14 CCS cases diagnosed between 2000 and 2025 were reviewed and their clinicopathological features were evaluated. PRAME expression was investigated for the differential diagnosis of melanoma.
Results: Nine(%64,2) cases were female. Median age was 35,9 years(11-64 years). The average tumour size was 6.6 cm (range 3–10). The most common location were foot(n:5) followed by

thigh(n:4),hand(n:2), inguinal-gluteal(n:2), and cruris(n:1). Histopathologically, tumours showed lobular growth patern. Spindle, epithelioid cells with clear cytoplasm showed low mitotic activity. Immunohistochemically all tumours were positive with HMB45 and S100, and focally positivity with MelanA, whereas other mesenchymal and epithelial markers were negative.
FISH was performed in seven tumours with EWSR-1 break apart probe. Six cases showed positive results with approximately 80% signal. Immunohistochemically PRAME was negative in eight tumours, whereas only one tru-cut biopsy was positive. The median follow-up time of eight cases was 53.5 months(6-216 months). Recurrence/metastasis was observed in five cases; five cases were alive whereas three patients had died.
Conclusion: Clear cell sarcoma is a rare and highly malignant neoplasm primarily affecting young adults. The genetic signature EWSR-1-ATF1 fusion is absent in melanoma, which is the major entity in differential diagnosis.
The results of this study show that the use of PRAME immunohistochemistry presents a valuable approach to minimizing diagnostic uncertainty and enhancing accuracy in differentiating CCS from melanoma and other histologically similar tumours.

OFP-07 Oral Free Paper Session Digestive Diseases Pathology - GI

OFP-07-001

Early-onset colorectal cancers differ from later-onset colorectal cancers, analysis of 651 cases with special emphasis to DNA MMR protein expression loss

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Background & Objectives: Early-onset colorectal cancer (CRC) is increasingly prevalent worldwide, yet its underlying causes remain unclear. Emerging evidence suggests that early-onset CRC exhibits distinct clinical, pathological, and molecular characteristics compared to late-onset disease. Younger patients are often diagnosed at more advanced stages and present with more aggressive histopathological features. We compared the clinicopathological characteristics and DNA mismatch repair (MMR) protein expression in early-onset and late-onset CRC cases.
Methods: A total of 651 CRC resection specimens were analysed, including 328 cases from patients under 50 years and 323 age-matched controls from patients over 50 years, randomized by including the subsequent resection following the study case collected from two reference centres. Tissue microarrays (5 mm) were extracted from tumour samples and immunohistochemically analysed for MMR proteins (MSH6, MSH2, MLH1, and PMS2). Tumour location, gender distribution, pT and pN stages, lymphovascular invasion (LVI), and perineural invasion (PNI) were statistically evaluated using parametric and non-parametric tests.
Results: Among the patients, 59.9% were male, and 40.1% were female. The median age for early onset cases were 43 years-old and 66 years-old for late onset ones. MMR protein loss was significantly higher in early-onset CRC cases ($p<0.05$, Chi-square). Most tumours (72.4%) were located in the left colon and predominantly exhibited moderately differentiated adenocarcinoma morphology. Stage T3 (70.4%) and N1 (60.4%) tumours were most common. N0 tumours were more frequent in younger patients than in the control group (43.3% vs. 35.8%, $p=0.05$, Chi-square). LVI was significantly lower in early-onset cases (41% vs. 51.6%, $p=0.007$).
Conclusion: Early-onset CRC differs significantly from late-onset CRC in terms of clinicopathological features and molecular profiles as higher ratio of MMR loss, lower likelyhood to lymphatic spread. These findings highlight the need for age-specific screening, diagnosis, and treatment strategies to improve patient outcomes.

OFP-07-002

Deep learning-based prediction scores in colorectal cancer and their association to tumour morphology, biology and predicted drug response

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Background & Objectives: Over the last few years, several deep learning (DL) models have been presented to predict colorectal cancer (CRC) patient survival directly from Haematoxylin-Eosin (H&E)-stained routine whole slide images (WSI). Unlike traditional studies, which require a predefined hypothesis and selection of features of interest, weakly supervised deep learning allows training on clinical endpoints without specifying in advance what the model should explicitly focus on. Such DL study results offer the unique opportunity to subsequently investigate tissue morphology and biology potentially driving these predictions, which may improve our understanding of the disease under investigation.
Methods: We performed a comparison of clinicopathological features, tumour morphology, biology, gene expression-based predicted drug response and H&E-inferred DL-based survival risk scores (low- vs high-risk as well as absolute risk scores) in 692 CRCs from two international cohorts.
Results: Clinicopathological risk factors such as grade of differentiation, lymph node status or percentage of tumour necrosis were significantly associated with higher DL-based risk scores (p-values < 0.05). CRCs with tumour cells located next to adipocytes were enriched in the DL-based high-risk group. The morphological review showed that spatial proximity of tumour cells to adipocytes, high degree of tumour budding, poor differentiation and signet-ring cell morphology were linked to DL-based high-risk scores. Transcriptomic and genetic subgroups showed no or only minimal association with H&E-inferred DL-based risk scores. Furthermore, DL-based low- vs high-risk CRCs were characterized by a differential drug sensitivity.
Conclusion: Our study highlights that DL-based risk scores derived from H&E-WSI closely align to established clinicopathological prognostic features, such as grading, lymph node status or spatial proximity of tumour cells and adipocytes. Moreover, DL-based risk groups seem

to be associated with a differential treatment response, underlining their potential to guide patient stratification in clinical routine.

OFP-07-003

Mucosal neural network alterations in HSV esophagitis: a semi-quantitative scoring analysis in comparison with gastroesophageal reflux esophagitis and healthy controls

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Background & Objectives: Herpes simplex virus(HSV) esophagitis is rare and usually caused by latent infection in the neural ganglia in immunocompromised patients. We aimed to investigate the impact of HSV infection on the oesophageal mucosa and mucosal neural network(MNN).
Methods: A total of 27 cases were analysed, including 9 patients with HSV esophagitis, 9 with gastroesophageal reflux disease(GERD) (evaluated according to Los Angeles classification and Lyon consensus) and 9 healthy controls (confirmed by endoscopy, high-resolution oesophageal manometry and 24-h pH-impedance monitoring). All samples were stained with S100 antibody and assessed semi-quantitatively (grade 1-3) for nerve fiber localization, density and nerve branching patterns. Additionally, oesophageal mucosal activity (EMA) was also scored based on histopathological features such as the presence of ulceration/erosion, basal cell hyperplasia, papillary elongation, dilated intercellular space, inflammatory cell (lymphocytes, eosinophil, polymorphonuclear leukocyte) infiltration and vascular dilation.
Results: Patients with HSV esophagitis were significantly older than healthy controls (67 vs. 43 years, p=0.013). EMA scores showed significant differences among groups: healthy controls (median: 4, range: 2-7), GERD (median: 14, range: 8-15), and HSV esophagitis (median: 11, range: 5-17) (p=0.000, ANOVA). MNN scores were also significantly different: healthy controls (median: 4, range: 3-5), GERD (median: 5, range: 3-6), and HSV esophagitis (median: 3, range: 0-5) (p=0.002, ANOVA).
Conclusion: HSV esophagitis was associated with increased EMA scores compared to healthy controls while MNN scores were lower, suggesting possible neural damage independent of inflammation. This implies that HSV may have a direct cytotoxic effect on oesophageal neural structures. Although investigated in a small group of cases these findings provide new insights into the neuropathological effects of HSV on the oesophageal mucosa and highlight the importance of MNNs in oesophageal disease pathology. Further research is needed to explore the mechanisms of HSV-induced neural damage and its clinical implications as well as the relationship of MNNs in different oesophageal pathologies.

OFP-07-004

Claudin 18.2 as an emerging and independent biomarker in gastric and gastroesophageal junction adenocarcinomas: a dual-centre cohort study

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Background & Objectives: Gastric cancer is characterized by molecular heterogeneity, with several biomarkers considered for therapeutic targeting, including HER2, mismatch repair proteins (MMR), and PD-L1. Claudin 18.2 has emerged as a therapeutically relevant biomarker. This study assesses its frequency and overlap with established biomarkers in a dual-centre cohort of gastric and gastroesophageal junction adenocarcinomas (G/GEJC) and related clinicopathological features.
Methods: A retrospective study included 126 patients diagnosed between 2019 and 2025 with G/GEJC from two institutions. HER2 (4B5, Ventana), MMR (Ventana), PD-L1 (28.8 and 22C3, Agilent), and Claudin 18.2 (43-14A, Ventana) were assessed by immunohistochemistry (IHC). HER2 was additionally evaluated by in situ hybridization (ISH) in 2+ cases. Claudin 18.2 was analysed in all cases for academic purposes. PD-L1 Combined Positive Score (CPS) was assessed in 36 patients, as it was not routinely tested in earlier cases due to lack of therapeutic indication. Associations were analysed using chi-square tests ($p < 0.05$).
Results: HER2 positivity was observed in 21 patients (16.7%), and deficient MMR (dMMR) in 28 (22.2%). Claudin 18.2 was positive in 44 patients (34.9%), and PD-L1 CPS $\geq$5 in 22 of 36 evaluated cases (61.1%). Among Claudin-positive patients, 15.9% were also HER2-positive, 13.6% were also dMMR, and 13.6% had PD-L1 CPS $\geq$5 (6 of 11 evaluated). HER2 positivity was more frequent in GEJ tumours ($p = 0.0031$). dMMR was significantly associated with HER2 negativity ($p = 0.022$), older age ($p = 0.008$), and non-GEJ tumours ($p = 0.021$). Claudin 18.2 and PD-L1 expression showed no significant association with other biomarkers or clinical features.
Conclusion: Claudin 18.2 was expressed in over one-third of cases and exhibited partial co-expression with HER2, dMMR, and PD-L1, without statistically significant associations. These findings support its role as an independent biomarker. Its integration into routine molecular profiling informs therapeutic stratification within multidisciplinary tumour board discussions.

OFP-07-005

Variation in p53 Immunohistochemistry assessment in Barrett's Oesophagus, a review of 1.150 patient cases by the Dutch Oesophageal Pathology Panel

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Background & Objectives: Assessing Barrett's Oesophagus (BE) related dysplasia is hampered by interobserver variability and guidelines advocate a second opinion. Ancillary P53-immunohistochemistry (IHC) has the potential to improve diagnostic consistency and clinical decision-making. Little is known however about the inter-pathologist variation assessing P53-IHC.
Methods: The Dutch oesophageal pathology panel accommodates centralized revision for BE-biopsies in The Netherlands, and consists of 15 pathologists who underwent a stringent training program. This study evaluates expert P53-IHC review in 1150 digitized consecutive panel revision patient cases between January 2015 and December 2024. Panel P53-IHC gold-standard (GS) assessment was determined as P53 wild-type, P53-overexpression, P53 null-mutation or P53 double-clone, when >75% of pathologists (minimum of 4) reached agreement, and otherwise discussed in monthly consensus meetings. If no consensus was reached, P53-IHC status was rendered equivocal. Referral P53-IHC assessment was compared to panel GS P53-IHC assessment.

Results: Of 1150 patient cases, 1690 P53-IHC assessments were reviewed. Overall accuracy of referral P53-IHC status compared to panel GS-P53 assessment was 75%. Highest agreement was observed in p53 wild-type (86%, 689/798) and P53 overexpression (81%, 515/634) cases, followed by double-clone (80%, 8/10) and null-mutation patterns (67%, 48/72). Referring hospital P53 wild-type were re-classified as P53 overexpression by panel revision in 7% (57/794) and vice versa in 9% (54/634). P53-IHC was assessed indeterminate by referring hospital in 180 of 1690 cases, and 166 of 180 were re-classified as wildtype (n=89), overexpression (n=59), null mutation (n=12) or double-clone (n=6); 14 were rendered equivocal. P53-IHC null-mutation was missed in 83/1690 of cases (5%).
Conclusion: Panel review of 1150 BE-patient cases shows inter-observer variation assessing P53-IHC. Wildtype is assessed as overexpression in 7% and vice versa in 9%. Null-mutations are missed in 5%, and initial P53 classification indeterminate in 11%. Clear guidelines for P53-IHC interpretation is needed, as accurate P53-IHC assessment has impact on diagnostic and clinical decision-making.

Funding: This research was funded with a grant by the MaagLeverDarmSticking (MLDS) with project number: MLDS-WO21-25

OFP-07-006

WNT1-Inducible Signaling Pathway Protein 3 (WISP3) as a biomarker for neoadjuvant CCRT response and prognostic indicator in rectal cancer: a retrospective cohort study

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Background & Objectives: Colorectal cancer ranks as the third most common malignancy worldwide. Fundamentally, cancer is characterized by dysregulated cell proliferation. The *WISP3* gene, also known as *cellular communication network factor 6 (CCN6)*, encodes WNT1-inducible signalling pathway protein 3 (WISP3). In aggressive subtypes of breast cancer, such as inflammatory and metaplastic carcinoma, WISP3 is recognized as a tumour suppressor.
Methods: Transcriptomic analysis of the GSE35452 dataset, with a focus on the Gene Ontology term "regulation of cell growth" (GO:0001558), identified WISP3 as the most significantly upregulated transcript in non-responders. Tumour samples from 343 primary rectal cancer patients who underwent neoadjuvant concurrent chemoradiotherapy (CCRT) followed by surgical resection were analysed. WISP3 expression was semi-quantitatively assessed via immunohistochemical staining, and statistical analyses were performed to evaluate its correlation with clinicopathological features and survival outcomes.
Results: Elevated WISP3 expression was significantly associated with greater tumour invasiveness pre- and post-treatment ($P \leq .002$), lymph node metastasis before and after therapy ($P \leq .005$), vascular invasion ($P = .006$), perineural invasion ($P = .041$), and poor response to neoadjuvant CCRT ($P = .031$). High cytoplasmic WISP3 immunoreactivity correlated with worse clinical outcomes, including disease-specific survival (DSS), local recurrence-free survival (LRFS), and metastasis-free survival (MeFS) (all $P \leq .0017$) in univariate analysis. Additionally, WISP3 was identified as an independent prognostic factor for reduced DSS, LRFS, and MeFS in multivariate analysis (all $P \leq .003$).
Conclusion: WISP3 plays a crucial role in rectal cancer progression and response to neoadjuvant CCRT, emerging as a novel prognostic biomarker that may help guide treatment strategies.

OFP-07-007

Ki67 Index and tumour size as dual diagnostic criteria for stratifying gastric fundic gland neoplasms: a multicentre clinicopathological validation study

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Background & Objectives: Gastric fundic gland neoplasms (GF-GNs), including oxyntic gland adenoma (OGA), fundic gland type gastric adenocarcinoma (GA-FG) and fundic gland mucosa type gastric adenocarcinoma (GA-FGM), are rare gastric tumours with low-grade nuclear atypia and indolent behaviour. This indolent nature poses diagnostic challenges in small biopsy specimens where architectural assessment is limited, necessitating quantitative biomarkers for accurate subtyping.
Methods: This multicentre study analysed 47 GF-GN cases with NGS and immunohistochemical staining, with thorough histological evaluation. Genomic alterations were analysed across histological subtypes using a 1021-related genes panel in 17 cases. AI-based approach was employed to quantify Ki67. ROC curve analysis, Decision Curve Analysis (DCA), and a diagnostic workflow integrating tumour size and Ki67 index were performed.
Results: Patients ranged from 42 to 79 years (median 60), with 22 males and 25 females. Histologically, 24 OGAs, 21 GA-FGs, and 2 GA-FGMs were identified. The tumours demonstrated well-formed glands, expanding with dense growth patterns comprising pale, blue-grey columnar cells with mild nuclear atypia. GA-FG/GA-FGM exhibited larger sizes ($p<0.0001$) and higher Ki67 indices (median 7.5%, range 2-26%) than OGA (median 1.9%, range 1-5%) ($p<0.0001$). ROC analysis set a Ki67 cutoff of 2.5% (AUC=0.9476, 90% sensitivity, 90.48% specificity) and a size threshold of 4.5 mm (94.74% sensitivity, 92.37% specificity) for distinguishing advanced subtypes. DCA confirmed the clinical utility of Ki67 (net benefit up to 0.9 at 0.3-0.6) and Size (0.8 at 0.2-0.4) models. Molecular profiling highlighted conserved Wnt signalling (GNAS 44.4%, CTNNB1 5.6%) across subtypes, with GA-FGM showing unique BRAF, MLL3, and MSH3 mutations.
Conclusion: This study validates that tumour size and Ki67 index effectively stratify indolent (OGA) versus progressive (GA-FG/GA-FGM) GF-GNs. DCA confirms the clinical benefit of these thresholds, with Ki67 offering superior performance in moderate-risk ranges. Integrating AI-quantified Ki67 and macroscopic measurements provides a high-accuracy diagnostic framework for biopsy interpretation, enabling conservative management of low-risk lesions.

OFP-07-008

UPK2 expression in colorectal cancer is linked to aggressive tumour histomorphology and distinct molecular features

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Background & Objectives: Uroplakin-2 (UPK2) is a marker primarily associated with urothelium and urothelial cancer, frequently utilized in differential diagnosis of tumours of unknown origin. This study examines the histopathological, immunological, molecular, and clinical characteristics of UPK2-expressing colorectal cancer (CRC).
Methods: Two independent CRC cohorts (N=1,851) were used to analyse UPK2 expression in relation to tumour histopathological features, immune cell densities analysed with multiplex immunohistochemistry, and chromosomal alterations evaluated using optical genome mapping. Additional molecular analyses were conducted in The Cancer Genome Atlas (TCGA) cohort (N=629) using bioinformatics approaches.
Results: UPK2 was expressed in 12% of CRCs. UPK2-positive CRCs were associated with poor prognostic factors, including advanced disease stage, lymphovascular invasion, tumour budding, and micropapillary growth pattern ($p<0.01$ for all). UPK2 positivity was associated with higher CRC-specific mortality in both cohorts (Cohort 1: HR for high vs. negative 1.97, 95% CI 1.00–3.88; Cohort 2: HR 3.33, 95% CI 2.15–5.16). In the larger cohort, this association remained independent of other prognostic parameters (multivariable HR for high vs. negative 2.31, 95% CI 1.46–3.65). Multiplex immunohistochemistry showed that UPK2 expression was linked to lower densities of $CD3^+$ T cells, $CD20^+CD79A^+$ B cells, $CD20^-CD79A^+$ plasma cells, and M2-like macrophages in both tumour epithelial and stromal regions. Optical genome mapping revealed that 33% of UPK2-positive CRCs (vs. 4.3% in others) exhibit copy number gain of the *UPK2* locus. UPK2-positive CRCs were associated with *TP53* mutation, Consensus Molecular Subtype 4, and the upregulation of genes related to keratinization and squamous differentiation, such as *KRT17* and *DSG3* ($p<0.01$ for all).
Conclusion: Our results indicate that UPK2 expression identifies a subset of CRCs characterized by poor prognosis, epithelial-mesenchymal transition, micropapillary architecture, and squamous-like differentiation. These findings advance the understanding of CRC heterogeneity and could contribute to the advancement of precision medicine.

Funding: This study was funded by Cancer Society of Northern Finland (to VKÄ), Oulu Medical Research Foundation (to VKÄ), Orion Research Foundation sr (to VKÄ), Cancer Foundation Finland (59-5619 and 69-7354 to JPV), Finnish Medical Foundation (6021 to JPV), Sigrid Jusélius Foundation (230229, 240241, and 250264 to JPV), and Finnish State Research Funding (to MJM, and JPV)

OFP-07-009

Basal-like subtype of oesophageal adenocarcinoma and it's morphological, molecular and clinical characteristics

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Background & Objectives: Oesophageal adenocarcinoma (EAC) and squamous cell carcinoma (ESCC) are the two main oesophageal malignancies, exhibiting distinct morphological and molecular characteristics that influence therapy response. The WHO classification also identifies adenosquamous carcinoma, which shares features of both entities. A basal-like subtype has been described in breast and pancreatic adenocarcinomas, characterized by cytokeratin 5 (CK5) or cytokeratin 6 (CK6) expression and associated with poor prognosis and chemoresistance. This study aimed to determine whether a basal-like subtype exists in EAC and to evaluate its prognostic impact and molecular characteristics.
Methods: Paraffin embedded tumour tissue from 953 operable EACs was analysed for CK5 and CK6 expression using immunohistochemistry. Cases exhibiting squamous tumour cell differentiation, including adenosquamous subtypes, were excluded. The remaining cases were then classified into three groups: negative, low-positive (<50% tumour cells), and high-positive (>50% tumour cells). Expression patterns were further analysed in primary-operated versus neoadjuvantly treated patients (CROSS or FLOT).
Results: Nine tumours exhibited high CK5 expression (0,9%), 27 had high CK6 expression (2,8%), and 4 showed high co-expression of CK5 and CK6 (0,4%). High CK5 expression correlated with worse survival (median OS: 11.93 vs. 22.57 months for negative and 13.90 months for low-positive; $p = 0.012$). In neoadjuvantly treated patients, high CK5 expression was an independent predictor of poor prognosis (n= 8, HR = 1.56, 95% CI = 1.08–2.24, $p = 0.017$). Co-expression of CK5 and CK6 also indicated worse survival (HR = 1.30, 95% CI = 1.08–1.56, $p = 0.005$).
Conclusion: This study is the first to identify a basal-like EAC subtype with poor prognosis, even post-neoadjuvant therapy. CK5 (alone or with CK6) is an accessible biomarker for this subtype, suggesting its potential for guiding personalized treatment strategies. Further research should explore its biological characteristics and therapeutic implications.

OFP-07-010

Biopsy is still the "gold standard" in the diagnosis of coeliac disease: the first validation study of the "coeliac algorithm"

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Background & Objectives: Diagnosis of coeliac disease (CD), due to heterogeneity in symptoms, serology and histology, can be difficult for all parties involved. Recently, a histologic diagnostic algorithm, namely, the "coeliac algorithm", based on TCRγδ intraepithelial lymphocytes (IEL) has been proposed. We, therefore, aimed to validate the algorithm prospectively in cases with flat mucosae and intraepithelial lymphocytosis.
Methods: Duodenal biopsies of 81 cases obtained for a suspicion of coeliac disease were studied for CD3 and TCRγδ IEL counts/100 enterocytes. The "coeliac algorithm" based on the TCRγδ IELs count>10.5 (step1) and TCRγδ+ IEL/CD3 ratio>14 (step2) was applied and diagnostic accuracy was determined in comparison to clinical and serologic data.
Results: Mean age was 22.6 (2-75) and 72.8%(n=59) were female, 27.2%(n=22) were male. Majority comprised of paediatric cases (61.7%) while 38.3% were adults. Using the algorithm, 59% of the cases were compatible with CD, 36% were in grey zone, and 5% were non-CD at step1 while step2 revealed that 96.5% were suggestive of CD and 3.5% of non-CD. Step1 classified 68% of the cases as type 3 and 54% as type 1 and through step2 evaluation, 3 additional type 1 cases and 25 more type 3 cases were detected. The diagnostic accuracy of step1 was 68.5% whereas step2, with the application of γδTCR/CD3 ratio, significantly improved the algorithm's accuracy up to 93.8% ($p<0.001$). When all cases were evaluated solely using step2 the diagnostic accuracy was 95,1% which was significantly higher compared to step1 ($p<0.001$). The algorithm yielded significantly higher diagnostic

accuracy compared to endoscopy (79.3%; p=0.007) and, though not significant, was even better than serology (91.4%).
Conclusion: Our findings highlighted the performance of the "coeliac algorithm", particularly, when TCRγδ+IEL/CD3 ratio is applied, ad therefore, successfully validated its use in the diagnosis of coeliac disease in a prospective cohort with high diagnostic accuracy superior to endoscopy.

OFP-07-012

Insights into the clinical prognosis of High-grade Appendiceal Mucinous Neoplasms: lymph node metastasis and peritoneal risks

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Background & Objectives: High-grade appendiceal mucinous neoplasm (HAMN) is a relatively recent term used to describe a rare epithelial neoplasm of the appendix characterized by pushing-type invasion and high-grade cytologic atypia. Its implications regarding lymph node spread and the necessity of right colectomy are subjects of ongoing debate. All cases undergoing right colectomy for pseudomyxoma were included from the French reference network for rare peritoneal cancers (RENAPE) database to explore lymph node and peritoneal spread.
Methods: We analysed data from 440 patients diagnosed with low or high appendicular mucinous neoplasm (LAMN, n=240 / HAMN, n=33) or appendicular adenocarcinoma (AA, n=167) who underwent right colectomy with lymph node dissection within the RENAPE network.
Results: Nearly 60% of the patients were female (n=249), with a mean age of 56.6 years (range: 21-83). No difference of number of appendiceal wall rupture among the three subsets. Lymph node metastases were identified only in 16.2% of AA (27/167), whereas none were found among LAMN/HAMN cases. In terms of peritoneal metastasis, a significantly higher proportion of cases were classified as high grade with/without signet cells in HAMN (69.2%) compared to LAMN (15.6%) and AA (44.0%). Following multimodal treatment, with no significant difference in terms of completeness of cytoreduction (p=0.429), In terms of peritoneal metastasis, a significantly higher proportion of cases were classified as high grade in HAMN, AA from HAMN, and AA compared to LAMN and LAMN from AA. HAMN and AA with appendicular perforation experienced significantly more peritoneal recurrences than LAMN. In cases confined to the appendiceal wall, HAMN and LAMN confined to the appendiceal wall had a lower tendency for peritoneal recurrences than AA ($p = 0.132$).
Conclusion: Our data suggest that HAMN is more prone to peritoneal dissemination as high-grade expansion rather than nodal spread.

OFP-07-013

Refining risk stratification in stage II colorectal cancer: the role of Stroma AReactive Invasion Front Areas (SARIFA)

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Background & Objectives: Colorectal carcinoma (CRC) remains a leading cause of cancer-related mortality. While adjuvant chemotherapy is recommended for high-risk stage II patients, its benefit remains uncertain, highlighting the need for novel prognostic markers. The Stroma AReactive Invasion Front Area (SARIFA), a zone where tumour cells interact with adipocytes without stromal reaction, has shown prognostic relevance. This study evaluates SARIFA's impact on risk stratification and therapy guidance in stage II CRC.
Methods: This retrospective cohort study included 293 stage II CRC patients who underwent curative-intent resection (2013–2023). SARIFA was assessed in H&E-stained slides. Clinicopathological characteristics, including established prognostic markers, were analysed. Univariate and multivariate analyses of recurrence-free survival (RFS) were performed using Kaplan-Meier curves and Cox regression models.
Results: SARIFA positivity was observed in 42.0% of patients and was associated with significantly worse RFS (median RFS: 28.1 vs. 31.0 months, HR: 1.85, 95% CI 1.03-3.33, $p = 0.040$). The combination of SARIFA-positive and at least one NCCN risk factor further worsened prognosis (HR = 2.43, 95% CI: 1.13–5.24, $p = 0.023$). SARIFA-positive cases had fewer examined lymph nodes ($p = 0.004$) and more frequent perineural invasion ($p = 0.004$). In the multivariate analysis, SARIFA showed a trend towards poorer RFS, maintaining its prognostic relevance (HR = 1.64, 95% CI: 0.91–2.96, $p = 0.102$). Additionally, older age (HR = 1.03, 95% CI: 1.001–1.07, $p = 0.043$) and higher lymph node count (HR = 0.96, 95% CI: 0.94–0.99, $p = 0.002$) were independent prognostic factors.
Conclusion: SARIFA is a promising prognostic biomarker in stage II CRC, providing cost-effective and reproducible risk stratification. It may aid therapy decisions by identifying patients who could benefit from adjuvant chemotherapy while minimizing overtreatment in low-risk cases. Prospective studies are now needed to validate SARIFA's role in optimizing personalized treatment strategies.

OFP-07-014

Testing practices in patients with BRAF^{V600E}-mutant metastatic colorectal cancer: data from a pooled analysis of European observational studies

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Background & Objectives: Between 8% and 12% of patients with metastatic colorectal cancer (mCRC) harbour $BRAF^{V600E}$ mutation, which is associated with poor prognosis and resistance to conventional therapies. BRAF testing is essential to identify this mutation and define optimal treatment sequence. This analysis used pooled data from 5 European studies to determine real-world management of patients with $BRAF^{V600E}$-mutant mCRC treated with encorafenib plus cetuximab (EC).
Methods: This retrospective, longitudinal, pooled analysis used data from real-world observational studies conducted across Europe between 2020 and 2024. Adult patients (age ≥18 years) who received an encorafenib-based regimen for $BRAF^{V600E}$ mutant mCRC were included. Pooled data included information collected at the start of treatment until the end of the observation period in each study. The primary objective was to assess baseline demographics and characteristics of patients initiating EC. Here, we describe BRAF testing practices in these patients, a secondary objective of the study.
Results: Among 709 patients, 54.4% were female, median age was 65 years, 33.7% were aged ≥70 years, 78.8% had ECOG PS 0–1, and 66.1% had right-sided primary tumour. At initial diagnosis, 70.9% of all patients presented with synchronous disease and the number of metastatic sites at EC initiation was 1 (36.6%), 2 (32.5%), or ≥3 (30.9%). All patients underwent BRAF testing, which was performed on archived tissue from primary tumour (76.8% of patients with available data) or metastasis (16.5%). The most common methods used for BRAF testing were next-generation sequencing (61.2% of patients with available data) and polymerase chain reaction (16.1% of patients with available data). EC was initiated as second-line therapy for 66.1% of patients, followed by third-line (21.3%) and fourth/later-line (7.9%); 4.7% initiated EC after prior systemic treatment (early relapse after adjuvant treatment).
Conclusion: BRAF testing should be conducted as early as possible at the time of mCRC diagnosis to optimize treatment decisions.

OFP-07-015

Enteroblastic differentiation in gastric adenocarcinoma: clinicopathological, immunohistochemical, and molecular findings

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Background & Objectives: Gastric adenocarcinoma with enteroblastic differentiation (GAED) is a rare and aggressive subtype of gastric cancer, characterized by clear cytoplasm and the expression of oncofoetal markers. This study aims to evaluate the clinicopathological and immunophenotypic features of GAED and to explore potential therapeutic targets, integrating immunohistochemistry and molecular techniques.
Methods: Eleven patients diagnosed with GAED were retrospectively analysed. Histological evaluation included tumour morphology, grade, and invasion patterns. Immunohistochemical staining was performed for AFP, glypican-3, SALL4, HER2, PD-L1, FOLR1, and CLDN18.2. HER2 status was further assessed using fluorescence in situ hybridization (FISH) in all cases with IHC score 2. Molecular profiling was performed using next-generation sequencing (NGS) on formalin-fixed, paraffin-embedded (FFPE) tumour tissue.
Results: The median age was 77 years (range: 62–90), with a male predominance (8/11). Tumour sizes ranged from 3 to 10 cm, and the enteroblastic component comprised 30–75% of the tumour area. All tumours expressed at least one enteroblastic marker, with glypican-3 positivity in 10/11 cases. HER2 overexpression (IHC score 2 or 3) was observed in four cases; FISH confirmed amplification in two of them. PD-L1 positivity (CPS ≥1%) was detected in five cases. FOLR1 was positive in three patients, while all cases were negative for CLDN18.2. Lymphovascular invasion was present in nine patients. Follow-up data showed that seven patients died of disease within 1 to 21 months after diagnosis; four patients were alive at last follow-up.
Conclusion: GAED is an aggressive form of gastric carcinoma with distinct immunophenotypic features. The frequent expression of HER2, PD-L1, and FOLR1 suggests that targeted therapies and immune checkpoint inhibitors may be viable treatment options. Integration of molecular testing, including FISH and NGS, may aid in the identification of novel biomarkers and treatment strategies.

OFP-08 Oral Free Paper Session Digestive Diseases Pathology - Liver/Pancreas

OFP-08-001

Clinicopathological behaviour of pancreatic neuroendocrine tumours (PanNETs) - subgrading G2 using Ki-67 proliferation index (Ki67PI) as G2a (3% to <10%) and G2b (10% to ≤20%)

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Background & Objectives: PanNETs are neoplasms graded as G1, G2 and G3 with different prognostic stratification. Recently, Eren and colleagues proposed subgrading G2 PanNETs, using Ki-67PI, as G2a (3% to <10%) and G2b (10% to ≤20%). Their study concluded that G2b PanNETs behave similarly to G3, indicating the need for a closer follow-up. Aim: to evaluate the clinicopathological behaviour of G1, G2a, G2b and G3 PanNETs.
Methods: A retrospective study was conducted and patients diagnosed with PanNETs between 2019 to 2024 were selected. Clinicopathological data were collected.
Ki-67 immunohistochemistry was performed for each tumour and its index was evaluated by digital pathology (Sectra algorithm for Ki-67). Tumours were graded according to their Ki-67PI as G1 (<3%), G2a (3-<10%), G2b (10-≤20%) and G3 (>20%). IBM SPSS was used for statistical analysis.
Results: A total of 42 patients (57.1% male; mean age 58 years) were diagnosed with PanNETs. Tumour sizes were 0.6 to 12.5cm (mean, 2.6cm). Considering Ki-67PI, 61.9% were G1, 16.7% were G2a, 14.3% were G2b and 7.1% were G3. There was statistic association between grade and distant metastases (p=0.03), perineural invasion (p=0.03), pT stage (p=0.001) and pN stage (p=0.015). There was no statistic association between disease-related death and vascular invasion. Perineural invasion was observed in 15 PanNETs (G1:n=4; G2a:n=4; G2b:n=4 and G3:n=3) and vascular invasion in 18 PanNETs (G1:n=7; G2a:n=5; G2b:n=4 and G3:n=2). Twenty-one tumours were pT1 (G1:n=17; G2a:n=3; G2b:n=1), 14 were pT2 (G1:n=8; G2a:n=2; G2b:n=3 and G3:n=1), 3 were pT3 (G1:n=1 and G2a:n=2) and 4 were pT4 (G2b:n=2 and G3:n=2). Eight tumours were pN1 (G1:n=2; G2a:n=1; G2b:n=3 and G3:n=2). Two patients died from PanNETs (G2b:n=1 and G3:n=1) and six had distant metastases (G2a:n=2, G2b:n=2 and G3:n=2).
Conclusion: Our study revealed that G2b subgroup has identical clinincopathological behaviour to G3 group, indicating the need for subgrading G2 PanNETs and a closer management of this subgroup.

OFP-08-002

High performance deep-learning model for the diagnosis of autoimmune hepatitis based on histological whole slide images

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Background & Objectives: Autoimmune Hepatitis (AIH) is a liver disease with a wide clinical spectrum, driven by an abnormal immune response against the liver parenchyma. Challenges persist especially in terms of accurate early diagnosis of acute onsets and differential diagnosis. Our work falls within the goals set by the fifth research workshop of the International Autoimmune Hepatitis Group for improving AIH diagnosis through a Deep-Learning Model (DLM) approach on liver biopsy's histology, in a setting close to real life.

Methods: Our training cohort comprised 143 index cases of untreated AIH and 158 control cases with a variety of differential diagnosis,from Pontchaillou Hospital, Rennes. Ground Truth was assigned based on the integrative diagnosis of the clinician. Biopsies were reviewed according to the IAIHG updated criteria, and the 2008 Simplified scoring system was computed. We trained a multiple-instance DLM from histology Whole Slide Images alone in order to design an interpretable classifier for the primo-diagnosis of AIH. The model was then tested on an external dataset of 61 AIH from Mondor Hospital, Paris.

Results: Our DLM "Artificial Intelligence On Liver Immunity (AIOLI)", evaluated with a stratified 5-fold cross-validation, achieved Sensitivity of 0.965 ± 0.038, Specificity of 0.861 ± 0.068, F1-score of 0.939 ± 0.035 and AUC of 0.911 ± 0.035 on the training dataset. Additionally, AIOLI achieved Sensitivity of 0.902 ± 0.29 on the external dataset. Retrieval of the five most and least predictive tiles allowed to identify morphological patterns used by the model for prediction.

Conclusion: We choose to tackle AIH diagnosis in a "real-life" setting, with an interpretable DLM able to segregate AIH from a wide variety of control cases with good performance. We plan to enhance our model's performance in future iterations by enriching our dataset, especially in metabolic- and toxic-diseases control cases, and to validate this approach with external datasets.

OFP-08-003

Histopathology, morphomolecular classification and clinical outcomes in hepatocellular carcinoma treated with immune-combined therapy: a prospective study on needle liver biopsies

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Background & Objectives: Hepatocellular carcinoma (HCC) histological subtypes (WHO 2019) are associated with prognosis, treatment response and a recently proposed morphomolecular classification. Our aim was to study histopathological features and morphomolecular subgroups in HCC treated with immune-combined therapy.

Methods: We prospectively evaluated 48 liver biopsies from 48 HCC patients [38 male, median age 69 years, BCLC stage A 3(6.2%), B 20(41.7%), C 25(52.1%)] treated with immune-combined therapy and followed-up 3-41(mean 11) months. Morphological examination and immunohistochemistry (IHC) for beta-catenin(B-CTNN), glutamine synthetase, TP53 and keratin 19 were applied to reflect HCC molecular classification based on Nault JC,J Hepatol 2018.

Results: Histological grade (WHO 2019) was 1 in 4(8.3%), 2 in 37(77.1%) and 3 in 7(14.6%) HCC. There were 30(62.5%) NOS, 9(18.8%) macrotrabecular-massive (MTM), 7(14.6%) steatohepatitic, 1(2.1%) clear-cell and 1(2.1%) scirrhous HCC. Morphomolecular subgrouping (n=41) highlighted 18(44%) proliferative and 23(56.0%) non-proliferative HCC. Morphomolecular class (n=27) was G1 in 2(7.4%), G2-G3 in 5(18.5%), G4 in 5(18.5%) and G5-G6 in 15(55.5%). MTM subtype positively correlated with mutated TP53 (p=0.012) and negatively with mutated B-CTNN (p=0.002) IHC pattern. Mean progression-free survival (PFS) was 7.7 months (2-34 months). At the end of follow-up, 31(64.5%) patients had progressed and 20(41.6%) patients were alive. Objective response-OR was observed in 6/48(12.5%) patients and was significantly related with overall survival-OS (p=0.009). Disease progression correlated with histological grade (p=0.036), mutated B-CTNN (p=0.027) and morphomolecular class (p=0.048). PFS correlated with morphomolecular class (p=0.035) and mutated TP53 (p=0.09). There was no significant correlation between histological subtypes and morphomolecular subgroups with OR, PFS or OS.

Conclusion: In HCC treated with immune-combined therapy, morphomolecular class can predict disease progression and PFS, while histological grade and mutated B-CTNN correlate with disease progression. Histological subtypes and morphomolecular proliferative/non-proliferative subgrouping do not have prognostic or predictive significance. Studies in a larger cohort are ongoing to validate these results.

OFP-08-004

Unraveling immune composition in pancreatic cancer for personalized immunotherapy

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Background & Objectives: Limited progress has been made towards effective immunotherapies for pancreatic ductal adenocarcinoma (PDA) patients. Treatment resistance remains a major roadblock toward improving survival. We have identified a subset of PDAs that carry alterations in a group of epigenetic genes named Complex Proteins Associated with Set1 (COMPASS)-like complex genes (CLCG). Approximately one-quarter of PDAs harbour CLCG alterations which commonly occur concomitantly with established driver mutations like KRAS and TP53 and are associated with high-grade histology, squamous or basal-like features, and poor patient survival compared with CLCG-wild type PDAs.

This study aims to dissect the complex immune composition of CLCG-mutated PDAs by single-cell spatial analysis and compare them with matched CLCG-wild type PDAs. Our goal is to identify vulnerabilities in this subset of PDAs for personalized immunotherapy.

Methods: We identified 15 PDA cases (CLCG mutation=8, wild type=7). The groups were matched for age, sex, and concomitant driver mutations. H&E slides and blocks were selected for single-cell spatial multiplex fluorescent immunohistochemistry (mfIHC) analyses. Ninety-seven stamped areas were analysed using Inform 2.6 software to assign identities to each cell based on IHC markers. R program was used to calculate cell count, percentage, and engagement.

Results: CLCG-mutated PDAs had a significantly lower number of antigen-presenting cells (APCs) and CD4 T cells with increased expression of immune checkpoint (IC) and exhaustion marker, TIGIT, on APCs (p=0.0031) and CD4 T cells (p=0.0053), supporting immunosuppression. There was no difference in the expressions of PD-L1 or another IC, TIM3. Interestingly, more CD4 T cells expressed TIGIT near tumour cells and APCs in CLCG-mutated PDAs. Furthermore, there was a loss of engagement between CD4 and CD8 T cells, and CD8 T cells and tumour cells in CLCG-mutated PDAs.
Conclusion: CLCG-mutated PDAs have a unique mechanism of immunosuppression that can guide personalized IC therapy.

Funding: Dr. Jiaqi Shi is supported in part by the National Cancer Institute of the National Institutes of Health under award number R37CA262209. This project is also funded by the Department of Pathology & Clinical Labs at the University of Michigan

OFP-08-005

Hepatocellular carcinoma demonstrates greater variance in nuclear morphometrics when compared to hepatocellular adenoma

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Background & Objectives: The differential diagnosis between hepatocellular adenoma and well-differentiated hepatocellular carcinoma (in non-cirrhotic liver) can be challenging, especially in a small biopsy with limited diagnostic material. Histological features and use of stains (reticulin in particular) are crucial, yet not always sufficient to differentiate between adenoma and carcinoma. In the current study we examined the nuclear morphometrical features of hepatocellular adenoma and carcinoma to identify any significant differences and assess whether they may be used to better differentiated between adenoma and carcinoma.
Methods: Full slide images from twenty four cases of well-differentiated hepatocellular adenoma and nineteen cases of hepatocellular adenoma were reviewed by a pathologist who captured fifty patches of either adenoma or carcinoma areas per case. An algorithm for nuclear segmentation and extraction morphometric features was used on each patch and provided parameters of size, shape, texture and stain intensity for each nucleus. A second cohort of nine adenomas and seven carcinomas was used for validation.
Results: The hepatocellular carcinoma nuclei were larger in size when compared to the adenoma nuclei and also showed a greater variance in size. Specifically, area and perimeter both showed a higher variance within the hepatocellular carcinoma group, in both cohorts ($p<.0001$). The hepatocellular carcinoma group also showed a larger area (microns), 26.321 ± 14.455 vs 23.899 ± 11.722 ($p<.0001$) and a larger perimeter length (microns), 18.915 ± 6.167 vs 17.839 ± 4.980 ($p<.0001$). Examination of the validation cohort highlighted similar trends for area (28.729 ± 14.449 vs 23.039 ± 10.671, $p<.0001$), perimeter (19.806 ± 6.119 vs 17.460 ± 4.676, $p<.0001$).
Conclusion: The results of this study suggest that hepatocellular carcinoma cells are larger in size and show a greater variance in size and texture when compared to hepatocellular adenoma. Further research may utilize these differences to better differentiate between well-differentiated hepatocellular carcinoma and hepatocellular adenoma.

OFP-08-006

Profiling the immune microenvironment during murine pancreatic carcinogenesis via deep learning

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Background & Objectives: Pancreatic ductal adenocarcinoma (PDAC) is characterized by its immunosuppressive tumour microenvironment. Emerging evidence suggests that the immune landscape of PDAC precursor lesions plays a pivotal role in early tumorigenesis. Genetically engineered mouse models (GEMMs) are essential in studying these precursor stages, as they enable temporal resolution of disease progression. This study aims to characterize the immune microenvironment of both human and murine PDAC precursor lesions using deep-learning approaches.
Methods: We analysed 140 murine tissue samples from 6 KC and 34 KPC mice using tissue microarrays. Samples included normal pancreas, acinar-to-ductal metaplasia (ADM), pancreatic intraepithelial neoplasia (PanIN), and invasive PDAC (central and peripheral regions), along with their respective microenvironments. OPAL 7-colour multiplex immunofluorescence staining was employed using two antibody panels: Panel 1 (anti-CD19, -CD3, -Tryptase, -F4/80, -CD163) and Panel 2 (anti-CD3, -CD4, -CD8α, -Granzyme B, -FoxP3, -PD-1). A total of 944 images (Panel 1) and 918 images (Panel 2) were acquired and analysed using convolutional neural networks (CNNs) including ResNet18, ResNet34, ResNet50, ResNet101, and ResNet152. Training utilized stochastic gradient descent with momentum and the Adam optimizer, employing transfer learning and 10-fold cross-validation.
Results: CNNs reached 91.8% accuracy with Panel 1 in distinguishing normal pancreas vs. precursors vs. PDAC, with F1-scores of 0.920 (normal tissue), 0.945 (ADM/PanIN), 0.913 (central PDAC), and 0.884 (peripheral PDAC). With Panel 2, a 92.2% accuracy was achieved, with F1-scores of 0.874 (normal pancreas), 0.934 (ADM/PanIN), 0.919 (central PDAC), and 0.922 (peripheral PDAC), respectively.
Conclusion: Despite a limited dataset, CNNs demonstrated solid accuracy in classifying the immune microenvironment of PDAC and its precursor lesions in GEMMs. Overlapping regions in multiplex immunofluorescence images present a limitation; however, the use of 10-fold cross-validation enhances reliability. We have already demonstrated similarly robust results in human pancreatic tissue samples. Currently, we are extending our analyses to encompass additional tasks, including spatial profiling of the immuno-infiltrate.

OFP-08-007

Primary mesenchymal tumours of the pancreas: a systematic literature review and outlook on machine-assisted diagnostics

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Background & Objectives: Primary mesenchymal tumours of the pancreas comprise less than 1% of pancreatic neoplasms and present a unique diagnostic challenge. Despite an increased number of published cases over the past decade, the data remains fragmented. We aimed to systematically review reported cases from the last 10 years to clarify the diagnostic spectrum, highlight age distribution, localization, outcome and common pitfalls. Furthermore, we aim to provide a data platform that could inform future machine-assisted diagnostic tools.
Methods: A systematic literature search was performed in Pubmed, Cochrane Library and Web of Science databases for English- language case reports and case series published between 2015 and 2025. Standardized evidence tables were used for the extraction of data. Studies with a confirmed diagnosis of a primary mesenchymal tumour originating from the pancreas with extractable data on histology, immunohistochemistry, molecular testings, clinical presentation and outcome were included. Mixed epithelial (e.g., carcinosarcomas) and metastatic mesenchymal tumours were excluded.
Results: We retrieved 332 unique records and included 98 studies that met our inclusion criteria. Histologic subtypes ranged from extraskeletal Ewing sarcoma and solitary fibrous tumour (SFT) to even less common entities such as leiomyosarcoma, liposarcoma, perivascular epithelioid cell

tumour (PEComa), angiosarcoma and undifferentiated pleomorphic sarcoma of the pancreas. Morphological features and key diagnostic markers (e.g., SMA, CD117, HMB-45, STAT6, CD34, EWSR1 rearrangements) helped establish definitive diagnoses. Clinical outcomes varied markedly, with some benign tumours being completely resectable and high-grade sarcomas exhibiting aggressive behaviour and early metastasis.
Conclusion: This comprehensive literature-based overview highlights the complexity of primary pancreatic mesenchymal tumours, underscoring the importance of thorough histopathological workup and ancillary testing. By uniting scattered case-level data, our collection offers pathologists and clinicians a valuable reference for recognizing these rare entities. In addition, these data also lay the groundwork for future development of machine-assisted diagnostic approaches, ultimately aiming to improve the diagnostic accuracy.

OFP-08-008
The incidence and prognostic significance of alternative telomere lengthening in hepatocellular carcinomas
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Background & Objectives: The mechanism involved in the maintenance of telomere length, apart from telomerase activation, is alternative telomere lengthening (ALT). ALT is defined in approximately 6-10% of hepatocellular carcinomas (HCC). The prognostic effect of ALT phenotype still remains unclear. This study aims to determine the incidence of ALT in hepatocellular carcinomas using the telomere-specific FISH method and the prognostic impact of ALT, and to contribute to the clinical management and potential treatment approaches of HCC.
Methods: In our study, ALT status was investigated by FISH method in 121 cases of HCC and the association between ALT positivity and clinicopathological features was evaluated statistically. In addition, for the first time in the literature, the presence of ALT in metastatic tumour tissues of the cases, when present, was investigated and whether there was a difference in frequency in primary or metastatic HCC tissues was evaluated.
Results: ALT positivity was observed in 11 cases (9%) including 8 conventional, 2 chromophobe and 1 clear cell HCCs. The rate of ALT positivity among metastatic HCCs was determined as 33.3%. ALT positivity showed strong statistical association with the presence of bizarre nuclei (9/11, 91.8%) ($p<0.001$), rather than morphological subtype (chromophobe subtype) association shown previously in the literature. The presence of ALT was found to be statistically associated with the risk of recurrence, presence and percentage of bizarre nuclei. Although the overall survival time was significantly lower in cases with ALT phenotype compared to those without (74,16/128,9 months), no statistically significance was detected.
Conclusion: In conclusion, our study which is the first to investigate the prognostic importance of ALT phenotype in HCCs and its frequency in metastatic HCCs, has shown that ALT has a potential negative prognostic impact and is observed more frequently in metastases than in primary HCCs.

OFP-08-009
Malignant solid pseudopapillary neoplasms: histological features, molecular alterations and survival outcomes
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Background & Objectives: Solid pseudopapillary neoplasms (SPNs) typically follow an indolent course with favourable outcomes after resection. Nevertheless, a small subset demonstrates malignant potential, characterized by lymphovascular invasion (LVI), increased mitotic activity, and metastasis –features associated with increased mortality. This study aims to evaluate the clinicopathological characteristics of malignant SPNs, assess relevant histological and immunohistochemical markers, and explore possible related molecular alterations.
Methods: We retrospectively analysed 61 SPN cases diagnosed between 2000 and 2025 at two academic pathology centres. Histopathological features including LVI, perineural invasion, mitotic activity, and capsular/parenchymal invasion were evaluated. Immunohistochemistry was performed for BAP1, β-catenin, CD10, progesterone receptor (PR), androgen receptor(AR), chromogranin, synaptophysin, and Ki-67. Next-generation sequencing (NGS) was performed on selected metastatic and histologically low-risk cases. Statistical analysis was conducted using SPSS version 30.
Results: Median age was 26 years (range: 8–71), and median tumour size was 6.5 cm (range: 1.5–22 cm). Of the patients, 86.9% were female (n=53) and 13.1% male (n=8). LVI was detected in 1.8%. Nuclear β-catenin expression was present in all cases. PR, AR, and BAP1 were positive in 84.1%, 77.5%, and 77.5%, respectively. BAP1 loss was more common in adults than in children ($p<0.05$). Median follow-up was 98.9 months. Metastasis occurred in four cases (liver, lung, and lymph nodes), with two deaths. Ki-67 ≥4% and increased mitotic activity were associated with higher mortality ($p<0.05$). Kaplan-Meier analysis revealed significantly worse overall survival in patients with high Ki-67 expression (≥4%,p=0.03), larger tumour size (≥5 cm,p=0.04), and presence of LVI (p=0.01). NGS revealed concurrent *CTNNB1* and *BRCA2* mutations in one metastatic case.
Conclusion: Although malignant SPNs are rare, recognition of histological risk factors and molecular alterations is essential for risk stratification and personalized management. Integration of immunohistochemical profiling and targeted sequencing may aid in identifying patients who could benefit from closer follow-up or novel therapeutic strategies.

OFP-08-010
Porto-sinusoidal vascular disease in metabolic-dysfunction associated steatotic liver disease
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Background & Objectives: The prognosis of metabolic dysfunction-associated steatotic liver disease (MASLD) largely depends on the presence of liver fibrosis. Non-invasive tests to assess fibrotic stage

are being developed, but are lacking diagnostic accuracy. This might be explained by fibrotic features not assessed in the currently used Brunt staging system and/or features of portosinusoidal vascular disease (PSVD) in liver histology.
Methods: We conducted a retrospective cohort study in patients with MASLD who underwent biopsy between 2015 and 2022. All biopsies with early stage disease, defined as Brunt F0-F2, were screened for eligibility and revised by two expert liver pathologists. In addition to the VALDIG criteria for PSVD, we subclassified the number of portal tracts showing obliterative portal venopathy (0, <50% or >= 50%). Perisinusoidal fibrosis was scored as 0, grade 1 (< 1/3), grade 2 (1/3-2/3) and grade 2 (> 2/3). Secondary endpoint was the correlation of histology with liver stiffness measurement (LSM).
Results: We included 136 patients [60% male, median age 50] with a median BMI of 30 kg/m^2, 15% having F1 fibrosis and 85% F2 fibrosis. The median LSM was 8.2 kPa. Obliterative portal venopathy was the most relevant finding in our cohort, occurring in 74% of biopsies, of which 35% had >= 50% of portal fields affected. Perisinusoidal fibrosis was present in 97% of biopsies, with 62% grade 1, 32% grade 2 and 3% grade 3 perisinusoidal fibrosis. We found a positive correlation between LSM and perisinusoidal fibrosis (r= .30, p=0.01). Obliterative portal venopathy did not correlate with LSM.
Conclusion: Obliterative portal venopathy is a frequent finding in patients with MASLD, together with various amounts of perisinusoidal fibrosis, potentially explaining the heterogeneity of LSM as measured with the Fibroscan. The extent of perisinusoidal fibrosis is not adequately taken into account in the current staging systems and correlates significantly with LSM.

OFP-08-011
Intratumoral bacterial abundance confers poor response to adjuvant gemcitabine in resected pancreatic cancer patients which is mitigated by postoperative antibiotics
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Background & Objectives: Adjuvant gemcitabine (aGC) is still a therapeutic mainstay after resection of pancreatic ductal adenocarcinoma (PDAC), but its efficacy is impaired by gram-negative intratumoral bacteria, suggesting a potential therapeutic implication of additive antibiotics. PDAC however contains several other bacterial strains capable of gemcitabine degradation.
Methods: Using immunohistochemistry and fluorescence-in-situ-hybridization on the samples of a large cohort of resected PDAC patients (n=342), we examined how the intratumoral bacterial abundance affected patient outcomes with respect to aGC therapy and whether the use of pre- or postoperative antibiotics (ABT) improved the prognosis. We confirmed the findings in several independent external cohorts (total n=297).
Results: High intratumoral bacterial abundance impaired aGC efficacy (disease free survival (DFS) 9.4 vs 19.1 months, p<0.001; overall survival (OS) 19.4 vs 34.0 months, p<0.001), which was mitigated by postoperative ABT application (DFS 7.9 vs 12.4 months, p<0.001, OS 15.2 vs 29.6 months, p<0.001). Postoperative ABT improved outcome of patients with low bacterial abundance in their tumours (DFS 15.1 vs 34.8 months, p<0.001, OS 28.5 vs 56.00 months, p<0.001).
Conclusion: High intratumoral bacterial abundance may predict poor response to adjuvant gemcitabine treatment, whereas postoperative ABT improves it. We propose postoperative ABT as potential additive treatment before or during aGC therapy after PDAC resection.

OFP-08-012
Deep proteogenomic characterization of solid pseudopapillary neoplasm (SPN) of the pancreas reveals specific protein markers, metabolic adaptation, immune microenvironment, and therapeutic targets
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Background & Objectives: Solid pseudopapillary neoplasm (SPN) is a rare neoplasm of the pancreas of unclear histogenesis. SPN accounts for 1-2% of pancreatic tumours and has a female predominance. The biology of SPN remains poorly understood, especially at proteome level. We report the first comprehensive integrated proteogenomic characterization of SPN and investigate differences to other pancreatic neoplasms.
Methods: We collected tissues from SPNs, pancreatic ductal adenocarcinomas, acinar cell carcinomas, pancreatoblastomas, well-differentiated pancreatic neuroendocrine tumours, and benign exocrine pancreatic tissues. Samples were exome-sequenced. LC-MS was performed on a Q Exactive Plus mass spectrometer. Metascape was used to conduct pathway enrichment analyses. Gene Set Enrichment Analysis was performed by projectingprotein expression onto GO, Hallmark, KEGG, and Reactome pathway sets. We calculated immune scores from the protein expression matrix of all samples. We inferred immune cell abundance using the xCell tool.
Results: We discovered that the SPN proteome is clearly distinct from that of other pancreatic entities, and that lysosome-related proteins were enriched in SPN, suggesting a possible link to metabolic adaptation mechanisms in low-nutrient environments since lysosomal degradation products are biological energy sources.
We also discovered that MITF, one of lysosomal process regulators, was highly specific for SPN and superior to TFE3. Furthermore, our proteome analysis found that SPN was an immune-cold tumour with low MHC class I molecule expression compared to pancreatic ductal adenocarcinoma. To expand possible treatment options for SPN, we conducted drug repositioning searches and identified 21 protein targets that could be targeted with already approved drugs.
Conclusion: We present the first mass-spectrometry-based, comprehensive, unbiased deep proteogenomic characterization of SPN. Our results contribute to a deeper understanding of the biology of SPN and the distinction of SPN from other pancreatic neoplasms such as PDAC, ACC, PBL, or PNET. Our discoveries of new SPN-specific protein biomarkers have direct implications for the development of novel therapeutic targets.

Funding: Funded by the Neuroendocrine Tumour Research Foundation (NETRF)

OFP-09 Oral Free Paper Session Pulmonary Pathology & Digital and Computational Pathology

OFP-09-001
Age, gender and skin site are associated with spatial distribution of mitoses in melanoma
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Background & Objectives: Melanomas can be sub-grouped into those arising in sun-exposed and non-sun-exposed skin regions. Numerous differences have been documented between these groups regarding their origin, microenvironment, mutational landscape, and prognosis. However, limited data exists on the spatial arrangement of melanoma. We developed a deep learning algorithm for mitosis

segmentation on whole H&E slides and used it to evaluate the spatial arrangement of mitosis in melanoma.
Methods: H&E slides from 27 melanoma cases were digitized. Demographic and clinical data were extracted from the pathology reports. The spatial organization of the mitosis on the tumours was analysed using the mitosis segmentation algorithm to identify the location of each mitosis. In 33 slides from 17 cases, the epidermis and the invasive front were annotated, and the relative locations of the mitoses were calculated.
Results: The mitosis algorithm detected 34,363 mitotic figures that underwent spatial analysis for each slide. Our analysis revealed significant differences in the spatial distribution and clustering patterns between patients younger than 70 and those older, as well as between sun-exposed and covered areas, and between tumours in males and females. In a second cohort of 9,176 mitosis, we annotate the epidermis and the invasive front, and found that in exposed areas, mitosis tended to be significantly closer to the invasive front than in covered areas.
Conclusion: Our algorithm enables mass segmentation and spatial analysis of mitosis in melanoma, revealing differences not typically noted in standard pathological examinations. Combining this with spatial analysis of other elements in melanoma, such as blood vessels and immune cells, and correlating results with clinical follow-up may lead to better understanding of the disease.

OFP-09-002
Deep learning-enhanced detection of invasive breast carcinoma in extensive ductal carcinoma in situ: a clinically validated human-AI approach
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Background & Objectives: Extensive intraductal carcinoma (EIC), a clinically significant DCIS subtype, presents diagnostic challenges particularly in detecting concurrent invasive components crucial for patient management. We developed a deep learning-based segmentation model for invasive carcinoma detection in EIC and evaluated a human-AI collaborative approach under real-world diagnostic conditions.
Methods: Using an expanded TiGER Challenge dataset, we addressed class imbalance through weakly-supervised pseudo-labelling, achieving ten-fold dataset expansion with minimal manual effort. Clinical validation involved 576 WSIs from 44 EIC patients (with/without invasion), comparing manual (4 pathologists), AI-standalone, and human-AI modes via two-round cross-validation, assessing sensitivity, specificity, NPV, IHC use, and diagnostic time.
Results: The AI segmentation model demonstrated consistent performance across all datasets, achieving weighted DICE scores of 0.8772 (training), 0.8531 (validation), and 0.8468 (test). The model maintained high segmentation accuracy for all critical tissue classes: invasive carcinoma, DCIS, and normal glandular tissue. In diagnostic performance comparisons, manual diagnosis by pathologists showed 82.7% sensitivity, 96.0% specificity, and 89.6% negative predictive value (NPV). Standalone AI analysis significantly increased sensitivity to 95.6% and NPV to 96.4%, though with reduced specificity (76.6%). The human-AI collaborative approach optimally balanced these metrics, achieving 95.1% sensitivity, 91.7% specificity, and 96.7% NPV. Significant clinical workflow improvements were observed in the human-AI collaborative mode, including reduced mean diagnostic time per slide by 41.4% (from 102.6s to 60.1s; $P<0.001$), decreased unnecessary IHC testing by 40.4% (from 52 to 31 cases in 226 WSIs with invasive components; $P=0.011$). Receiver operating characteristic (ROC) analysis revealed superior diagnostic performance in the human-AI collaborative mode (AUC 0.904 vs 0.847 for manual diagnosis; $P=0.0124$).
Conclusion: This human-AI system demonstrates clinically meaningful improvements in EIC diagnosis, showing strong potential for routine implementation to enhance precision and workflow efficiency.

OFP-09-003
Predicting response to neoadjuvant therapy using artificial intelligence on digitized pathology slides: a systematic review
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Background & Objectives: Neoadjuvant therapy (NAT) is an important treatment strategy in oncology. However, not all patients benefit equally from NAT, and a personalized prediction of response to NAT is needed to improve treatment decision-making and patient survival. Artificial intelligence (AI)-driven approaches have shown potential in predicting treatment response. Despite increasing research in this domain, a systematic review of AI applications in NAT assessment with pathology features is lacking. Therefore, we present a comprehensive overview of studies that applied AI-based methods to Haematoxylin and Eosin (H&E) stained histopathology slides for NAT response prediction.
Methods: A systematic search was conducted in Medline, Embase, Web of Science, Cochrane Central Register of Controlled Trials, and Google Scholar. Two reviewers independently screened the identified studies, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.
Results: After removal of duplicates, 235 studies were screened for eligibility based on the exclusion criteria. 26 relevant studies that predicted NAT response using H&E-stained pathologic slides were included and reviewed. 11 studies presented an end-to-end deep learning approach, directly predicting NAT response from H&E slides, while 14 studies used AI to extract biomarkers, after which a second model predicted NAT response. To extract features, 12 studies used a supervised machine learning approach. 6 studies demonstrated that multimodal approaches, especially combining H&E slides with radiomics features, improved the performance of AI in predicting pathological complete response.
Conclusion: The current literature demonstrates that pathological features hold the potential to predict NAT response. Promising biomarkers have recently emerged such as HER2 for breast cancer; however, further investigation is needed for other cancer types. Moreover, to develop reliable, robust, and accurate models, larger datasets are essential. Additionally, these models should be interpretable to gain the trust of clinicians who will use them in the future, necessitating future research into their clinical applicability.

OFP-09-004
Granulomatous inflammation in a cohort of 188,880 lower endoscopy biopsy specimens
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Background & Objectives: Granulomatous inflammation is an uncommon pathologic finding; however, it is clinically significant. Its prevalence and call rate are not routinely assessed. This work sought to assess the call rate of granulomatous inflammation, by anatomical site, pathologist, submitting MD and polyp status.

Methods: A Hugging Face/Pytorch multilayer perceptron (MLP)-large language model (BERT) was used in conjunction with transfer learning to interpret lower endoscopy biopsy specimens (LEBS). Pre-processing was done with string matching which selected reports with "granuloma" and extracted text fragments with "granuloma". Specimens with the word "granuloma" were randomly audited to assess accuracy of the approach.
Results: The cohort had 188,880 LEBS out of which 1,290 specimens were labelled by two individuals and used to train a MLP-BERT model. Pre-processing identified 173,053 LEBS without the term "granuloma". A partial string matching found two instances where "granuloma" was misspelled. The remaining 15,827 of 188,880 LEBS were classified by MLP-BERT and 1,344 were positive. Accuracy was assessed in a random subset of the 15,827 and was correct in 1494 of 1500 LEBS. Non-polyp specimens (NPS) (108,734/188,880) had 1,307 granulomas present. In logistic regression of NPS, pathologist and submitting MD predicted granulomas (both $P<0.0001$) and anatomical location did not ($P>0.1$). Among pathologists reading >600 NPS LEBS the mean/std/median/max/min granuloma rate was 1.2%/1.6%/0.6%/6.7%/0.03%. 8/30 pathologists reading >1000 NPS LEBS were 99.9% confidence interval outliers on a funnel plot centred on the group median rate (0.6%). "Negative for granuloma" (and text variants) rate median/max/min was 4%/62%/0%.
Conclusion: Granulomatous inflammation does not appear to vary by anatomical location in LEBS. Granuloma call rates were similar for 22/30 pathologists suggesting moderate concordance. Reporting of the negative finding has very high variability. There appears to be room for diagnostic rate optimization; however, the accuracy of individual pathologist rates should be confirmed with targeted reviews, as reporting style may impact MLP-BERT classification.

OFP-09-005
H&E analysis of tumour microenvironment features with prognostic implications in lung adenocarcinoma
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Background & Objectives: Lung adenocarcinoma is the most common subtype of lung cancer and a leading cause of cancer related mortality. Digital pathology and AI algorithms allow for the automatic extraction of quantitative morphological and spatial information from H&E stained whole-slide images (WSIs). We establish a fully automated pipeline that segments tumour tissue compartments and classifies individual tumour, immune, and stromal cells, resulting in useful parameters for the assessment of the tumour microenvironment and aggressivity. We study the prognostic relevance of these parameters across several international patient cohorts and survival endpoints.
Methods: The pipeline includes preanalytical modules (tissue detection and rigorous quality control), tissue segmentation algorithm (all tumour-relevant classes), and a previously validated single cell segmentation and classification algorithm allowing detection of tumour cells, lymphocytes, plasma cells, eosinophils, neutrophils, and connective tissue cells. The parameters include overall stromal cellularity assessment, abundance of single cell types in different compartments and spatial parameters deciphering different patterns in cellular neighbourhoods. We extensively analyse intratumoral heterogeneity in the context of these parameters. We utilize one exploratory cohort (n = 431) and four independent validation cohorts (total n = 912) with available follow-up data.
Results: We show independent prognostic value of multiple parameters such as overall stroma cellularity, intraepithelial and stromal lymphocyte quantities, and stroma composition with regard to connective tissue cells and granulocytes. We define 10 types of local cellular neighbourhoods, 7 of them associated with prognosis in validation studies. We show that the patterns of organization of connective tissue cells in the stroma are of significant importance for tumour aggressivity.
Conclusion: We establish a computational pipeline for lung adenocarcinoma that allows for the extraction of fully explainable prognostic parameters directly from routine H&E stained histological slides. These parameters have independent value and can be a foundation for advanced grading systems, fine-grained patient risk stratification, and personalization of oncological therapy.

OFP-09-006
Multimodal whole slide foundation model for pathology
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Background & Objectives: The field of computational pathology has been transformed with recent advances in foundation models that encode histopathology region-of-interests (ROIs) into versatile and transferable feature representations via self-supervised learning (SSL). However, translating these advancements to address complex clinical challenges at the patient and slide level remains constrained by limited clinical data in disease-specific cohorts, especially for rare clinical conditions.
Methods: We propose the Transformer-based pathology Image and Text Alignment Network (TITAN), a multimodal whole-slide vision-language model for general-purpose slide representation learning in histopathology. Building on the success of knowledge distillation and masked-image modelling for patch encoder pretraining, TITAN introduces a novel paradigm that leverages millions of high-resolution regions-of-interest ($8{,}192 \times 8{,}192$ pixels) for large-scale, resolution-agnostic pretraining and scalable WSI encoding.
Results: Trained using 336K WSIs across 20 organ types, vision-only TITAN produces general-purpose slide representations that can readily be applied to slide-level tasks such as cancer subtyping, biomarker prediction, outcome prognosis, and slide retrieval tasks, outperforming supervised baselines and existing multimodal slide foundation models. To augment TITAN with language capabilities, we further finetune by contrasting with 423K synthetic fine-grained ROI-captions generated with PathChat, a multimodal generative AI copilot for pathology, and with 183K pathology reports at slide level. Through comprehensive evaluation across a large range of clinical tasks, including the first application to rare cancer retrieval across 43 rare cancer types, we demonstrate the efficacy of our vision-language

pretraining approach, showcasing the general-purpose capability of our slide foundation model.
Conclusion: We introduce a multimodal whole-slide foundation model for pathology, TITAN, that combines and elevates successful recipes of self-supervised learning from the patch level to the slide level. Without any finetuning or requiring clinical labels, TITAN can extract general-purpose slide representations and generate pathology reports that generalize to resource-limited clinical scenarios such as rare disease retrieval, few-shot, and zero-shot classification.

OFP-09-007

Evaluation of tumour budding in lung adenocarcinomas a retrospective study about patients received sublobar resection

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Background & Objectives: The presence and prognostic significance of tumour budding are less investigated particularly in patients diagnosed with pulmonary adenocarcinoma who underwent sublobar resection. We aimed to examine the extent of tumour budding semi-quantitatively and evaluate its prognostic impact on overall survival (OS) and recurrence-free survival (RFS).
Methods: In our retrospective cohort investigation, the number of stromal tumour buds in a hot spot and in 10 medium power fields were recorded on histological slides. Other clinicopathological data were obtained from clinical charts. As statistics, Kaplan-Meier analyses and Cox regressions were applied.
Results: Altogether 61 patients were included. The presence of tumour budding was more frequent in high-grade adenocarcinomas ($p<0.001$) with vascular- ($p=0.025$) lymphovascular spread ($p<0.001$), lymph node metastasis ($p=0.002$) and pleural invasion ($p=0.02$). The results of tumour budding assessment in hot spot and in 10 medium power fields were statistically similar. Concerning OS and RFS data, in univariate models, stage, lymphovascular and pleural invasion, spread through air spaces (STAS), and tumour budding were significant prognostic markers, respectively. In multivariate analysis, higher stage (HR: 7.9; 95%CI: 2.44-12.07; $p=0.007$), lymphovascular spread (HR: 4.62; 95%CI: 1.31-16.4; $p=0.018$) and tumour budding (HR: 3.03; 95%CI: 1.04-10.43; $p=0.019$) were found to have impact on OS data. Regarding RFS estimates, STAS (HR: 5.01; 95%CI: 1.61-15.62; $p=0.005$) and tumour budding (HR: 3.20; 95%CI: 1.24-8.27; $p=0.016$) were independent prognostic markers.
Conclusion: Tumour budding is a less investigated unfavourable prognostic factor among pulmonary adenocarcinomas. However, lobar resection is the gold standard treatment for primary pulmonary neoplasms; sublobar resection is an alternative therapeutic modality for patients with decreased respiratory capabilities. The intraoperative demonstration of presence of tumour budding may be an argument for the escalation of the sublobar resection into a lobar surgery along lymphadenectomy.

Funding: Hetényi Géza grant 5S766 (A202)

OFP-09-008

p53 immunohistochemistry as a surrogate biomarker for TP53 mutational status in lung cancer

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Background & Objectives: TP53 is a pivotal tumour suppressor gene in humans. In lung cancer, it has been established as both a prognostic and predictive biomarker. Immunohistochemical analysis of p53 (p53 IHC) as a surrogate marker of TP53 mutational status is well established in endometrial, ovarian, and colorectal carcinomas. However, its applicability in lung cancer remains uncertain. This study aimed to evaluate the utility of p53 IHC as a surrogate biomarker for TP53 mutational status in lung cancer.
Methods: A total of 112 lung cancer cases with both p53 IHC and next-generation sequencing (NGS) data were analysed. p53 expression patterns were categorised into three groups: wild-type, overexpression and null. For analytical purposes, p53 IHC results were classified as either wild-type or aberrant (including overexpression and null patterns). TP53 mutational status was determined using four different commercial NGS panels. Statistical analyses were performed using IBM® SPSS® Statistics 25.
Results: Most samples were obtained from biopsies (42%), surgical specimens (38%) and cytology (20%). Adenocarcinoma was the predominant histological subtype (80 cases, 71%), followed by squamous cell carcinoma (8 cases, 7%). Aberrant p53 expression was observed in 65 cases (58%), with overexpression being the most prevalent pattern (91%). TP53 mutations were detected in 58 cases (52%) via NGS. The correlation between p53 IHC and TP53 mutational status yielded a sensitivity of 96.6%, a specificity of 83.3%, a positive predictive value of 86.2%, and a negative predictive value of 95.7%. A "substantial agreement" was observed between both methods ($\kappa = 0.802$).
Conclusion: These findings support the use of p53 immunohistochemistry (IHC) as a surrogate biomarker for evaluating TP53 mutational status in lung cancer. p53 IHC is advocated as a reliable diagnostic and prognostic tool, particularly in settings where next-generation sequencing (NGS) is unavailable.

OFP-09-010

Artificial intelligence-assessed LKB1 immunohistochemical expression better differentiates LKB1-*impaired* and LKB1-*proficient* non-small cell lung cancers rather than NGS analysis

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Background & Objectives: LKB1-mutated non-small cell lung cancers (NSCLCs) display an aggressive phenotype, with unique tumour microenvironment features. However, the correlation between *LKB1* mutational status and protein expression is poor. We recently identified IL-6 stromal expression as a feature of LKB1-*impaired* NSCLCs. Our aim is to compare the efficacy of *LKB1* mutational status and immunohistochemical expression in discriminating IL-6 expressing LKB1-*impaired* NSCLCs.
Methods: We retrieved 36 cases of KRAS-mutated lung adenocarcinoma. Immunohistochemistry for LKB1 (Ley37D/G6, Santa Cruz Biotechnology) and IL-6 (10C12, Leica Biosystems) was performed. A machine learning (ML) algorithm was created to distinguish tumour and stroma for both IHC-staining; IL-6 was evaluated as positive cells/mm2, LKB1 with a modified H-score (mH-score), accounting absolute cell number. *LKB1* mutational status was assessed by Ion-Torrent NGS.

Results: NGS analysis showed 7 cases (19%) with *LKB1* pathogenic or likely-pathogenic variants (MUT), 4 cases (11%) with *LKB1* VUS and 25 *LKB1* wild-type cases (70%) (WT). We calculated the ratio between IL-6 expression in stromal and tumour cells and we found no difference in MUT+VUS versus WT, but an almost statically significant (p=0,05) difference between MUT (mean IL-6 S/T = 3,84) and VUS+WT (mean IL-6 S/T = 1,30 and 1,06). We distinguished LKB1 high-expressor (17 cases) and low-expressor (17 cases), based on the median LKB1 pathologist-assessed H-score (30), but no difference was established in IL-6 expression. Exploiting our ML algorithm, we chose a cutoff of mH-score = 0,2 to distinguish high- and low-expressor, and we identified a higher stromal IL-6 expression in LKB1 low-expressor compared to LKB1 high-expressor (p=0,0452), and no difference in tumour cell IL-6 expression (p=0,362).
Conclusion: An increased stromal cell IL-6 production was guessed in pathogenic *LKB1*-mutated NSLCs and endorsed in LKB1 low-expressor. Artificial intelligence-assessed LKB1 immunohistochemical expression overperforms mutational status and pathologist-assessed H-score in identifying LKB1-*impaired* NSCLCs. Further analyses are needed to better characterize LKB1-*impaired* tumours.

OFP-09-011
Integrated molecular analysis depicts molecular signatures associated with response to tyrosine kinase inhibitors in advanced NSCLC
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Background & Objectives: Tyrosine kinase inhibitors (TKI) are the mainstay of treatment in oncogene addicted non-small cell lung cancer (NSCLC). However, resistance to TKI invariably occurs during treatment course but data on drug resistance-related mechanisms are largely missing. Therefore, we designed a study to deeply characterize the genomic and epigenetic signatures associated with TKI response in oncogene-addicted NSCLC patients.
Methods: Sixty samples from advanced NSCLC patients treated with TKI at first line were analysed for genomic profiling using the Oncomine Comprehensive Assay Plus (ThermoFisher Scientific) panel, including 44 EGFR-mutated and 16 ALK-fused cases. Additionally, 52 cases (46 in overlap with NGS testing, 36 EGFR-mutated and 16 ALK-fused cases) were analysed using a PCR-based global miRNome assay (miRCURY LNA miRNA PCR kit, Quiagen). Potential targets of significantly deregulated microRNA and their biological functions were predicted by STRING and MirDIP softwares.
Results: In EGFR-mutated cases, progressive disease during therapy was associated with lower tumour mutational burden, presence of TP53 co-mutations and gains in Chr1q. Shorter time to progression was observed in cases harbouring TP53 co-mutations and gains in Chr5p and Chr7p. In ALK-fused cases, no molecular characteristic was significantly associated with type of response. However, shorter time to progression was observed in cases with HLA A gene loss. MicroRNA profiling clustered both EGFR and ALK-altered cases into 3 main clusters not significantly associated with specific profiles of responsiveness. However, good and bad responders showed significant deregulation of a set of microRNA. In EGFR-mutated, the most differentially regulated miRNAs were miR-423-3p, miR-744-5p and miR-455-3p, with a main predicted interference of the transforming growth factor-β pathway, whereas in ALK-fused cases immune-related chemokine pathway was deregulated through the modulation of miR-135a-5p, miR-331-3p and miR-196a-5p.
Conclusion: The present data claim the role of extended molecular testing to predict response to TKI in oncogene addicted NSCLC and identify novel potential predictive biomarkers.

OFP-09-012
Loss of Claudin-18 in immunohistochemistry: a potential specific biomarker to differentiate lung adenocarcinoma from lung cancer mimickers
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Background & Objectives: Lung cancer (LC), particularly lung adenocarcinoma (LUAD), is often diagnosed at an advanced stage, with limited biopsy samples available for molecular testing. Claudins, especially *Cldn18.1*, play a crucial role in lung epithelial barrier function and may impact LUAD progression. Reduced *Cldn18.1* expression in LUAD has been linked to increased YAP activity, promoting cell proliferation. This study aims to evaluate *Cldn18.1* expression in LUAD using immunohistochemistry, exploring its potential as a diagnostic tool.
Methods: We analysed 164 lung surgical resection samples and 51 diagnostic biopsy samples from patients with clinically suspected pulmonary neoplasms, including CT-guided core needle biopsy (CNBs), transbronchial biopsy (TBBs), and cell block (CBs). Immunohistochemical staining for *Cldn18.1* was performed on 4 µm sections using the Ventana platform, with AT1 and AT2 cells as internal controls. *Cldn18.1* expression was evaluated semi quantitatively, stratifying cases by the percentage of tumour-positive cells in 10% intervals.
Results: *Cldn18.1* expression was observed in normal alveolar cells in all cases. Conversely, *Cldn18.1* was absent in all lung cancer histotypes except for LUAD. In invasive Non-Mucinous LUAD (NM-LUAD), 68% of cases showed no expression, 27.8% exhibited 1-49% positivity, and only 4.2% displayed expression in more than 50% of tumour cells. Conversely, all Invasive Mucinous LUAD (IM-LUAD) cases showed positive staining in at least 50% of tumour cells. Mixed IM/NM-LUAD and Colloid-LUAD exhibited either variable or no protein expression. In small biopsy samples, most LUAD (79.3%) showed a lack of *Cldn18.1* expression. LUAD with mucinous features demonstrated widespread *Cldn18.1* staining, while LUAD with colloid features and NSCLC-NOS were negative.
Conclusion: *Cldn18.1* demonstrates a trend of reduced IHC expression in LUAD, except for IM-LUAD. This loss of expression may serve as a useful marker for diagnosing LUAD in small tissue samples, particularly in cases with limited material and in diagnostically challenging cases.

OFP-09-013
Current approaches, barriers, and future directions in mesothelioma diagnostics: results from an Italian national survey
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Background & Objectives: This nationwide survey aimed to evaluate current diagnostic practices, adherence to international guidelines, and key challenges faced by Italian pathologists in diagnosing pleural mesothelioma (PM), an aggressive malignancy with rising therapeutic complexity.
Methods: A 38-item questionnaire was distributed electronically to Italian pathologists involved in PM diagnostics. The survey explored demographics, biopsy procedures, immunohistochemical and molecular practices, educational needs, and barriers to research collaboration.
Results: Fifty-five pathologists with diverse experience levels and institutional affiliations participated, predominantly from academic medical centres. Marked variability emerged in tissue sampling and biobanking practices. Diagnostic challenges included accurate recognition of sarcomatoid/desmoplastic features, limited adipose tissue in biopsies, and difficulties in histotype subclassification. Most pathologists employed multidisciplinary discussions and molecular analyses (e.g., BAP1, MTAP) for inconclusive cases. While immunohistochemistry was routinely used, especially calretinin, WT1, and BAP1, standardized reporting protocols and molecular tools like p16 FISH and MTAP IHC were inconsistently adopted. Research-oriented practices, such as biobanking, were limited by institutional infrastructure and the absence of standardized protocols. Although digital pathology infrastructure was not broadly identified as a limiting factor, case-sharing logistics (e.g., paraffin block transport) posed challenges. Participants expressed a strong need for enhanced access to molecular diagnostics, national case repositories, and training on novel biomarkers.
Conclusion: This survey underscores diagnostic variability and resource gaps in PM pathology across Italy. Standardizing histopathological protocols, expanding access to molecular tools, and fostering structured national collaboration are key steps toward improving diagnostic precision. Targeted training initiatives and support for biobanking and multicentre research efforts will be critical for advancing both diagnostic and therapeutic outcomes in PM.

OFP-09-015
Pneumoconiosis, a retrospective study
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Background & Objectives: Exposure-related lung diseases constitute a group of occupational, preventable diseases caused by the inhalation of organic and inorganic dust. The number of affected patients remains high, although it is likely underestimated. Currently, treatment is very limited once the fibrotic stage is reached. Our role as pathologists is crucial, as our diagnoses must clearly establish the presence of foreign elements and the body's response to them.
Methods: A descriptive and retrospective study consisting of 64 patients incidentally diagnosed with pneumoconiosis through biopsy or analysis of surgical specimens from patients without an initial clinical suspicion. Cases were collected between January 9, 2020, and September 25, 2023. Data regarding occupational activity or environmental exposure were gathered as recorded in electronic medical records and corresponding clinical reports.
Results: The majority of patients were diagnosed with mixed pneumoconiosis from coal dust and silicates, with a predominance of male patients and a mean age of 69 years. Information was available in 62.5% of medical records, revealing that these patients worked in the construction industry. A total of 54.6% of patients presented respiratory symptoms, which were generally attributed to COPD. In 25% of cases, neither the patient's occupation nor any environmental or occupational exposure was documented in the medical records.
Regarding disease staging, 78% of patients were diagnosed in the macular or nodular stage, while 22% had progressive massive fibrosis.
Conclusion: It is essential to raise awareness among healthcare professionals about the importance of conducting a thorough medical history, including the patient's occupational and environmental background. The goal of identifying pneumoconiosis at early stages depends on awareness of the disease, as it is often underdiagnosed by pulmonologists, primary care specialists, and even pathologists.
Examining non-neoplastic areas in patients undergoing lung resection for cancer is crucial, as there are numerous lesions that must be properly diagnosed.

OFP-10 Oral Free Paper Session Endocrine Pathology & Head and Neck Pathology

OFP-10-001
Deep-learning based recognition of reticulin stain distinguishes germline mutated from sporadic paragangliomas
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Background & Objectives: Grounded on digital pathology, computational pathology exploits the power of artificial intelligence to develop algorithms, which can learn to recognize patterns and anomalies that may elude the human eye on whole slide images (WSI). We recently observed a structural heterogeneity of reticulin framework patterns in pheochromocytomas-paragangliomas (PPGL), possibly genetically-linked. This study aims to develop a deep learning algorithm which predicts PPGL genetic profile from reticulin stained WSI.
Methods: A total of 104 PPGL (90 pheochromocytomas, 14 paragangliomas) were retrieved from the University of Turin pathology files from 2000 to 2023. All clinical, pathological and NGS genetic data were available. Two genetic outcome categories (Sporadic vs Germline mutated) were trained on 39 reticulin stained WSI by means of weakly supervised labels with 2785/10000 iterations, in an extra complex modality and a field of view of 150 μm. The analysis was performed on an untrained dataset of 24 WSI. The performance of the algorithm was considered correct if >70% WSI area was assigned to a single label. Validations on the rest of the dataset and on an external dataset are ongoing. The latest version of Aiforia Create (Version 6.2) was used.
Results: In 19/24 WSI, the algorithm correctly identified the profile (10 germline and 9 sporadic cases). As a weakly supervised model, the algorithm identified WSI regions contributing the outcome prediction. Strikingly, a reticulin framework made of a repertoire of nests from very small to large size (1-2 cells to 10-15) was the feature of germline cases, while wide areas of disrupted reticulin fibres were commonly found in sporadic cases. The cases with discrepant prediction had mixed patterns, possibly intratumor heterogeneity-related.
Conclusion: This novel deep learning model offers solid promises to standardize reticulin framework assessment and to offer pathologists and clinicians a practical tool for identifying patients who should be prioritized for genetic testing.

OFP-10-002
Hormone-associated subtypes of pulmonary neuroendocrine tumours: correlation with clinicopathological, transcriptional signatures, therapy targets and outcome
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Background & Objectives: Recently pulmonary neuroendocrine tumours (NETs) were subgrouped by immunohistochemical expression of transcription factors (TFs) such as OTP, ASCL1, TTF1. The signatures correlated with clinical characteristics. However, the role of hormone expression remained unexplored. This study aimed to identify hormone-associated NET subgroups and clarify their correlation with TF signatures and clinicopathological characteristics.
Methods: We immunostained 111 resected NETs from multiple institutions (2000–2024) for the hormones GRP, ACTH, calcitonin, serotonin, the TFs OTP, ASCL1, TTF1, treatment relevant markers such as SSTR2 and DLL3, and SOX10 to identify sustentacular cells. The results were correlated with clinicopathological features as well as outcome (progression free survival).
Results: Cluster analysis based on hormone expression identified three groups: The largest group expressed GRP (63/111, 57%) with or without other hormone expression and was statistically associated with female sex (79%), non-smoking (67%), peripheral location (36%), spindle cell morphology (60%), ASCL1/OTP expression (67/78%), DLL3 positivity (71%), and presence of sustentacular cells (all $p<0.05$). The second group that expressed no hormones (29/111, 26%) and the third group with serotonin expression (19/111, 17%) shared following features: male sex (59-47%), smoker (69-50%), central location (86-88%), trabecular pattern (48-37%), absence of ASCL1/OTP expression, and sustentacular cells but differed in SSTR2 and DLL3 expression (all $p<0.05$). In addition, within the GRP group, an ACTH subgroup (28/63, 25%) could be distinguished from a calcitonin-subgroup (16/63, 14%). The ACTH-subgroup was associated with older age (median 71), neuroendocrine cell hyperplasia, high DLL3, TTF1 expression, but was negative for SSTR2 (all $p<0.05$). The calcitonin subgroup showed better outcome than the others ($p=0.03$).
Conclusion: Hormonal profiling identifies three clusters closely related to TFs signatures, clinicopathological features, therapy related molecule expression and prognosis and refines pulmonary NET-subclassification by stratifying patients and guide therapeutic strategies.

OFP-10-003

Investigation of the diagnostic and prognostic significance of IGF-2 And FGFR-4 in adrenocortical neoplasms by immunohistochemistry and real-time PCR

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Background & Objectives: Adrenocortical carcinomas are rare tumours diagnosed by various multifactorial algorithms. It is relatively easy to distinguish carcinomas with metastatic or periadrenal tissue invasion from adenomas, but there are difficulties in the diagnosis of organ-limited carcinomas. In addition to histopathological findings, biomarkers are needed for these tumours. In our study, we aimed to investigate the importance of IGF-2 and FGFR-4 in adenoma-carcinoma differentiation and prognostically in these tumours.
Methods: A total of 74 patients diagnosed with adrenocortical neoplasia and 19 adrenal gland for control were included in the study. IGF-2 and FGFR- 4 were studied by immunohistochemical method and real-time(RT) PCR from formalin-fixed paraffin-embedded blocks. Histopathologic, clinical findings and ki67 proliferation index and results were evaluated together.
Results: Patients with a Helsinki score of >17 and/or a ki67 proliferation index of > 9% had a statistically significant relationship with poor prognosis (mortality). IGF-2 is a significant biomarker for adenoma-carcinoma differentiation when administered by immunohistochemical and RT-PCR methods. We found a strong and significant positive correlation between IGF-2 immunohistochemistry and PCR. There is a significant correlation between IGF-2 immunohistochemical (protein) values and recurrence, metastasis, mortality and between IGF-2 mRNA (RT-PCR) values and metastasis in carcinomas. FGFR-4 isn't a useful biomarker in adrenocortical tumours in terms of diagnosis and prognostics when administered by immunohistochemical and/or RT-PCR.
Conclusion: Adrenocortical tumours, especially organ-confined carcinomas, are challenging lesions for pathologists. We have shown that when histopathological criteria, reticular framework, ki67 proliferation index and IGF-2 are evaluated together, carcinomas can be distinguished more easily and the rate of misdiagnosis can be reduced. In addition, we found that Helsinki score, ki67 index and IGF-2 are prognostically important in these tumours. We have shown that FGFR-4 isn't useful in distinguishing between adenomas and carcinomas, nor is it prognostically helpful. Therefore further studies are needed to evaulete FGFR-4 expression in adrenocortical tumours.

Funding: Cukurova University Scientific Research Projects and Federation of Turkish Pathology Societies

OFP-10-004

Autophagy as a mechanism involved in Radioiodine-Refractoriness in papillary thyroid carcinoma

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Background & Objectives: Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy. Despite its excellent prognosis, some PTC's variants are associated with an increased risk of recurrence. One of the major causes of local recurrence and distant metastasis is the resistance to Radioiodine (RAI) therapy.
Methods: In this study, we evaluated the expression of >700 immune-related genes in tumour microenvironment (TME) of patients affected by PTC, stratified according to RAI treatment response. In detail, 25 PTCs were subdivided into two categories: RAI resistant (R), RAI sensitive (T); while 6 patients were classified as normal patients (with normal tissue). Normal patients were considered as a reference category. To predict specific interactions between proteins, translated from the identified genes, a specific *in silico* analysis was performed to construct protein networks for R and T categories.
Results: For the R network, among the 49 differential expressed genes, 14 genes resulted as the most relevant interaction nodes, including IL-6, ITGAM, CASP3, RELA, RELB, CASP8, ITGB2, C3, JAK3, PPARG, CLEC7A, TNFRSF10B, CDH5, BCL2. At variance, for the T network, among the 31 differential expressed genes, 11 genes resulted as the most important interaction nodes, including HMGB1, IKBKB, IRAK4, MAVS, TLR7, NOD2, ITGB3, CD28, IFNAR1, CD19, CD7. Interestingly, in regards of autophagy, in the R group the pro-autophagic gene IL-6 resulted upregulated, while the anti-autophagic gene BCL2 resulted downregulated. Conversely, in the T group the key pro-autophagic gene HMGB1 resulted down-regulated.

Conclusion: RAI resistance remains a significant obstacle in the treatment of PTC. Our study suggests that in PTC RAI resistance may be driven by the capacity to activate autophagy. The investigation of process of autophagy, and the involved pathways, in the TME could be an important step for the modulation of RAI refractoriness to improve therapeutic strategies and patients' management.

OFP-10-005

Tumour microenvironment of anaplastic thyroid carcinoma: implications for patient survival

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Background & Objectives: Anaplastic thyroid carcinoma (ATC) is a highly aggressive malignancy with nearly 100% mortality and limited treatment options. The tumour microenvironment (TME) plays a critical role in ATC progression, particularly immune checkpoint molecules, tumour-associated macrophages (TAMs), and adhesion molecules like E-cadherin.
This study investigates the expression of PD-L1, PD-1, TAM infiltration, and E-cadherin loss in ATC and evaluates their impact on patient survival.
Methods: A retrospective cohort of 22 ATC patients treated at King George's Medical University, Lucknow, India, between January 2017 and August 2022, was analysed. Immunohistochemical staining assessed PD-L1 and PD-1 expression, TAM density, and E-cadherin loss. Statistical correlations between these markers and overall survival were examined.
Results: Immunohistochemical evaluation revealed PD-L1 expression in 68.2% of cases, with a median tumour proportion score (TPS) of 50. PD-1 expression was limited to inflammatory cells. E-cadherin loss was observed in over 69% of cases, suggesting disrupted cell adhesion. TAM infiltration was elevated in 58.8% of patients and correlated significantly with PD-L1 expression ($p = 0.02$). Survival analysis demonstrated a mean overall survival of 3 months, with high PD-L1 expression, elevated TAM density, and increased PD-1 expression associated with shorter survival ($p < 0.001$). Patients expressing PD-L1 had a mean survival of 2.4 months compared to 4.1 months for those without PD-L1 expression ($p < 0.05$). Similarly, high PD-1 expression in inflammatory cells correlated with poorer outcomes (mean survival of 2.5 months versus 4.5 months for low expression; $p = 0.03$).
Conclusion: The findings highlight the critical role of immune markers within the TME in ATC prognosis. The association of PD-L1, PD-1, and TAM density with poor survival underscores the potential of immunotherapeutic strategies. Further research is needed to validate these biomarkers for guiding treatment approaches in ATC.

Funding: ICMR

OFP-10-006

The effect of tumour microenvironment on prognosis and lymph node metastasis in oral squamous cell carcinoma

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Background & Objectives: Oral squamous cell carcinoma (OSCC) constitutes 90% of oral cavity cancers. Low survival rates show that current staging and grading systems are not sufficient for prognostication. Tumour microenvironment (TME) is shown to play a crucial role in cancer biology. This study aims to investigate the impact of TME components such as cancer-associated fibroblasts (CAF), tumour-infiltrating lymphocytes (TILs), tumour budding (TB), desmoplastic reaction (DR), tumour-stroma ratio (TSR) on prognosis and lymph node metastasis (LNM) as well as their potential effect on tumour progression in OSCC.
Methods: H&E slides of 129 OSCC cases diagnosed between 2017-2023 in Marmara University Hospital were histomorphologically evaluated for TSR, TB, DR and TILs. CAF density was assessed using α-SMA immunohistochemistry. Effect of each parameter on survival and their association with LNM, stage and other adverse histologic features were investigated statistically.
Results: Cases with high TB showed more aggressive features including higher depth of invasion (DOI), perineural-lymphovascular invasion, worst pattern of invasion, higher T stage and higher rates of LNM. Higher CAF density, immature stroma and low TSR were associated with higher TB, higher rates of LNM and other mentioned adverse features. High TIL density was associated with antitumoral activity, as they were linked to lower TB, lower DOI and lower rates of LNM. In univariate analysis, high TB, high CAF density, immature stroma, low TIL density and low TSR were associated with poor overall survival. In multivariate analysis, high TIL density in total tumour area and high TSR were associated with better overall survival. High CAF density and low TIL density were associated with worse progression-free survival in univariate analysis, while in multivariate analysis, these parameters did not show independent effects.
Conclusion: This study demonstrates that TME has a significant impact on prognosis, LNM and tumour progression in OSCC. Further research is needed to explore the prognostic value of related parameters and their role in tumour progression.

OFP-10-007

Histomolecular profiling of benign oncocytic neoplasms in the parotid gland

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Background & Objectives: Oncocytic neoplasms of the salivary gland are rare and include oncocytomas (O) and nodular oncocytic hyperplasia (NOH). While these proliferations have traditionally been considered benign, their molecular characteristics and classification remain debated. This study aimed to characterize the histomolecular features of oncocytic proliferations and investigate their potential as a distinct pathological entity using transcriptomic analysis and immunohistochemical (IHC) markers.
Methods: A cohort of 23 cases of oncocytic proliferations, including O, NOH, oncocytic neoplasms of uncertain malignant potential (ONUMP), and NOH/O hybrid cases, was analysed. Immunohistochemistry was performed for various markers, including CK7, p40, p63, SOX10, PLAG1, HMGA2, PTGER3, and GLUL. Whole Exome RNA sequencing and targeted transcriptomic profiling were conducted to assess gene expression patterns and clustering among oncocytic

lesions and other salivary gland tumours. Statistical analyses included clustering methods and differential gene expression comparisons.
Results: Transcriptomic clustering revealed that oncocytic proliferations, including O, NOH, NOH/O, and ONUMP, formed a distinct molecular group, separate from conventional salivary gland tumours. Notably, *GLUL* (*Glutamine Synthetase*) was significantly underexpressed in oncocytic proliferations in comparison to conventional salivary gland tumours. These findings suggest a shared molecular signature among these lesions, distinct from other benign and malignant oncocytic tumours.
Conclusion: This stu.dy identifies oncocytic proliferations as a unique molecular entity, which we propose to name Low-Grade Oncocytic Tumours (LGOT). The consistent low expression of *GLUL* provides robust IHC markers to differentiate LGOT from other salivary gland neoplasms. These findings support a refined classification of oncocytic salivary gland lesions and have potential diagnostic implication. Further validation in larger cohorts is required.

OFP-10-008

The hidden threat: how occupational exposures drive inverted sinonasal papilloma and may contribute to its malignant transformation

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Background & Objectives: Inverted sinonasal papillomas (ISPs) are benign epithelial tumours with a recognized potential for malignant transformation into squamous cell carcinoma (ISP-SCC), occurring in 2–7% of cases. While the mechanisms underlying this progression remain unclear, occupational exposure to carcinogens has been proposed as a contributing factor. This study investigates the association between occupational exposure and both the development and malignant transformation of ISPs using a multidimensional approach.
Methods: We conducted a retrospective analysis of 32 patients (22 with ISP and 10 with ISP-SCC), based on a standardized questionnaire from the Italian Register of Sino-Nasal Tumours. All samples were analysed for p53 and p16 via immunohistochemistry, and for high-risk and low-risk HPV using reverse-transcriptase real-time PCR. Focus was placed on exposure to IARC Group 1 and 2A carcinogens. Hierarchical clustering (HC) using Gower distance and complete linkage was performed, incorporating variables such as smoking, gender, allergic rhinitis, septal deviation, turbinate hypertrophy, nasal spray use, and occupational/extra-occupational exposures. HPV data were excluded from clustering due to the limited sample size and low positivity rate. Malignant transformation was evaluated in relation to cluster composition.
Results: In the ISP group (n=22), 68.2% were male, mean age 61.1 years, with lesions mainly in the nasal cavity and maxillary sinus. Occupational exposure was present in 41%. The ISP-SCC group (n=10) was 50% male, mean age 64.4 years, with 40% reporting occupational exposure. HC identified three clusters. Cluster 1 (n=18) had high smoking prevalence; Cluster 2 (n=7), composed entirely of ISP-SCC cases, showed the highest occupational exposure and lowest smoking rates; Cluster 3 (n=7) had low exposure and high nasal spray use.
Conclusion: All ISP-SCC cases grouped into the cluster with predominant occupational exposure, supporting a possible role of occupational carcinogens in malignant transformation. Larger studies integrating HPV data are warranted.

OFP-10-009

Comparative analysis of the WHO reporting system for head and neck cytopathology and the Milan System for Reporting Salivary Gland Cytopathology

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Background & Objectives: The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) standardizes the classification of salivary gland fine-needle aspiration (FNA) samples. The newly introduced WHO Reporting System for Head and Neck Cytopathology consolidates categories to improve diagnostic utility, notably merging Non-Neoplastic (NN) and Benign Neoplasm (BN) into a single "Benign" category. This study compares the risk of malignancy (ROM) across categories in both systems using a large cohort of FNA samples.
Methods: We evaluated 2,218 salivary gland FNA samples collected at the Institute Curie, Paris (1954–2022), with 1,356 having histological follow-up. Samples were classified according to the MSRSGC (Non-Diagnostic [ND], NN, Atypia of Undetermined Significance [AUS], BN, Salivary Gland Neoplasm of Uncertain Malignant Potential [SUMP], Suspicious for Malignancy [SM], Malignant [M]) and the WHO system (Insufficient/Inadequate/Non-Diagnostic, Benign, Atypical, Neoplasm of Uncertain Malignant Potential [NUMP], SM, M). ROM was calculated for each category, and diagnostic performance metrics were assessed.
Results: In the MSRSGC, ROM was: ND 50% (n=2), NN 16.8% (n=149), AUS 0% (no cases), BN 4.3% (n=514), SUMP 50% (n=2), SM 56.1% (n=66), and M 98.2% (n=623). In the WHO system, ROM was: Insufficient/Inadequate/Non-Diagnostic 50% (n=2), Benign 7.1% (n=663), Atypical 0% (no cases), NUMP 50% (n=2), SM 56.1% (n=66), and M 98.2% (n=623). The WHO's "Benign" category, combining NN and BN, balanced the NN's higher ROM (16.8%) and BN's lower ROM (4.3%) into 7.1%. In conclusive categories (MSRSGC II, IVa, V, VI), the diagnostic metrics for both systems were: sensitivity 93.3%, specificity 93.9%, positive predictive value (PPV) 94.2%, and negative predictive value (NPV) 92.9%.
Conclusion: Both systems effectively identify malignancy. The WHO system's merger of NN and BN into "Benign" streamlines reporting and reduces variability, though it may mask clinically significant differences between non-neoplastic and benign neoplastic lesions.

OFP-10-010

Multiplex *in situ* expression profiling of lung-cancer-associated genes in the development of squamous cell carcinoma of the larynx and hypopharynx

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Background & Objectives: Previous studies suggest similar gene expression patterns in lung carcinoma and squamous cell carcinoma of the larynx and hypopharynx (LHSCC); however, the role of lung-cancer-associated genes in the development of LHSCC from precancerous lesions remains poorly understood.
Methods: We performed multiplex *in situ* hybridization, using Human multi-tissue and cancer gene panel (Xenium, 10X Genomics) consisting of 377 genes, including 63 lung-cancer-associated genes. We first compared *in situ* expression of lung-cancer-associated genes between normal mucosa and invasive carcinoma. We further compared expression between different stages of LHSCC development. We included biopsy samples from three patients with normal mucosa, four patients with low-grade dysplasia, one patient with high-grade dysplasia, one patient with carcinoma *in situ* and two patients with invasive carcinoma.
Results: Totally, we observed 127 differentially expressed genes between normal mucosa, dysplasia and LHSCC. Among them, 28 differentially expressed genes were lung-cancer-associated, including well-known oncogenes (e.g. *MDM2* and *MET*), transcription factors (e.g. *EHF*), cytokeratins (e.g. *KRT7*), glycoproteins (e.g. *LAMP3, PDPN*), enzymes (e.g. *PLCG2, CYP4B1*), cytokines (e.g. *CCL5, CXCL2*) and other immune response-related genes (e.g. *MALL*). Interestingly, some of the genes have been described to be related to nasopharyngeal carcinoma (e.g. *SNTN, TSPAN19, UPK3B*), but not to other head and neck carcinomas. Two of the genes have not yet been reported in head and neck carcinomas (*SFTA2, EDN1*).
Conclusion: Almost half of the analysed lung-cancer-associated genes were differentially expressed in various stages of LHSCC development. Our study confirms similarities in gene expression profiles between lung carcinoma and LHSCC, suggesting similar pathogenesis between the two cancer types.

OFP-10-011

Re-evaluation of difficult salivary gland tumour cases among 125 consultation cases: according to 5th WHO Blue Book

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Background & Objectives: The classification of salivary gland tumours (SGTs) was changed in 5th WHO blue book published in 2024, mainly based on their molecular characteristics. I have received 125 consultation cases of SGTs, and sometimes experienced difficult cases. My aim is re-evaluation and re-diagnose of such cases, based on recent evidence, according to 5th WHO blue book.
Methods: During 1998-2021, I experienced 125 consultation cases of SGTs. Among such cases, I selected especially difficult or rare 8 cases and re-diagnosed them using additional immunostainings.
Results: Case 1 (53y/o. F. Parotid) was re-diagnosed cystic epithelial-myoepithelial carcinoma (EMC) ex pleomorphic adenoma (PA) from combined congenital dystrophic cyst and PA. Case 2 (81 y/o. M. Oral floor) was re-diagnosed sialadenoma papilliferum from intraductal carcinoma. Case 3 (59 y/o. M. Parotid) was re-diagnosed mucoacinar carcinoma ex PA with bone formation and tumour-associated lymphoid proliferation (TALP) from mucoepidermoid carcinoma with TALP. Case 4 (33 y/o. F. Parotid) was re-diagnosed cystic EMC with bizarre cells from basal cell adenoma. Case 5 (74 y/o. M. Parotid) was re-diagnosed striated duct adenoma from so-called monomorphic adenoma, due to diffuse S-100 protein immunostaining. Case 6 (77 y/o. F. Sublingual) was mucinous adenocarcinoma showing signet-ring cell feature. Case 7 (82 y/o. M. Parotid & Lymph nodes) was re-diagnosed secretory carcinoma with high-grade transformation (HGT) from acinic cell carcinoma with HGT, due to S-100 protein, mammaglobin and MIB-1 immunostaining. Case 8 (76 y/o. F. Upper Lip) was re-diagnosed mucinous adenocarcinoma (previously termed as "papillary cystadenocarcinoma") from non-intestinal-type adenocarcinoma.
Conclusion: The diagnosis of SGTs is sometimes very difficult. Some cases could be re-diagnosed using adequate surrogate markers against their molecular characteristics, whereas others need the molecular examinations for the exact diagnosis. As low-grade carcinomas were especially misdiagnosed as benign tumours, careful observation and exact examination are essential.

OFP-10-012

Trem2-expressing multinucleated giant macrophages are a biomarker of good prognosis in head and neck squamous cell carcinoma

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Background & Objectives: Patients with head and neck squamous cell carcinomas (HNSCC) often have poor outcomes; yet integrating novel prognostic biomarkers into clinical practice is challenging. Alongside conventional tumour-associated macrophages (TAM), a proportion of HNSCC patients contains large macrophages termed multinucleated giant cells (MGC). These MGC are performing a foreign body reaction against extracellular keratin produced by carcinomatous cells. While MGC presence is well documented in keratinizing SCC, their biology is not well understood and studies suggest varying impact of MGC on patient survival. Thus, we investigated their potential pronostic impact in HNSCC. Additionally, we designed a deep-learning method to automate MGC quantification and we employed spatial transcriptomic and proteomic approaches to explore their related tumour-microenvironment.
Methods: We had access to two cohorts of HNSCC patients from The Cancer Genome Atlas (TCGA, n=110 patients) and Gustave Roussy (GR, n=284 patients). We quantified the number of MGC per mm^2 of tumour creating an MGC density biomarker. Then, we developed a deep-learning algorithm to automatically quantify the number of MGC and the number of tumour cells, and computed the automatic MGC biomarker as the MGC-to-tumour-cells ratio. The model was trained on TCGA and validated on GR cohort. Finally, we performed spatial transcriptomic (Visium) and proteomic (CosMx) analyses on tumour slides.
Results: Here, we report that the presence of MGC in HNSCC, associates with longer Overall Survival (OS) and Progression Free Interval (PFI). The automatic biomarker was also associated with longer OS and PFI. With spatial-omics approaches we observed an increase in central memory CD4 T cells and a decreased in regulatory T cells. We identified an MGC-specific RNA signature resembling to TREM2-expressing mononuclear TAM, which cluster in keratin-induced granulomas.
Conclusion: Herein, we observed that MGC density associates with a good prognosis in HNSCC patients and we described their related tumour-microenvironment, paving the way for more personalized therapies.

Funding: Programme de Recherche Translationnelle en Cancérologie 2022 Institut National du Cancer PRT-K 2022. Prix Fonds Recherche 2021 de la Société Française de Pathologie

OFP-10-013

Pathological predictors of recurrence in oral squamous cell carcinoma: analysis of 1,365 cases from a high-prevalence region

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Background & Objectives: This study aims to evaluate the pathological factors predicting recurrence in oral squamous cell carcinoma (OSCC) and to propose a practical scoring system for risk stratification based on key clinicopathological parameters.
Methods: A retrospective cohort analysis was performed on 1,365 consecutive OSCC patients who underwent surgical resection at our tertiary-care oncology centre from January to December 2019. Clinicopathologic parameters were correlated with recurrence and survival outcomes. The statistical analysis included 836 treatment-naive patients who completed therapy and had either adverse events or a minimum follow-up of one year. Survival analysis utilized Kaplan-Meier and log-rank tests, while multivariate predictors were assessed via multiple logistic regression. Optimal cut-offs for tumour size, tumour thickness, and depth of invasion (DOI) were determined through Receiver Operating Characteristic analysis.
Results: The cohort had a mean age of 53 years, with a male-to-female ratio of 5.7:1. Buccal mucosa (45.8%) was the most common tumour site. The mean tumour size was 3.29 cm, and mean DOI was 10.6 mm. Perineural and lymphovascular invasions were noted in 28.3% and 3% of cases, respectively. The most frequent worst pattern of invasion (WPOI) was pattern 4 (73.7%). Lymph node metastases occurred in 52.9% of patients, with extranodal extension present in 60.3% of these cases. Recurrences occurred locoregionally in 18.6% of cases, and distant metastases developed in 6.1%. Multivariate analysis identified lymph node metastasis (HR=1.8, $p<0.001$), WPOI 5 (HR=1.7, $p=0.004$), and DOI >10 mm (HR=1.69, $p<0.001$) as significant independent predictors of recurrence. A scoring system derived from hazard ratios (scores ranging from 0 to 4) effectively categorized patients into low, intermediate, and high-risk groups.
Conclusion: Lymph node metastasis, DOI >10 mm, and WPOI 5 significantly predict OSCC recurrence. This risk stratification scoring system can guide oncologists in patient management and follow-up.

OFP-10-014

A comparison of molecular genetic features of primary and recurrent sinonasal intestinal type adenocarcinoma

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Background & Objectives: Intestinal-type sinonasal adenocarcinoma (ITAC) arises predominantly in the ethmoid sinus of male patients with occupational exposure to wood and leather dust. ITACs carry a poor prognosis with local recurrences as the main cause of death. Recurrent tumours can arise several years after primary treatment and with a different histological subtype. We performed whole exome sequencing (WES) on pairs of primary and recurrent tumours to investigate if the recurrences are clonal with primary tumours or if they could in fact be second primary tumours.
Methods: Paraffin embedded primary and recurrent tumour samples of 16 cases were collected and DNA was successfully extracted in 15 cases. Relapse time between primary and first recurrence ranged from 1 to 13 years.
Results: WES was successful in 12 primary and all 15 recurrent tumours. Pairwise comparison showed clonal gene mutations in all 12 pairs. Shared mutations included TP53 (4 cases), APC (3 cases), MAPK pathway genes NF1 and KRAS (each 1 case) and PI3K pathway gene MTOR (1 case) and have been described previously in ITAC. In addition, we found tumour pairs with not yet reported mutations in DNA repair pathway gene FANCD2 (2 cases) and DNMT3B (1 case), and SWI/SNF pathway genes SMARCD1, ARID1A and EZH1 (each 1 case). We also found TP53 and ARID1A mutations unique to the recurrence in 2 instances. Two mutations occurred in the primary tumour only, affecting TP53 and NF1 (each 1 case).
Conclusion: Recurrent ITACs are clonal with corresponding primary tumours, also in cases with a long relapse-free time, and should not be considered second primary tumours. In this relatively small series, two-thirds of ITAC harboured actionable mutations in primary tumour that were retained in recurrences. This indicates that personalized treatment of recurrent ITAC may be based on actionable mutations observed in the primary tumour.

OFP-10-015

Molecular characterization of epithelial-myoepithelial carcinoma: insights from mutation and transcriptomic profiling

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Background & Objectives: Epithelial-myoepithelial carcinoma (EMC) is a rare malignancy of the salivary glands, representing less than 1% of all epithelial salivary gland tumours. It is characterized by a biphasic arrangement of inner ductal epithelial cells and outer clear myoepithelial cells. Advances in molecular pathology have identified specific genetic alterations in salivary gland tumours, with HRAS hotspot mutations being frequently associated with EMC. This study aimed to analyse the molecular characteristics of EMC and compare its genetic profile to other head and neck tumours with RAS mutations.
Methods: A retrospective analysis of EMC cases was conducted using histological, immunohistochemical, and transcriptomic approaches. Cases were selected from the archives of Lyon Sud University Hospital and Centre Léon Bérard. Whole-exome RNA sequencing was performed on 14 EMC cases and a comparative cohort of various salivary gland neoplasms. Immunohistochemistry was conducted to assess epithelial and myoepithelial markers. Statistical analyses included differential gene expression and clustering methodologies to establish molecular relationships among tumours.
Results: The study included 14 EMC cases, with a mean patient age of 74.5 years. The majority were located in the parotid gland. *HRAS* mutations were identified in 8 cases, predominantly *HRAS* Q61R. Other genetic alterations included *STAT5B*, *NOTCH1*, and *PIK3CA* mutations. Gene fusions, such as *HMGA2*::*WIF1*, were detected in two cases. Transcriptomic analysis showed EMC clustering closely with basal cell adenoma and separated to pleomorphic adenoma.
Conclusion: EMC exhibits a distinct molecular profile with frequent *HRAS* mutations and transcriptomic similarities to basal cell adenoma. The findings suggest that EMC shares genetic pathways with other salivary gland neoplasms, highlighting *HRAS* as a potential diagnostic marker. Further research is warranted to explore the clinical implications of these molecular alterations.

OFP-11 Oral Free Paper Session Uropathology & Nephropathology

OFP-11-001

Large language model–expert concordance in IgA nephropathy scoring using Oxford classification

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Background & Objectives: Large language models (LLMs) are increasingly used to support histopathological evaluation. However, the degree to which LLM-derived scores align with human assessments in complex pathological conditions remains uncertain. In this study, we used ChatGPT-4o, an LLM developed by OpenAI, to generate lesion scores for cases of IgA nephropathy. Given the clinical importance of consistent and accurate lesion scoring, evaluating the concordance between LLM output and expert interpretation is essential. This study aimed to assess the agreement between LLM-generated scores, expert-revised scores, and original pathology reports based on Oxford classification parameters.
Methods: A total of 127 kidney biopsy reports were scored by ChatGPT-4o, a revising expert pathologist, and according to the original report. Each case was assessed using five Oxford parameters: M, E, and S (scored as 0 or 1), and T and C (scored as 0 to 2). Cases with complete scores across all three sources (n = 105) were included in the final analysis. Agreement between sources was evaluated using Cohen's Kappa, Spearman correlation, Wilcoxon signed-rank tests, and Friedman's test.
Results: ChatGPT-4o and revised expert scores showed near-perfect agreement (Cohen's Kappa = 0.970; Spearman Rho = 1.000; Wilcoxon p = 0.7855). Agreement between ChatGPT-4o and original reports was lower (Kappa = 0.799), as was agreement between revised and original scores (Kappa = 0.819). Friedman's test indicated a statistically significant difference across the three sources ($\chi^2 = 6.71$, p = 0.035).
Conclusion: ChatGPT-4o demonstrated high concordance with expert-reviewed scoring, suggesting that LLMs may aid in identifying inconsistencies in original pathology reports. These findings highlight the potential of LLMs as tools for quality control and decision support in renal pathology. While not a replacement for human judgment, LLMs show promise as reliable adjuncts to improve scoring consistency. Further validation in broader diagnostic workflows is needed.

OFP-.11-002

Two classifications, one disease: Oxford and Banff reveal distinct IgA nephropathy profiles in children and adults

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Background & Objectives: IgA nephropathy is the most common primary glomerulonephritis, diagnosed through kidney biopsy. The Oxford classification describes histological lesions in native kidneys, while the Banff classification is used in transplant pathology but provides additional insight into inflammatory and vascular changes. The aim was to compare Oxford and Banff classification parameters in paediatric and adult patients, in light of differing therapeutic strategies.
Methods: This retrospective study included 253 patients with biopsy-proven IgA nephropathy: 105 paediatric and 148 adult. Clinical data (haematuria, proteinuria, renal function, comorbidities) and histological parameters (glomerular, tubulointerstitial, vascular changes) assessed by Oxford and Banff classifications were compared across age groups.
Results: Paediatric patients more frequently had macroscopic haematuria and IgA vasculitis symptoms ($p<0.001$), while adults had significantly worse renal function (higher urea/creatinine, lower GFR) and frequently suffered from hypertension and diabetes. According to the Oxford classification, adults had more chronic glomerular ($p=0.005$) and tubulointerstitial lesions ($p<0.001$). The Banff classification revealed a higher frequency of both acute inflammatory (t, i, i-IFTA, ti) and chronic (ct, ci) interstitial lesions, as well as vascular changes (cv, ah, aah) in adults ($p<0.05$).
Conclusion: Oxford and Banff classifications reveal significantly more chronic and inflammatory changes in adults. The combined use of both scoring systems can enhance diagnostic precision and guide individualized management in IgA nephropathy. These findings highlight the need for age-tailored therapeutic strategies. The Banff classification adds value in detecting acute inflammation in native kidneys and may improve risk stratification and long-term prognosis.

OFP-11-003

MicroRNA-371~373 cluster is released in testicular germ cell tumours via extracellular vesicles

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Background & Objectives: Extracellular vesicles (EVs) are membrane-derived particles with important roles in cell communication. EV-derived microRNAs (miRNAs) have been considered potential cancer biomarkers. The miR-371~373 cluster has been proposed as a biomarker of testicular germ cell tumours (TGCTs), but to date it is unknown if they are carried in EVs. We aimed to isolate EVs from different TGCT sample types (cell lines, tissue and plasma), and assess the presence of the miR-371~373 cluster.
Methods: A total of 9 TGCT cell lines, 12 patient-derived tissue explants (tumour and normal testicular parenchyma), and matched plasma samples were used. Healthy blood donor plasma samples were used as controls. Conditioned media were retrieved after cells and tissues were cultured in medium. EVs were isolated by a differential ultracentrifugation protocol, divided into two populations (large EVs (lEV) and small EVs (sEV)), and characterized according to MISEV guidelines, including western blot, nanoparticle tracking assay and electron microscopy. EV-RNA was extracted and miR-371a-3p, 372-3p and 373-3p were tested by RT-qPCR for all sample types.
Results: EV-miRNA levels derived from cell lines paralleled the cells inner total RNA, corroborating our hypothesis that these miRNAs are secreted into EVs. We successfully isolated and characterized EVs from conditioned media in culture with TGCT fresh tissue (tumour and normal parenchyma) and from matched plasma samples. Tumour tissues released significantly higher number of particles into the medium when compared to normal tissue, both for lEV and sEV. MiR-371a-3p levels for tumour-derived EVs were significantly higher than in normal tissue/healthy blood donors-derived EVs, both in tissue and plasma. Upon differentiation of NT2 cells with ATRA, both cellular and EV-derived miR-371~373 cluster were downregulated, recapitulating the observations in teratoma tissues.
Conclusion: A significant part of the circulating miR-371~373 cluster is transported in EVs. This protected secretion mechanism highlights the relevance of this miRNA cluster in TGCTs biology.

Funding: NTT holds a PhD fellowship from Fundação para a Ciência e Tecnologia (FCT) - 2022.09566.BD. The authors would like to acknowledge the funding from miREpiTestis – 'Unveiling miR-371-373 cluster epigenetic reprogramming and downstream targets in testicular germ cell tumours' (PI190-CI-IPOP-23-2023)

OFP-11-004

The clinical utility of immunohistochemistry for GPNMB and SOX9 in the differential diagnosis of renal neoplasia with oncocytic features

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Background & Objectives: In addition to oncocytoma (Onc) and chromophobe renal cell carcinoma (chRCC), the current WHO classification includes a category of other oncocytic tumours of the kidney. Many of these entities have overlapping morphologic and immunophenotypic features. Herein, we evaluated the clinical utility of immunohistochemistry (IHC)-based markers, including GPNMB and SOX9, to reliably separate these tumours.
Methods: IHC was performed on whole slide sections of representative cases of Onc (n=14), chRCC (n=14), (*MTOR/TSC1/2*-mutated) low grade oncocytic tumour (LOT; n=13) and eosinophilic vacuolated tumour (EVT; n=5), and *FLCN*-mutated tumours (FMT; n=39). The IHC panel included CD117, CK7, L1CAM, GPNMB, and SOX9. In addition, IHC for cathepsin K was performed in a subset of cases (EVT, n=5; FMT, n=38). IHC results were quantified using H-scores (product of intensity of staining and percentage of positive cells, range: 0-300).
Results: IHC for CD117 and CK7 had expected results: CD117+/CK7- for all ONC and EVT, CD117+/CK7+ for all chRCC, and a CD117-/CK7+ immunophenotype for all LOT. In contrast, FMT showed low expression of CD117 and scattered positivity for CK7 (H-scores of 17 and 65, respectively). With regards to other traditional markers, L1CAM lacked expression in Onc, chRCC and EVT in contrast to LOT and FMT (mean H-scores of 257 and 184, respectively). With regards to newer markers, GPNMB showed absence of staining in Onc, and higher expression in the rest (mean H-scores, chRCC: 171, LOT: 130, EVT: 230, FMT: 265), while SOX9 showed absence of staining in Onc, LOT and EVT, variable positivity in chRCC (mean H-score: 80), and frequent positivity in FMT (mean H-score: 211).
Conclusion: Our results suggest that IHC for markers such as GPNMB (negative in Onc) and SOX9 (variable and diffuse positivity in chRCC and FMT) may complement traditional markers such as CD117, CK7, L1CAM and cathepsin K in the differential diagnosis of oncocytic renal neoplasia.

OFP-11-005

Nested urothelial carcinoma: a rare subtype needs an optimized treatment approach - a multicentre retrospective study

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Background & Objectives: Nested urothelial carcinoma (N-UC) is a challenge for diagnosis and optimal treatment strategy. This multicentre study aims at evaluating prognostic endpoints according to disease extent [non-muscle invasive (NMIBC) and muscle invasive (MIBC)], presentation and treatment [Bacillus Calmette-Guérin (BCG), radical cystectomy (RC) and chemotherapy (CT)].
Methods: Data were collected from 61 patients with N-UC across 5 centres over a 10-year period (2013–2023). Patients were stratified according to time of nested-subtype diagnosis (onset vs recurrence), disease extent (NMIBC vs MIBC) and initial treatment (BCG±RC vs RC only vs RC+CT). Kaplan-Meier analysis was used to assess median progression free survival (mPFS) and median overall survival (mOS).
Results: 15 NMIBC and 26 MIBC were identified, with a median follow-up of 30.6 months. Of the 15 NMIBC, 80% received initial BCG. Patients with N-UC at onset had worse mPFS and mOS [99.6 months (95% CI: 55.2-NR) and 107.3 months (95% CI: 71.6-NR) respectively], than those with N-UC at recurrence [mPFS of NR (95% CI: 42.1-NR) and mOS of 138.4 (95% CI: 51.7-NR)]. According to treatment, the best mPFS and mOS were recorded among patients receiving RC+CT [mPFS = 99.6 months (95% CI: 55.2-NR) and mOS = 107.3 months (95% CI: 107.3-NR)]. Those receiving BCG followed by RC had a mPFS of 84.2 months (95% CI: 68.1-NR) and mOS of 85.9 months (95% CI: 71.6-NR), while those undergoing RC alone apparently had the worse mPFS (42.1 months, 95% CI: 42.1-NR) and mOS (51.7 months, 95% CI: 14.7.1-NR). None of these differences were statistically significant.
Conclusion: This study represents the largest case series of nested urothelial carcinoma. It suggests limited benefit from BCG treatment and most of NMIBC lastly need CT. Diagnosis at recurrence and combination of RC and CT tend to better survivals. Further analyses are ongoing to expand case number and evaluate pathologic features.

OFP-11-006

An audit of correlation between tumour size and renal sinus invasion in renal cell carcinoma

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Background & Objectives: Renal sinus invasion (RSI) is an important prognostic indicator in renal cell carcinoma (RCC), which upstages a tumour to pT3a and influences treatment decisions, including eligibility for immunotherapy. RCCs measuring >7cm have RSI in >90% of cases. This audit aimed to assess the correlation between tumour size, presence of RSI, and sinus sampling in RCC specimens at our centre.
Methods: A retrospective search of the laboratory information system for nephrectomy specimens containing carcinoma examined over a 58-month period was performed. Pathological data collected included histological subtype, tumour size, ISUP grade, and pTNM stage including RSI status (macroscopic and microscopic).
We used the 'Invasive Carcinoma of Renal Tubular Origin Histopathology Reporting Guide, 1st edition (2017). International Collaboration on Cancer Reporting; Sydney, Australia' as our standard.
Results: • 130 cases were identified, with 43% of tumours measuring >7cm and RSI present in 62%.
• 69% of clear cell RCCs >7cm had RSI.
• 63% of tumours were pT3a or higher, with RSI present in 63.4% of these.
• 48% of high-grade RCCs (ISUP 3/4) had RSI versus 29% in low-grade RCCs (ISUP 1/2).

• Macroscopic and microscopic assessment of RSI was discordant in 16% of cases.
• 31% of specimens did not have any blocks labelled as renal sinus, with the terms renal hilum or
pelvis used in 73% of these cases.
• The median number of blocks of renal sinus taken was 1.
Conclusion: The detection of RSI in our audit was 21% lower than the expected standard, with undersampling of the renal sinus and underestimation of macroscopic features likely significant factors. Our results highlight several key areas for improvement, including meticulous macroscopic examination and appropriate renal sinus sampling in tumours >7cm.
Frequent mislabelling of blocks demonstrates the need for differentiation of these terms in guidelines.
Inconsistency in the macroscopic assessment of RSI underscores the need for experienced macroscopic examiners.

OFP-11-007

B-cell antitumor immunity: prognostic role in penile squamous cell carcinoma

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Background & Objectives: Penile squamous cell carcinoma (pSCC) displays the worst prognosis among male genital tumours, and is characterized by slowly increasing incidence and stagnant mortality. Several prognostic markers have been recently identified, including tumour infiltrating lymphocytes (TILs), mostly focusing on T-cells. The prognostic role of B-cells has not yet been sufficiently described in pSCC.
Methods: 152 cases of invasive pSCC with available FFPE tumour tissue were analysed. Whole tissue sections have been examined immunohistochemically for p53, CD20, CD138. The cohort was classified into p53 mutated (overexpression+negative) vs. wild type. B-cell immunoscore (B-IS) divided the cohort based on the expression of the two B-cell/plasma cell markers (CD20 and CD138) counted separately in tumour centre and tumour invasion front per mm2; into the high/low status using the median value of each of the four categories. The B-IS distinguishes five groups: the cases with high status in all four categories belong to B-IS 4, the cases with low status in all belong to B-IS 0. Cox regression and Pearson's chi squared test were used.
Results: The patients with pSCC displaying low B-IS (0-1, n=51) showed significantly worse overall survival (OS) compared to those with high B-IS (2-4, n=101): HR=1.89, 95%CIs 1.18-3.03, p=0.009). Similarly, shorter OS was found in tumours with low CD20+cells in tumour centre (HR=1.67, 95%CIs 1.04-2.7, p=0.033) and low CD20+cells in tumour invasion front (HR=1.69, 95%CIs 1.05-2.7, p=0.029). Of note, high B-IS was strongly associated with a mutated p53 profile (OR=4.76, 95%CIs 1.32-25, p=0.011). High CD20+ cells in invasion front were associated with histological grade 3 (OR=2.44, 95%CIs 1.15-5.26, p=0.015).
Conclusion: High number of tumour infiltrating B-cells is a favourable prognostic marker in pSCC, but displayed unexpected association with mutated p53, which is known as a key detrimental prognosticator. Deeper discussion and research to elucidate the role of p53 in B-cell mediated antitumor immunity are warranted.

Funding: Czech Health Research Agency, NU21J-03-00019

OFP-11-008

BK polyomavirus (BKPyV)-associated urothelial carcinoma in renal and non-renal transplant recipients: a clinicopathological and molecular study

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Background & Objectives: Urothelial carcinoma expressing BK polyomavirus (BKPyV) Large-T antigen (LTag) may represent a distinct tumour entity in transplant recipients. We aimed to identify yet unknown cases and to assess how patients with BK virus nephropathy (BKVN) after non-renal organ transplantation and those with BKPyV-positive urothelial carcinoma differ from renal transplant patients with BKVN.
Methods: We searched the pathology archives of Hannover Medical School over a 20-year period for cases of BKVN and BKPyV-associated urothelial tumours, including patients after solid organ and stem cell transplantation. Identified cases were morphologically re-evaluated and underwent SV40-LTag immunohistochemistry. The clinical course of BKVN patients was analysed retrospectively. Viral isolates from tumour samples were genotyped and sequenced.
Results: 14 of 42 urothelial carcinomas in transplant recipients were SV40-LTag positive by immunohistochemistry. These occurred equally in renal and non-renal transplant patients. SV40-LTag-positive cases were significantly associated with previous BKV infection (p=0.021), tacrolimus-based immunosuppression (p=0.001), and the micropapillary variant (p=0.0002). All 10 successfully amplified isolates belonged to the predominant European genotype Ib-2. Sequencing of BKPyV genomes isolated from tumours showed rearrangements in regulatory elements, including duplications and deletions, particularly in the non-coding control region (NCCR).
Conclusion: BKPyV-associated urothelial carcinoma affects both renal and non-renal transplant recipients. Previous BKVN and tacrolimus therapy are potential risk factors. Early post-transplant BKPyV replication may represent a necessary prerequisite for later tumorigenesis. The observed restructuring of the NCCR may be associated with increased pathogenicity.

OFP-11-009

Comparison of the two urinary markers Bladder EpiCheck and Xpert BC Monitor in the follow-up of 648 patients with non-muscle invasive bladder cancer

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Background & Objectives: The surveillance of patients diagnosed with non-muscle invasive bladder cancer (NMIBC) relies mainly on cystoscopy and cytology. At the Hospital of Bozen two urinary markers based on real-time polymerase chain reaction (PCR) are routinely analysed alongside: Bladder EpiCheck Test, based on DNA methylation alterations associated with bladder carcinoma (BC), and Xpert BC Monitor,

which measures the levels of five target mRNAs. The aim of this study is to confirm the diagnostic accuracy of these urinary markers and to compare them with each other and with urinary cytology and/or histology in the same cohort of patients undergoing follow-up for NMIBC.
Methods: The 648 patients enrolled in this prospective study (for a total of 1900 samples) were tested with urinary cytology, cystoscopy, Bladder EpiCheck and Xpert BC Monitor. Suspicious lesions were biopsied or removed transurethrally, and the samples were reported according to the TNM classification of bladder cancer.
Results: 200 samples were excluded due to invalid values. Of the remaining 1700, 158 showed a recurrence of NMIBC, specifically 106 LG NMIBC and 52 HG NMIBC. The other 1542 cases were negative on cystoscopy and/or histology. The overall sensitivity of cytology was 25.3%. Based on tumour grade, it was 8.4% for LG tumours and 59.6% for HG tumours. Running both tests and considering a result positive if either test was positive, Bladder EpiCheck and Xpert BC Monitor together identified 78.4% of tumours (124/158), 71.6% of LG tumours, and 92.3% of HG tumours.
Conclusion: Xpert BC Monitor and Bladder EpiCheck achieved excellent results. The negative predictive value (NPV) was higher than that of cytology, especially when used together (97%). Their sensitivity was significantly higher than that of cytology in both tumour groups, LG and HG. Together they identified 92.3% of HG tumours. Their specificity was high, but it did not reach the one of cytology.

OFP-11-010
ADAR2, Androgen Receptor (AR), and PD-L1 expression in papillary urothelial carcinoma: implications for prognosis and therapy
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Background & Objectives: Bacillus Calmette-Guérin (BCG) is standard therapy for urothelial carcinoma in situ. Emerging evidence suggests roles for Androgen Receptor (AR), Adenosine Deaminase Acting on RNA 2 (ADAR2), and Programmed Death Ligand 1 (PD-L1) in urothelial carcinoma, with modulation of the tumour microenvironment. This study aimed to investigate these markers in papillary urothelial carcinoma, correlating their expression with clinicopathological features and patient outcomes.
Methods: A retrospective, multi-institutional study was done analysing 128 patients with papillary urothelial carcinoma. Seventy-seven had low-grade papillary urothelial carcinomas (all Ta), and 51 high-grade papillary urothelial carcinomas (11 Ta and 40 T1). Immunohistochemistry was performed on tissue sections to assess AR, ADAR2, PD-L1 expression, and tumour-infiltrating lymphocytes (TILs, CD4/CD8 ratio). Receiver operating characteristic (ROC) curve analysis determined optimal cutoffs for high and low expression. Statistical analyses examined associations between marker expression, clinicopathological parameters, and recurrence-free survival (RFS).
Results: All 77 low grade papillary urothelial carcinomas presented low AR/high ADAR2 levels. Of the 51 high-grade papillary carcinomas, 25/40 T1 cases and 1/11 Ta cases showed high AR/low ADAR2 levels. High AR expression correlated with lower ADAR2 expression ($P < .0001$), higher PD-L1 expression ($P < .0001$) and higher CD4/CD8 ratio ($P < .0001$). Patients with low AR, high ADAR2, and low PD-L1 expression, had better RFS ($P < 0.0001$). Additionally, miR-200a-3p and INF-γ were significantly higher in tumours with low AR/high ADAR2 expression.
Conclusion: This study shows that AR, ADAR2, and PD-L1 expression are significantly associated and are prognostic indicators in papillary urothelial carcinoma.

OFP-11-011
Stroma AReactive Invasion Front Areas (SARIFA) - a promising prognostic biomarker in muscle-invasive urothelial bladder cancer
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Background & Objectives: SARIFA (Stroma AReactive Invasion Front Areas) describes an entity-independent histopathological biomarker with prognostic and possibly predictive relevance. It is assumed that direct contact between tumour cells and adipocytes leads to activation of the tumour's lipid metabolism, providing the tumour cell with significant survival advantages. The prognostic relevance of SARIFA has previously been described in gastrointestinal and prostatic adenocarcinomas. This study investigates the relevance of SARIFA in muscle-invasive urothelial carcinomas (miUC) of the urinary bladder.
Methods: SARIFA is defined as ≥5 tumour cells in direct contact with at least one adipocyte. A single focus is sufficient for classification as SARIFA-positive. The total cohort included samples from 559 miUC patients who underwent radical surgery with curative intent. Cases with poor scan quality or unclear results despite discussion between three pathologists were excluded (n=33).
Results: The prevalence of SARIFA was 56% (296/526). In pT2 carcinomas, the prevalence rate was 31% (SARIFA of submucosal or intramuscular adipose tissue). The prevalence rates of SARIFA were 48% for conventional urothelial carcinomas (UC), 58% for UCs with divergent differentiation (>95% squamoid), 61% for UC with subtype histology, 77% for UC with sarcomatoid dedifferentiation, and 83% for small-/large-cell neuroendocrine UCs (Chi-square $P<0.001$). Median disease-specific survival was 22.9 months in the SARIFA group and 89.7 months in the non-SARIFA group (Log-Rank $P<0.001$). Multivariable Cox regression analysis (adjusted for pT, pN, histology, L, V, biological sex, age, grading), revealed a 1.40-fold higher risk of disease-specific mortality (HR=1.40, 95% CI 1.02–1.93, P=0.033) in SARIFA-positive patients.
Conclusion: After investigations in the gastrointestinal tract, we now present SARIFA as a prognostic marker in the urogenital tract. Following recently published data on prostate carcinomas, we demonstrate the prognostic significance of SARIFA in miUC of the bladder as well. Detailed analyses with additional data from independent validation cohorts will be presented at the conference.

OFP-11-012
AI-assisted prostate cancer grading: validation study on diagnostic accuracy and efficiency
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Background & Objectives: Prostate cancer (PC) is the fourth most common cancer and a leading cause of cancer-related death globally. Accurate grading is essential, as the Gleason score is a crucial predictor of biochemical recurrence and prostate cancer-specific mortality. AI-based solutions have significant potential for enhancing diagnostic accuracy in PC. This study aims to evaluate the performance of an AI algorithm in detecting and grading prostate carcinoma at a tertiary care centre.
Methods: This retrospective analysis included 254 prostate biopsy slides, with 2-3 slides selected per case to enhance dataset diversity.

AI-generated results were compared to the ground truth established by two senior genitourinary (GU) pathologists. The algorithm classified cases as benign, malignant (with Gleason patterns 3, 4, or 5), or benign with ambiguous foci (AMF) needing further review. Key performance metrics included sensitivity, specificity, and ISUP grade concordance (identical grade, 1 or 2 grade differences).
Results: The AI algorithm correctly identified 149 slides as benign (true negatives) and 77 as malignant (true positives), with 17 false positives. Two slides were excluded due to rare atypical acini. Nine slides were flagged for AMF, later confirmed as malignant by pathologists. The AI algorithm demonstrated high sensitivity (100% considering AMF as malignant and 89.5% excluding AMF) and specificity (89.7%). Complete ISUP grade concordance was achieved in 38 of 86 malignant slides, with only 2 showing a 2-grade difference.
Conclusion: The AI algorithm has proven to be a reliable and efficient clinical decision support tool, demonstrating high accuracy in prostate cancer detection and grading. While AI serves as an auxiliary resource, pathologist review remains essential for all cases. This validation underscores AI's potential to enhance pathology processes and improve diagnostic efficiency.

OFP-12 Oral Free Paper Session Molecular Pathology & Haematopathology

OFP-12-001
Anti-oxidants protect Nucleic Acids integrity during paraffin embedding of glyoxal and formaldehyde-fixed tissues

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Background & Objectives: Nucleic Acids (NA) integrity purified from Formalin Fixed Paraffin Embedded (FFPE) tissues represents a pivotal checkpoint in the era of Precision Medicine. Although it is known that most of the NA quality issues are related to the cross-linking between nucleotides and nearby proteins and to the fragmentation induced by formaldehyde, we also reasoned that oxidative events during tissue processing might affect the NA chains. Pursuing improvements in NA preservation, we focused on the two main steps of tissue handling: fixatives and paraffin embedding.
Methods: We envisioned four parallel fixation protocols *per* sample: we compared the standard of care method with neutral buffered formalin (NBF) to the Glyoxal Acid-Free (GAF), a di-aldehyde that only forms unstable links with guanine. Moreover, antioxidants (AO) were added to paraffin for both NBF (NBF-AO), and GAF (GAF-AO) processing. We applied all fixations and embedding workflows on 16 human cancer specimens. A cohort of 100 retrospective, NBF-fixed colorectal cancers (CRCs) were used as external control. We assessed DNA quality using the DNA Integrity Number (DIN) obtained by the TapeStation Assay.
Results: Starting from the different fixatives, GAF ($median_{DIN}$:6) better preserved DNA compared to the matched NBF tissues ($median_{DIN}$:3.75). The retrospective FFPE-CRCs confirmed a superimposable, strong fragmentation induced by NBF ($median_{DIN}$:3.1). The addiction of the AOs to paraffin improved the fragment size for the NBF fixation ($median_{DIN}$:4.85), with the most preserved DNA purified from GAF-AO processed tissues ($median_{DIN}$:7.3). Considering the standard of care (NBF) and the best performing protocol (GAF-AO), we induced a 2-fold increase for DIN, implying a shift from a median size of 2.1 Kbp to 11.2 Kbp.
Conclusion: We prospect a novel, paradigm shifting protocol for DNA preservation in paraffin embedded tissues, based on the reduction of the oxidation during the tissue processing, opening the way to more reliable and reproducible genetic analyses..

OFP-12-002
Spatiotemporal organisation of residual disease in mouse and human BRCA1-deficient mammary tumours and breast cancer

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Background & Objectives: Breast cancer remains one of the prominent causes of death worldwide. Although chemo- and immunotherapeutic agents often result in substantial reduction of primary or metastatic tumours, remaining drug-tolerant tumour cell populations, known as minimal residual disease (MRD), pose a significant risk of recurrence and therapy resistance. Here, we aimed to characterize the spatiotemporal organisation of therapy response and MRD in BRCA1;p53-deficient mouse mammary tumours and human clinical samples using a multimodal approach.
Methods: By focusing on our genetically engineered mouse model for *BRCA1*-mutated breast cancer, we integrating single-cell RNA sequencing (scRNA-seq), spatial transcriptomics (ST), and imaging mass cytometry (IMC) across multiple treatment time points, and characterized dynamic interactions between tumour cell subpopulations and their surrounding microenvironment. Our dataset includes more than 30 individual ST samples spanning multiple timepoints and chemotherapy treatments, complemented by pathological annotations, cell type abundances, and several gene set signatures. This is further supplemented with scRNA-seq data and integrated with IMC for a direct assessment of drug uptake and the associated transcriptional changes. To translate our findings from the mouse model into human disease, we analysed 5 human BRCA1-deficient breast cancer ST samples, characterizing intratumoural heterogeneity and molecular features across species.
Results: Our analysis identifies a distinct, drug-tolerant epithelial-mesenchymal transition (EMT) cancer cell population, which exhibits a conserved expression program in human BRCA1-deficient tumours and significantly correlates with adverse clinical outcomes. We further reveal the spatial distribution of residual EMT-like tumour cells within specific anatomical niches, providing a framework for understanding the persistence of MRD and potential therapeutic vulnerabilities.
Conclusion: Our data yield a comprehensive molecular roadmap of MRD that may open new avenues for therapeutic strategies targeting EMT-driven drug tolerance and tumour relapse.

OFP-12-003
Sestrin3 links aromatic amino acid sensing to proteasome dynamics and tumour progression

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Background & Objectives: The aromatic amino acids (AAAs)—tyrosine, tryptophan, and phenylalanine—have been shown to regulate proteolysis by governing the subcellular distribution of the proteasome between the nucleus and cytoplasm. This dynamic plays a critical role in cancer cell adaptation to stress, and proteasome recruitment was demonstrated to serve as an essential survival mechanism. While mTOR was shown to mediate this response, the upstream sensors through which AAAs influence proteasome localization and cell fate remain unclear. This study aimed to identify the molecular mediator of AAA sensing and its potential role in cancer biology.
Methods: We performed a CRISPR-Cas9 knockout screen, targeting 20 candidate proteins implied in mTOR signalling, to uncover regulators of AAA-induced proteasome translocation. Hits were validated using confocal microscopy, co-immunoprecipitation, mass-spectrometry, and functional rescue assays. The role of the identified mediator was further tested in animal tumour models, and its expression patterns were evaluated in human cancer datasets.
Results: We identified Sestrin3 (SESN3) as a critical mediator of AAA-driven proteasome translocation. SESN3 knockout abrogated nuclear-to-cytosolic proteasome translocation in response to nutrient stress, while ectopic re-expression rescued this function. Mechanistically, AAAs disrupted SESN3's interaction with the GATOR2 complex, particularly with WDR59 and MIOS, thereby relieving its inhibitory effect on mTOR. SESN3-deficient cells showed constitutive mTOR lysosomal localization, independent of amino acid availability. In vivo, SESN3-deficient tumours were significantly smaller (94.1% reduction, $p = 4.5\times10^{-11}$) and exhibited nuclear-restricted proteasome distribution without any intervention. Analysis of human datasets revealed consistent SESN3 overexpression in multiple aggressive tumour types.
Conclusion: Our findings uncover a previously unrecognized signalling axis in which SESN3 serves as a sensor of AAAs, linking nutrient cues to proteasome localization and mTOR activation. SESN3 appears to be a tumour-promoting factor and a candidate oncogene, whose expression may serve both as a biomarker and a potential therapeutic target across cancer types.

OFP-12-004
Spatial tissue proteomics of non-small cell lung cancer (NSCLC)
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Background & Objectives: Lung adenocarcinoma, the predominant subtype of non-small cell lung cancer (NSCLC), exhibits significant molecular heterogeneity, characterized by oncogenic driver mutations, gene rearrangements, and amplifications. Despite advances in targeted therapies and immune checkpoint inhibitors, a substantial proportion of NSCLC cases lack identifiable driver alterations and limiting treatment options. Additionally, resistance mechanisms to therapy remain poorly understood. This study aims to utilize spatial tissue ultrasensitive mass spectrometry (MS)-based proteomics to explore tumour heterogeneity, signalling pathways, and metabolic states beyond genetic alterations, with the goal of identifying novel predictive biomarkers and mechanisms of therapy resistance.
Methods: Retrospective NSCLC samples from formalin-fixed and paraffin-embedded (FFPE) tissues were analysed with deep visual proteomics. Wer employed histology-guided laser-capture microdissection (Leica LMD7) followed by ultrasensitive LC-MS/MS proteomics. Samples were measured with the EvoSep One LC system, coupled to a timsTOF pro 2 (Bruker) mass spectrometer in dia-PASEF scan mode. Additionally, we use patient-derived tumour samples obtained from fine-needle aspirates and cytological smear preparations.
Results: With our approach, we quantified over 5,000 protein groups per sample from approximately 30,000 µm² of FFPE tissue, corresponding to 200–300 tumour cells. Spatially resolved tissue proteomics reveal tumour-specific protein signatures and alterations in signalling pathways in NSCLC depending on the histomorphological subtype, grading and presence or absence of known driver mutations. Notably, this approach also uncovers intratumoral heterogeneity and characteristics of the tumour microenvironment, which may influence immune evasion and variability in therapeutic response.
Conclusion: Morphology-guided ultrasensitive spatial MS-based proteomics is an emerging and powerful approach to study pathophysiology at an unbiased (i.e. untargeted), quantitative and system-wide level. By uncovering tumour-specific proteomic signatures of a few hundred tumour cells with spatial resolution, MS-based tissue proteomics enhances our understanding of tumour heterogeneity and the interaction with its microenvironment, and paves the way for more precise, individualized treatments in NSCLC.

Funding: FONDATION POUR LA RECHERCHE NUOVO SOLDATI

OFP-12-005
A crucial role of DUSP8 in glioblastoma by endothelial transdifferentiation inhibition of Glioblastoma Stem-like Cells
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Background & Objectives: Glioblastoma is the most common malignant brain tumour in adults, characterized by increased VEGF levels, leading to abnormal angiogenesis. While patients respond to VEGF inhibitors, resistance develops over time. Recent studies suggest that glioblastoma stem-like cells (GSCs) can transdifferentiate into endothelial-like cells (GdECs), contributing to resistance to anti-VEGF therapies.
Methods: GSCs were isolated from GBM surgical samples and transdifferentiated into GdECs. Endothelial markers expression was confirmed by flow cytometry, while gene and miRNAs expression was assessed through RNA extraction, qRT-PCR and RNA-seq. Protein analysis was performed with WES technology. Combined ISH/IHC was performed directly on patient tissue to visualize the localization and co-expression of DUSP8 and miR-1825. Drug cytotoxicity experiments were carried out to evaluate selective inhibitors effects on GSC viability. In vivo, xenograft mice were used to evaluate tumour growth, microvessel density and DUSP8/miR-1825 interaction.
Results: We identified a signature of three miRNAs (miR-4516, miR-1281, and miR-1825) that distinguishes GSCs from GdECs. Gene Set Enrichment Analysis (GSEA) revealed the involvement of these miRNAs in angiogenesis, hypoxia, and reactive oxygen species (ROS) metabolism. Specifically, high miR-1825 levels negatively regulate DUSP8 expression. Molecular analysis showed that low DUSP8 levels activate the MAPK signalling pathway leading to high microvascular density ($p=0.041$) and poor overall survival ($p=0.0062$) in GBM patients. Furthermore, DUSP8-overespressing xenograft displayed reduced tumour spread, while those with silenced DUSP8 exhibited increased invasion ($p<0.001$). Pharmacological inhibition of MAPK signalling with ralimetinib impaired GdEC viability and reduced tube

formation ability (p<0.001), highlighting its potential therapeutic relevance.
Conclusion: These findings suggest that regulating the miR-1825/DUSP8 pathway could be a therapeutic strategy to inhibit tumour vascularization in GBM.

OFP-12-006
Enhancing *BRCA* mutation detection in metastatic prostate cancer: the critical role of early testing and sample quality
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Background & Objectives: Metastatic prostate cancer frequently harbours DNA damage repair (DDR) mutations, particularly in *BRCA1 and BRCA2* genes, which are actionable targets for poly(ADP-ribose) polymerase (PARP) inhibitors. Early detection of these mutations is crucial for optimizing therapeutic strategies. However, pre-analytical factors such as tissue storage duration and DNA degradation significantly impact next-generation sequencing (NGS) success rates, potentially affecting patient eligibility for targeted therapies.
Methods: This multicentre study retrospectively analysed 954 formalin-fixed paraffin-embedded (FFPE) tissue samples (559 biopsies and 395 surgical specimens) from 11 italian institutions. The impact of storage duration (categorized into seven intervals: 0–12 months, 13–24 months, 25–36 months, 37–48 months, 49–60 months, 61–72 months, and >72 months), DNA concentration, and DNA fragmentation on NGS success rate was evaluated. Logistic regression and Cox proportional hazards models were used to assess correlations between these variables and sequencing outcomes.
Results: NGS success rate declined progressively across all participating centres over the seven storage intervals, with the highest success rate observed in samples stored for 0–12 months (87.8%) and a significant decrease beyond 72 months, where the success rate dropped to approximately 50% (p<0.001). This sharp decline highlights the detrimental impact of prolonged storage on DNA integrity. Higher DNA concentrations and fragmentation indices were associated with improved sequencing success (p<0.001). Surgical specimens demonstrated superior success rate (83.3%) compared to biopsies (72.8%), likely due to better DNA preservation.
Conclusion: Timely *BRCA1/2* mutation testing is essential to maximize the identification of metastatic prostate cancer patients eligible for PARP inhibitors. Surgical specimens are more reliable than biopsies for *BRCA1/2* detection. Early *BRCA* testing should be proposed in high-risk and very high-risk prostate cancer patients. Standardization of formalin fixation time, DNA extraction, and sequencing protocols across diagnostic centres is crucial for improving patient access to personalized therapies.

OFP-12-007
SPOP mutations and MMR deficiency are associated with high PD-L1, low TIL and high Gleason Score in prostate cancer
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Background & Objectives: The application of immunotherapy in prostate cancer (PCa) has met with limited success to date, with only a small subgroup of patients experiencing significant clinical benefits. This modest response rate stresses the urgent need to refine patient selection. The aim of this retrospective study was to explore the relationship between SPOP mutations and MMR/MSI status with the expression of AR, PD-L1 and TIL (as CD4/CD8 ratio) in a cohort of PCa cases.
Methods: A total of 153 PCa patients were selected. Immunohistochemistry for CD4, CD8, and PD-L1 was performed, with PD-L1 expression evaluated using the Combined Positive Score (CPS). SPOP mutations were analysed by exon sequencing. MMR/MSI status was assessed by immunohistochemistry and the EasyPGX® ready MSI kit (Diatech, Jesi, Italy), respectively. The expression levels of AR and CD274 were examined with qRT-PCR. The role of SPOP silencing on the expression of CD274 was evaluated using SPOP interfering RNAs on two prostate cancer cell lines (LNCaP, PC3) and western blot analysis.
Results: SPOP mutations, identified in 14 out of the 153 samples (9.15%), were associated with higher PD-L1 expression and lower TIL (both p<0.0001), higher Gleason score and higher PSA level (both p<0.0001). Patients with SPOP mutations had increased mRNA levels of CD274 and AR compared to non-mutated patients (p=0.0006 and p=0.0148, respectively). Silencing SPOP expression with specific siRNA led to a significant up-regulation of PD-L1 expression in both cancer cell lines. MMR/MSI status was significantly correlated with higher PD-L1 expression (p<0.0001), lower TIL (p=0.0004), and higher Gleason score (p=0.001).
Conclusion: Our study supports SPOP mutations and MMR/MSI status as potential biomarkers for better identifying PCa patients who could be more susceptible to immunotherapy. Further research is required to validate these findings and translate them into clinical practice.

OFP-12-008
Exploring the relationship between BRAF V600E and PD-L1 in histiocytic dendritic cell neoplasms: a potential link to immune escape?
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Background & Objectives: Histiocytic and dendritic cell neoplasms (HDCNs) are very rare malignancies. Although data are limited, *BRAF* mutations may negatively impact disease progression. In aggressive subtypes like histiocytic sarcoma (HS), treatment

response is generally low, though some patients have shown responses to anti-PD-L1 therapies. This study aimed to investigate the relationship between PD-L1 expression, *BRAFV600E* mutation, histopathological, clinical, and prognostic features of HDCNs.

Methods: We retrospectively analysed 108 patients diagnosed with HDCN between 2006-2025, evaluating histopathological features (necrosis, fibrosis, atypia, immune microenvironment), laboratory and viral data (LDH, CRP, EBV, CMV), risk organ and CNS involvement, treatment response, disease-free survival (DFS), recurrence, and overall survival (OS). PD-L1 expression was assessed by SP263 immunohistochemistry and quantified in tumour and immune cells using 5%, 10%, 20%, and 50% cutoffs. BRAF status was evaluated immunohistochemically.

Results: The mean age was 31.06 years, with 64.2% being male. Subtypes included 65 LCH, 11 BPDCN, 8 HS, 7 RD, 6 JXG, 3 EC, 3 FDHS, 3 IDHS, 1 LCS, and 1 ALK-H. Among 94 evaluable patients, 29 (30.9%) were BRAF-positive. PD-L1 positivity at 5%, 10%, 20%, and 50% cutoffs was 50%, 35%, 26.6%, and 7.4%, respectively. At 5% cutoff, PD-L1 positivity was seen in 83.3% of HS, 80% of RD, 56.1% of LCH, 50% of FDHS and IDHS, 16.7% of JXG, and 100% of LCS and ALK-H, but was absent in EC. PD-L1 positivity was significantly associated with BRAF mutation at 5%, 10%, and 20% thresholds (p=0.014, 0.005, 0.010). Multisystem-involvement was associated with shorter DFS (p=0.001); BRAF and PD-L1 were not directly related. Kaplan-Meier analysis showed 1-year and 5-year OS rates of 90% and 78%, respectively.

Conclusion: Recent study shows *BRAFV600E* promotes immune evasion via PD-L1 in melanoma and papillary thyroid carcinoma. Our findings support this in HDCNs, especially HS with high PD-L1 positivity (83.3%), suggesting anti-PD-L1 therapy as a potential option.

OFP-12-009

Can morphologic features predict TP53 abnormalities in acute myeloid leukaemia post-cytotoxic therapy?

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Background & Objectives: TP53 mutations frequently occur in acute myeloid leukaemia post-cytotoxic therapy (AML-pCT) and are linked to treatment resistance, complex cytogenetics, and poor prognosis. Identifying morphological characteristics predictive of TP53 abnormalities may enhance diagnostic accuracy and clinical management. This study aimed to evaluate the impact of TP53 abnormalities in AML-pCT.

Methods: This study evaluated 50 AML-pCT patients diagnosed between 2010-2025. Bone marrow (BM) morphology was reviewed, and p53 immunohistochemistry (IHC) was performed in 48 patients, with cytogenetic data available for 26 patients. TP53 abnormality was defined as either ≥5% nuclear p53 expression in blasts or deletion of chromosome-17p. Blast cells were graded (G1–G3) based on nucleolar prominence, particularly eosinophilic nucleoli.

Results: The median age of patients was 63 years, with females comprising 52%. The most frequent primary malignancies included hematolymphoid (24%), breast (18%), gastrointestinal (16%) cancers. The median time from primary cancer to AML diagnosis was 39 months. TP53 abnormalities were detected in 54%. Nucleolar grading revealed G1 in 12 (24%), G2 in 14 (28%), and G3 in 21 (42%) patients. Grade 3 blasts (prominent eosinophilic nucleoli) were significantly more common in TP53-abnormal patients (73.1%,p< 0.001). BM-hypercellularity was also more frequent in the TP53-abnormal group (70%,p=0.01). Dysplastic changes were common in all patients.TP53-abnormal patients showed less mature granulocytic lineage cells, though not statistically significant. Notably, one cytogenetically TP53-mutant case lacked detectable p53 protein expression by IHC but had G3 blasts. Median overall survival was identical (3 months) in both groups; however, mean survival was shorter in the TP53-abnormal group (5.20 vs 15.14 months), without statistical significance(p=0.468).

Conclusion: In conclusion, specific morphologic features such as prominent eosinophilic nucleoli and hypercellularity in BM morphology are indicative of TP53 abnormalities in AML-pCT, potentially aiding early detection and diagnostic precision. While p53 IHC provides valuable insights, confirmation through molecular or cytogenetic methods remains indispensable for definitive diagnosis.

OFP-12-010

Genomic profiling of primary cutaneous follicle centre lymphoma reveals major differences from systemic follicular lymphoma with cutaneous involvement and identifies two distinct PCFCL clinicopathological subgroups

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Background & Objectives: Primary cutaneous follicle centre lymphoma (PCFCL) is a rare, indolent cutaneous lymphoma that responds well to local treatment. Differentiating it from systemic follicular lymphoma with cutaneous involvement (FL-CI), which requires systemic treatment and has a worse prognosis, remains challenging. While genetic alterations in systemic follicular lymphoma are well understood, mutations in PCFCL remain unclear. Molecular characterization could aid in diagnosis, reveal different mechanisms driving oncogenesis, and identify distinct patient subgroups.

Methods: We analysed the clinicopathological characteristics and mutational profile using an NGS panel including 120 genes involved in follicular lymphoma pathogenesis. The cohort consisted of 27 PCFCL samples (24 patients), 13 FL-CI samples (10 patients), and the reanalysis of 50 systemic FL samples. The study included two synchronous tumours in one patient (PCFCL) and sequential samples from four patients (2 PCFCL, 2 FL-CI). BCL2 rearrangement analysis was performed using FISH, and clonality was assessed by NGS.

Results: PCFCL showed lower CD10 positivity, with an absence of BCL2 rearrangement (one case), compared to FL-CI. FL-CI exhibited recurrent mutations in chromatin-regulating genes (CREBBP (90%), KMT2D (90%), EP300 (30%)) and overlapped with the mutational profile of systemic FL. We also describe two groups of PCFCL cases: 55% harboured mutations in immuno-scape genes (IRF8, FAS, CIITA, B2M), which were mutually exclusive with 20% of PCFCL cases showing mutations in STAT6 DNA-binding or SH2 domains. These cases showed increased CD23 (5/5) and CD10 positivity (4/5), as well as CREBBP mutations (4/5).

NGS-based B-cell clonality analysis in synchronous and sequential tumours from the same precursor B-cell revealed significant mutational and pathological diversity in PCFCL recurrences. In contrast, FL-CI relapses showed greater genetic and histological stability.

Conclusion: We present the largest cohort of PCFCL, including genomic and clinicopathological data, identifying recurring genetic and pathological features to improve clinical management, differential diagnosis, and characterization of novel subgroups in this rare disease.

Funding: Ramon y Cajal contract (RYC2021-031306-I, Ministerio de Ciencia, Spain)

OFP-12-011

Transcriptional reprogramming of splenic endothelial cells in myelofibrosis

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Background & Objectives: The spleen plays a central role in blood filtration and immune regulation, supporting both steady-state and stress-induced haematopoiesis. Littoral endothelial cells (ECs) are a unique subset of splenic ECs, yet their transcriptional identity remains largely undefined. This vascular niche is particularly relevant in myelofibrosis (MF), where the spleen becomes a major site of extramedullary haematopoiesis (EMH). We aimed to define the native transcriptional profile of human splenic littoral ECs and characterize their molecular reprogramming upon EMH establishment in MF.

Methods: We performed whole-transcriptome digital spatial profiling on 48 regions of interest (ROIs) of FFPE splenic tissue sections from two healthy donors and two MF patients (one Primary MF, one Polycythemia Vera-associated MF). CD8A and CD3E were used as markers to identify splenic littoral ECs (CD8+CD3−) and distinguish them from non-endothelial compartments (CD3+; CD8−CD3−).

Results: In healthy spleen, differential gene expression analysis identified a unique littoral EC signature, consisting of 417 genes upregulated in EC ROIs (adj-p < 0.01, logFC > 0.58). This included NR5A1, a key regulator of splenic vasculature development, along with hallmark genes BLNK, NR0B2, SIGLEC11, STAB2 and IL34. The signature was validated against two reference single-cell atlases of human vascular cells, confirming its specificity for splenic ECs. In MF, the expression of splenic EC signature genes was dampened, indicating a global attenuation of littoral EC identity in favour of genes involved in EC stress response and potentially supporting EMH, including NOS2, NOX4, FOXC1, CX3CL1, PDGFB, and CSF3. Additionally, inflammatory pathways were upregulated, with increased expression of class-I IFN genes, IL6, and complement factors C3 and C5, suggesting a shift toward a pro-inflammatory endothelial state.

Conclusion: Our study delineates the transcriptional landscape of native littoral ECs and uncovers their reprogramming in MF, marked by a transition from intrinsic endothelial identity to a stress-adaptive state.

Funding: This study was supported by the Italian Foundation for Cancer Research (AIRC)

OFP-12-012

Megakaryocytic activation (M-ACT): a novel morphological predictor of fibrotic progression in philadelphia-negative myeloproliferative neoplasms

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Background & Objectives: Philadelphia-negative myeloproliferative neoplasms (MPNs) exhibit variable clinical courses, including progression to myelofibrosis (MF). Current prognostic models lack morphological features associated with fibrotic evolution. This study evaluates Megakaryocytic Activation (M-ACT), a novel morphological parameter, as a predictor of fibrotic progression in MPNs and explores underlying mechanisms.

Methods: We analysed bone marrow biopsies from 450 MPN patients [150 polycythemia vera (PV), 250 early/prefibrotic primary myelofibrosis (PMF), 50 essential thrombocythemia (ET)] at diagnosis. M-ACT was defined by coexisting: 1) megakaryocytic (MK) emperipolesis; 2) MK clustering; and 3) peri-MK fibrosis. Progression-free survival (PFS; progression to overt MF) was assessed. An in vitro model was also developed. CD34+ stem cells were isolated from bone marrow aspirates of patients with Philadelphia-negative MPNs exhibiting M-ACT (n=20), not exhibiting M-ACT (n=20), and healthy controls (n=10). Megakaryocyte differentiation was induced, with CD42+ cell quantification after 15 days. Soluble mediators in culture medium were analysed.

Results: M-ACT was present in 65% PV patients and in 55% early/prefibrotic PMF ones, but absent in ET. M-ACT correlated with splenomegaly, elevated white blood cell count, lactate dehydrogenase, platelet count, JAK2V617F allele burden (PV), and CALR mutations (PMF). M-ACT patients had significantly worse PFS (P<0.0001). Multivariate analysis confirmed M-ACT as an independent predictor of fibrotic progression. In vitro studies showed increased CD42+ cells in cultures from M-ACT-positive patients. Megakaryocytes from M-ACT-positive patients showed higher pro-fibrotic cytokine levels (TGF-β, PDGF) in the culture medium.

Conclusion: M-ACT is a readily assessable morphological parameter that independently predicts fibrotic progression in PV and early/prefibrotic PMF, potentially aiding in differentiating ET from early/prefibrotic PMF. The in vitro model shows that M-ACT megakaryocytes present pro-fibrotic features.

SY-02 Quantitative morphology in electron microscopy - methods old and new

SY-02-004

Electron microscopy in renal pathology. A hospital's experience with an outsourced electron microscope

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Background & Objectives: Electron microscopy (EM) remains vital to the diagnostic repertoire of pathologies; however, in the case of renal pathology, it is essential for certain morphological entities. Fewer and fewer hospitals have an electron microscope and rely on their nearest university or a private company. Our study analyzes turnaround times since our institution's electron microscope ceased to operate in 2020.

Methods: We analysed the response times for sample submission and the ability to view the sample by our centre's pathology team. We analysed the referred cases, nonviable samples (without glomeruli), and the agreement between the paraffin-embedded and ultrastructural diagnoses.

Results: During the period 2020-2024, a total of 326 electron microscopy studies were requested. 318 samples corresponded to renal pathology, the rest to cardiac, nerve, or skeletal muscle pathology. Twelve samples were not representative because they lacked glomeruli or were poorly processed. The mean response time for image viewing, including tissue processing, was 27 days. The level of agreement between the paraffin-embedded and ultrastructural diagnoses was 83%.

Conclusion: Access to EM services remains vital, but is increasingly being outsourced to external centres. Pathologists depend on accurate images and ultrastructural reports to inform the diagnosis. It is

necessary to create hospital referral units to centralize cases, reducing dependence on external centres and increasing quality and efficiency.

Computational Symposium – Selected abstracts

CP-01 Foundation models in pathology

CP-01-004

Leveraging AI for medical laboratories ISO 15189:2022 accreditation and compliance: a histopathology proof-of-concept on documentation and workflow efficiency

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Background & Objectives: As pathology services adopt increasingly complex regulatory frameworks, the demand for scalable digital solutions to manage accreditation workflows has never been greater.
Berkshire and Surrey Pathology Services (BSPS), an ISO 15189:2022 accredited pathology service within the United Kingdom, leverages the iPassport platform to manage its extensive document archive, exceeding 15,000 items, encompassing standard operating procedures (SOPs), work instructions, and quality records. BSPS launched a proof-of-concept using Large Language Models (LLMs) to audit and refine SOPs for potential noncompliance, streamline updates, and reinforce operational excellence.
Methods: We leveraged pre-trained cloud-based models (OpenAI and Mistral), in conjunction with locally deployed quantized models on Msty (Q4 DeepSeek R1 and Mistral Small). Standardised instructions ensured consistency across models. Execution times were documented, and staff contributed by reviewing standard operating procedures to provide practical compliance feedback. This allowed efficient document review and supported ongoing quality improvement initiatives.
Results: LLM-based analysis significantly outperformed manual review. Each model required approximately two minutes per document, compared to twenty minutes for human evaluators. While all models generated relevant suggestions and logical reconstructions, performance varied. Locally deployed models, while faster than human review, occasionally produced nonfactual outputs. Staff engagement was limited, further highlighting the value of automation.
Conclusion: This study shows that LLMs can effectively detect noncompliance issues, identifying up to three times more findings than manual reviewers. Both cloud-based and locally deployed AI models showed strong performance. Human oversight was retained as a critical final validation step, ensuring compliance accuracy and mitigating risks associated with model hallucinations. This initiative informs the development of Project BESSIE (Baseline Enhanced Semantic System for Intelligent Embeddings), a targeted governance AI designed to support ISO-aligned clinical workflows. Our findings position LLMs as a transformative force for accreditation-readiness, quality improvement, and operational efficiency in digital pathology services.

CP-01-005

Analysis of histopathology data drift in a real-world data set over an 8-year period reveals laboratory- and instrumentation-induced variability

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Background & Objectives: AI solutions in histopathology are susceptible to data drift arising from changes in laboratory preparation, slide scanner variability, and other factors. Continuous monitoring after deployment can help combat this problem, which is often performed indirectly by analysing how AI model responses may change over time. Methods to *directly* monitor complex histopathology data, on the other hand, are not well established. We developed a method to directly evaluate data drift in whole-slide images (WSIs) which we applied to slides scanned over an eight-year period to mimic a real-world AI deployment with sample sizes supporting fine-scale time resolution.
Methods: We analysed 5,781 WSIs of Ki-67 breast slides acquired between 2016-2023 at the time of diagnosis (and therefore not contaminated with artifacts associated with retrospective slide scanning). We trained an autoencoder on WSIs from 2016 (reference set) and, using a novel computational paradigm, evaluated data from 2017-2023 to detect deviations from the reference. As a negative control, we held out 50% of the 2016 samples for analysis. As positive controls, we analysed 52 Ki-67 WSIs using a different slide scanner and a set of ER/PR-stained slides scanned alongside the reference data.
Results: Positive control images were strongly separable from reference data, confirming that the model was capable of detecting scanner-induced and even subtle stain differences. In contrast, data drift was of much lower magnitude with occasional deviations that quickly returned to baseline.
Conclusion: This study addresses the unmet need to directly monitor data drift in histopathology for quality assurance after an AI model is put into production. We discovered that scanner-induced differences are far more dominant than laboratory-induced variability at our site. These results not only demonstrate a novel method for AI monitoring but also underscore that best practices in local site validation may be a bigger priority than histology laboratory standardization for ensuring AI safety.

CP-01-006

Enhancing pathologist accuracy and agreement in reporting for prostate cancer: a clinical validation study

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Background & Objectives: International bodies, including ICCR, ISUP and GUPS have provided recommendations regarding minimum data sets for reporting prostate core biopsy (PCB) and Transurethral resections of the prostate (TURP). The use of artificial intelligence (AI) is a potential solution for discrepancies in diagnostic agreement among pathologists. We sought to demonstrate how our model enhanced agreement between pathologists in classifying key clinical findings when assessing whole slide images (WSI).
Methods: The diagnostic accuracy and overall agreement of 29 pathologists were evaluated by classifying PCB and TURP WSIs (n = 1735). Accuracy was evaluated by the per-subject Area Under the Curve (AUC) and overall agreement by the Interclass Correlation Coefficient (ICC).
Results: Analysis of pathologist performance revealed that when assisted with AI, pathologists demonstrated improved diagnostic accuracy and overall agreement in identification of Gleason patterns for both PCB and TURP specimens. When assisted with AI, pathologists' accuracy of acinar adenocarcinoma in PCBs improved from an AUC of 0.84 to 088 for Gleason pattern 3, 0.93 to 0.94 for Gleason pattern 4, and from 0.91 to 0.89 for Gleason pattern 5. Similarly, in TURP specimens, AI-assisted pathologists reported AUC improvements from 0.83 to 0.84 in Gleason pattern 3, 0.91 to 0.91 in Gleason pattern 4, and 0.87 to 0.92 in Gleason pattern 5. Further on this, interobserver classification of Gleason patterns of AI

assisted pathologists was overall in 'Good' agreement (0.75 > ICC > 0.90) for Gleason Patterns 3, 4 and 5 compared to unassisted with 'Moderate' to 'Poor' agreement (0 > ICC >0.75).
Conclusion: The diagnostic assistance provided by the AI algorithm improves pathologist accuracy and overall agreement. AI applications have the potential to enhance patient care by increasing pathologist diagnostic agreement in Gleason grading accuracy, as well as reducing interobserver variability.

CP-01-007
Deepath-SCC: a deep learning model for accurate tissue origin identification in squamous cell carcinoma
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Background & Objectives: Squamous cell carcinoma (SCC) is a common malignancy that arises in various organs. Despite differences in anatomical location, SCCs and urothelial carcinoma (UC) often exhibit similar histomorphological features and immunophenotypes, making it challenging for conventional pathological methods to determine their origin accurately. To address this challenge, we developed and validated Deepath-SCC, a deep learning model designed to improve the accuracy and interpretability of SCC tissue origin identification.
Methods: In this retrospective multicentre study, we assembled a dataset of H&E-stained whole-slide images (WSIs) encompassing nasopharyngeal carcinoma (NPC), head and neck/oesophageal SCC (HNE), lung SCC (LUSCC), cervical SCC (CSCC), and UC. We trained Deepath-SCC, a deep learning-based classifier designed to identify the tissue of origin of pan-SCC directly from H&E-stained slides, without requiring manual tumour region annotation. Model performance was evaluated using the area under the receiver operating characteristic curve (AUROC) and accuracy metrics for tissue origin classification.
Results: Our analysis included 2,144 patients with confirmed diagnoses. In the validation cohort of 865 specimens, Deepath-SCC demonstrated exceptional performance, achieving accuracy of 93.3% (807/865) and AUROCs ranging from 0.975 for UC to 0.995 for NPC. Among 803 high-confidence predictions (similarity score >0.51), the model achieved an overall accuracy of 96.1% (772/803). For primary SCCs, Deepath-SCC attained an overall accuracy of 96.9% (659/680), with subtype-specific accuracies ranging from 94.7% for NPC to 98.5% for LUSCC. For metastatic SCCs, the model achieved an overall accuracy of 91.9% (113/123), with subtype-specific accuracies ranging from 78.6% for LUSCC to 100% for NPC.
Conclusion: The Deepath-SCC model offers a promising, efficient, and cost-effective solution for identifying the tissue origin of SCC, particularly for cases with unknown primary or multiple primary SCC.

CP-01-008
Prospective evaluation of deepath-MSI for microsatellite instability assessment in colorectal cancer: a novel whole slide image-based approach versus promega MSI assay
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Background & Objectives: Microsatellite instability (MSI) plays a critical role in colorectal cancer (CRC) diagnosis and treatment, particularly for guiding immunotherapy decisions. The Promega MSI assay is widely used but has limitations in terms of cost, time, and tissue requirements. This study aimed to compare the consistency of Deepath-MSI, a whole slide image (WSI)-based approach, with the traditional Promega MSI assay in assessing MSI status in CRC.
Methods: A total of 728 primary CRC specimens were prospectively enrolled, all of which underwent Promega MSI assay testing. Samples with fewer than 100 tiles or unclear diagnoses were excluded, leaving 636 samples for analysis. Among these, 490 surgical specimens (24 MSI-H and 466 MSI-L or MSS) and 146 biopsy specimens (11 MSI-H and 135 MSI-L or MSS) were included. The Promega MSI assay served as the gold standard, and performance metrics including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were evaluated for Deepath-MSI.
Results: In the 490 surgical specimens, the overall AUROC was 0.982, with an accuracy of 91.84% (450/490). Using a 0.4 threshold, Deepath-MSI showed sensitivity of 95.83% (23/24), specificity of 91.63% (427/466), PPV of 37.1% (23/62), and NPV of 99.77% (427/428). In the 146 biopsy specimens, the overall AUROC was 0.924, with an accuracy of 88.36% (129/146). Using a 0.2 threshold, sensitivity was 81.82% (9/11), specificity was 88.89% (120/135), PPV was 37.5% (9/24), and NPV was 98.36% (120/122). Overall, Deepath-MSI reduced the need for traditional PCR testing by 87% in surgical specimens and 82% in biopsy samples.
Conclusion: Deepath-MSI provides a highly accurate and efficient alternative to traditional MSI detection methods in CRC. It significantly reduces reliance on costly and time-consuming PCR-based assays, making MSI detection more accessible and less resource-intensive. The integration of Deepath-MSI into clinical practice has the potential to streamline diagnostic workflows and improve patient care.

CP-02 Sustainability & interoperability

CP-02-003
Commercial artificial intelligence solutions in histopathology: a 2025 market landscape from a european perspective
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Background & Objectives: Artificial intelligence (AI) is increasingly becoming a component of digital pathology workflows. Amidst the transition to the In Vitro Diagnostic Regulation (IVDR) across Europe, there is increasing interest in understanding the current landscape of regulatory-cleared AI-based tools in histopathology. This study aims to provide a comprehensive overview of CE-marked and FDA-cleared AI software for diagnostic histopathology, focusing on clinical applications, regulatory trends, and market dynamics relevant to the European setting.
Methods: A structured review was conducted across regulatory databases (FDA, EUDAMED), vendor documentation, press releases, and curated AI repositories. Inclusion criteria encompassed AI tools approved for diagnostic use on whole-slide images (WSIs) in histopathology or cytopathology, bearing CE marking (under IVDD or IVDR) and/or FDA clearance. Key data points included pathology subdomain, stain type, subspecialty, use case, regulatory status, approval

specifications (e.g., scanner regulatory applicability), and integration capabilities.
Results: As of March 2025, 60 CE-marked AI tools were identified from 23 vendors (14 headquartered in Europe). Of the 60 tools, 87% are still operating under the legacy IVDD framework, and 13% of tools are certified under IVDR (i.e., Class C). To date, only three solutions have received FDA clearance. The most common clinical applications include prostate cancer detection, quantification, and grading (n=12), biomarker quantification in breast cancer (ER, PR, HER2, Ki-67) (n=16), and lymph node metastasis detection (n=5). Most tools analyse WSIs from H&E- (n=30) or IHC-stained (n=27) slides. Public resources widely lack detailed information regarding regulatory approval conditions, intended use, system integration, and evidence-substantiated claims of clinical-grade AI-based algorithms in pathology, therefore, the complete dataset will be made available at https://pathology.healthairegister.com.
Conclusion: CE-marked AI solutions in pathology are expanding across various subspecialties, primarily addressing high-throughput diagnostic tasks. For safe clinical adoption and to support purchase decision-making, ongoing efforts towards AI-based pathology market transparency are critical.

CP-02-004
Building a database of tumour immunohistochemical profiles from PubMed abstracts using large language models
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Background & Objectives: Immunohistochemistry (IHC) is essential in diagnostic pathology for tumour classification, prognostication, and treatment decisions. Whilst many IHC markers are well established, others lack consistent evidence with IHC-tumour data often fragmented, outdated, or restricted by subscription. To address this, we leveraged large language models (LLMs) to extract structured IHC-tumour profiles from PubMed abstracts at scale. Our objective was to develop an automated pipeline for building a comprehensive IHC-tumour database.
Methods: A two-stage LLM-based pipeline was developed. First, PubMed abstracts were classified for relevance using a fine-tuned LLM (Gemma2) trained on 1,000 examples. Second, IHC-tumour profiles (tumour type/site, marker name, positive counts) were extracted in structured format using a prompt-based method trained on 462 examples. Marker and tumour names were normalised to Unified Medical Language System (UMLS) concepts to ensure consistency using a SapBERT model. Extracted data were compared against ground truth and reference data (PathologyOutlines) to assess concordance and added value.
Results: Abstract classification was achieved with 91.5% accuracy. From 107,759 abstracts identified for 50 common IHC markers, 30,481 were classified by the model as relevant. IHC-tumour profiles were extracted with a correct output rate of 63.3% (n=98). Across all markers, the total cohort size was over 5 million with an average of 854 per marker. Examining 50 IHC-tumour profiles, 10 lacked reference data, 18 only had qualitative data and 22 had quantitative data all but one within 5% of the calculated. For example, TTF1 showed 79% positivity (3410/4315) in lung adenocarcinoma, within the reference range (65–93%).
Conclusion: This study demonstrates the potential of LLMs to systematically extract and structure IHC-tumour data from biomedical literature. With further refinement, this pipeline will enable the creation of a scalable, prospectively updated open-access granular IHC-tumour database to support diagnostic accuracy, efficiency and research in pathology.

Funding: NIHR Academic Clinical Lectureship, The Jean Shanks Foundation, The Pathological Society of Great Britain & Ireland, Rosetrees Trust

CP-02-005
Artificial intelligence program to engage a broad segment of an academic pathology department
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Background & Objectives: Artificial intelligence (AI) is transforming anatomic pathology. Currently, only limited algorithms are available for clinical application. The algorithm development effort is predominantly in industry. However, pathologists have the domain expertise in pathology with knowledge of the problems that will benefit from AI. The objective of this program is to engage a broad segment of an academic pathology community in AI algorithm development.
Methods: The program is in its sixth year. The platform was developed over the first two years. The platform requirements included an intuitive user interface, diverse algorithmic modelling options, seamless mechanism for discovery to clinical deployment transition, and scalable over time. A vended product was selected. To engage pathologists without prior AI experience, a support system was created that included lectures, open office hours, one-on-one tutorials, short videos for specific topics, ticketing system for questions/problems, data science and project management guidance.
Results: In the first two years of algorithm development (years 3 and 4 of the program), there was an emphasis on project management with at least monthly meetings with a project manager to help resolve problems and allow the investigators to meet their milestones. The first two cohorts included 114 unique users working on 57 projects. Nearly all of the projects progressed to algorithm development and approximately 50% resulted in USCAP abstracts. For the next two years, the same resources are available, but the intense project management was no longer needed. The program continues to have an average of 89 unique users/year working on 25 projects of which twelve are new projects.
Conclusion: Engagement of the pathology community in algorithm development has benefited the pathology staff and trainees with enhanced understanding of AI, interest in developing algorithms, collaborating with vendors, as well as extending their efforts to other AI methods such as foundation models.

CP-02-006
Optimization of large-scale digital scanning operations at a tertiary cancer centre
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Background & Objectives: Memorial Sloan Kettering Cancer Centre in New York is an early adopter of digital pathology. After 17 years of increased digital scanning growth in several hospital locations, the clinical digital pathology operations were consolidated to one central, dedicated, newly built laboratory adjacent to the histology laboratory. The design and build of the new laboratory infrastructure was completed in December 2023, with full clinical operations that started in

January 2024. The resulting quality and productivity gains of the 2024 operations were studied and analysed.
Methods: The planning process for the infrastructure needs was summarized from planning records. The operational data that was collected in the 2024 scanning of >1.4 million slides was compared to the 2023 records. Scan data, turnaround times, rescan rates, instrument failures and downtime data were analysed based on observational and scan team dashboard data. Staffing data were obtained from departmental records.
Results: An increase in digital scanning productivity and a decrease in turnaround times was observed for the 2024 year in comparison to the 2023 operation. This also included a decrease in instrument failures and rescan needs. There were changes in our 24 hours/day staffing needs and training needs not just for the digital scan team but also for the histology laboratory, pathologists, office assistants, slide file room clerks and administration. New digital workflows allowed the digital scanning operation to reach the milestone of prospectively scanning all the departmental in-house cases by the end of 2024. Lessons learned from the new laboratory transformation will be shared in this presentation.
Conclusion: A centralized dedicated digital pathology laboratory adjacent to the histology laboratory allowed the quality expansion of the clinical digital scanning at our institution. This improved lean digital pathology operation is a step towards sustainable digital pathology workflows in a high volume, large pathology department.

Funding: This work was funded in part through the NIH/NCI Cancer Centre Support Grant P30 CA008748

CP-02-007
Deep learning for lymph node metastases detection: toward a unified and accurate pan-cancer diagnostic model
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Background & Objectives: Lymph node metastasis is a key prognostic factor in many malignancies and can be particularly challenging, especially in micrometastases. While they have been extensively explored in specific cancers (e.g., breast or gastric), fewer studies have addressed this issue in a comprehensive pan-cancer context. By leveraging state-of-the-art deep learning methodology, this study introduces a unified framework for detecting and classifying both macroscopic and micrometastatic lymph node involvement across various tumour types.
Methods: A total of 1,030 lymph node whole-slide images were retrospectively collected from patients diagnosed with skin, head and neck, colon, lung, kidney, pancreas, breast, endometrial, and prostate cancers. This in-house dataset was organized into four classes: normal (n=570), melanoma (n=243), squamous cell carcinoma (n=114), and adenocarcinoma (n=103). Each whole-slide image underwent processing with the Trident toolbox and feature extraction using UNIv2. An attention-based multiple-instance learning framework was then employed for the final classification.
Results: Across all tumour types, the proposed model achieved an AUC of 0.976 and a balanced accuracy (BAC) of 0.928. When considering all metastatic lesions as a single class, performance improved to an AUC of 0.984 and a BAC of 0.967. Subgroup analyses demonstrated robust detection of micrometastases, highlighting the model's ability to identify even small or early-stage lesions.
Conclusion: These preliminary findings suggest that this AI-driven approach can reliably detect both macroscopic and micrometastatic spread across multiple cancer types. Future work will focus on external validation to confirm its clinical utility and applicability for large-scale screening. Additionally, evaluating the algorithm's performance in more complex clinical cases and refining the integration process into standard diagnostic workflows will be crucial for maximizing its real-world impact.

Poster Sessions

PS-01 Poster Session Breast Pathology

PS-01-001
Clinicopathological features of breast carcinoma with Ultra-Low Risk MammaPrint® result: a comparative analysis with low-risk cases
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Background & Objectives: MammaPrint® is a 70-gene expression signature that stratifies early-stage breast carcinoma into Low-Risk (LR) and High-Risk groups, supporting personalized treatment decisions. Within the LR, it further identifies an Ultra-Low Risk (U-LR) subset with an exceptionally low probability of distant metastasis. Patients in this group may safely forgo adjuvant chemotherapy and potentially reduce endocrine therapy without compromising long-term outcomes. While the clinical implications of U-LR are gaining recognition, its associated histopathological characteristics remain underexplored.
Methods: We retrospectively analysed patients diagnosed with early-stage luminal breast cancer between 2012 to 2023 who had an available MammaPrint® result. Patients classified as LR and U-LR were selected. Clinicopathological variables—including histological type and grade, tumour size, lymph node status, lymphovascular and perineural invasion, tumour-infiltrating lymphocytes (TILs), progesterone receptor expression (Allred score), Ki-67 index, and recurrence were collected. Statistical analysis was performed using Chi-square/Fisher's exact test or Student's t-test, as appropriate.
Results: Among 470 patients in the MammaPrint® cohort, 215 (46%) were classified as LR and 53 (11%) as U-LR, separately. Significant differences were observed: no U-LR tumours were grade 3 ($p = 0{,}042$), and U-LR tumours showed lower nuclear grade ($p = 0.012$). U-LR tumours were also smaller (1.5 vs 1.7cm, $p = 0{,}022$) and had a lower Ki-67 index (8% vs 13%, $p < 0{,}001$). No other histopathological differences were found. Although not significant, there were no U-LR recurrences, compared to 12 in LR ($p = 0{,}080$).
Conclusion: Our findings offer valuable insight into the histopathological profile of U-LR tumours identified by MammaPrint®. These tumours are characterized by favourable features, including lower grade, smaller size, and reduced proliferation (Ki-67 index). The absence of recurrences in the U-LR group supports its potential role in identifying patients who may safely reduce endocrine treatment while maintaining excellent outcomes. Further studies on long-term follow-up are necessary.

Funding: Research funded by Carlos III Health Institute (PI22/01892, PMP22/00054), Spain

PS-01-002
Clinicopathologic characteristics and tumour-infiltrating lymphocyte patterns in HER2-low vs. HER2-0 triple-negative breast cancer
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Background & Objectives: Triple-negative breast cancer (TNBC) comprises a heterogeneous group of tumours with distinct clinicopathologic, and molecular characteristics. HER2-low, a subset of TNBC, is gaining therapeutic relevance. This study evaluates differences in clinicopathologic features and immune microenvironment between HER2-low and HER2-0 TNBC.
Methods: A retrospective analysis was conducted on surgically resected specimens from 60 newly diagnosed, treatment-naive TNBC patients. HER2 status was determined by immunohistochemistry (IHC), with interobserver agreement among three independent reviewers evaluated using Fleiss' Kappa ($p<0.05$). Clinicopathologic features, along with tumour-infiltrating lymphocytes (TILs), distribution patterns (fully-inflamed, immune-desert, stroma-restricted, margin-restricted), and heterogeneity (>10% variation across tumour areas) were compared between HER2-low and HER2-0 TNBC.
Results: HER2-low TNBC comprised 63% (38/60) of cases. Median age was 63 (IQR: 42–75) for HER2-low and 62 years (IQR: 48–76) for HER2-0. No significant differences were observed in tumour size, grade, lymph node status, or TILs density (all p-values >0.05). TILs distribution patterns were similar across both groups, with immune-desert being the most common phenotype, although these patterns were not properly applicable in all cases. TILs heterogeneity was more frequent in HER2-0 TNBC (45% vs. 27%, p=0.2). Tertiary lymphoid structures were rare (2/60). Invasive breast carcinoma of no special type (IBC, NST) was more common in HER2-low (82% vs. 59%), while metaplastic (23% vs. 2.6%) and medullary (14% vs. 2.6%) carcinomas were more frequent in HER2-0 cases. Substantial HER2 evaluation interobserver agreement (0.707) was noted, with 8.6% clinical critical disagreement rate.
Conclusion: Our findings suggest that HER2-low and HER2-0 TNBC exhibit comparable clinicopathologic features, except for a higher prevalence of IBC, NST, in HER2-low cases, while medullary and metaplastic carcinomas were primarily HER2-0. TILs density and distribution patterns were similar, with greater TILs heterogeneity in HER2-0 TNBC. Disagreements among expert pathologists with similar training background underscore the need for enhanced standardization and ongoing training for HER2-low expression.

PS-01-003

Extracellular matrix remodelling in breast cancer: the role of BMP-1, LTBP-1, and Fibulin-4 in tumour invasiveness and liver metastases

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Background & Objectives: Breast cancer is one of the most common malignancies in women, with a high propensity for liver metastasis. This study evaluates BMP-1, LTBP-1, and Fibulin-4 expression across breast cancer subtypes and liver metastases to clarify their roles in tumour invasion and metastasis. As regulators of extracellular matrix (ECM) remodelling and latent TGF-β activation, these proteins may contribute to tumour–stroma interactions and metastatic progression.
Methods: Immunohistochemical staining for BMP-1, LTBP-1, and Fibulin-4 was performed on 69 samples, including 8 intraductal carcinomas, 24 invasive ductal carcinomas, 22 invasive lobular carcinomas, and 15 breast cancer liver metastases. Staining extent and intensity were each scored from 0 to 3, and their product was used to calculate a final immunohistochemistry (IHC) score. Marker expression levels were compared among tumour groups to evaluate their role in invasion and metastasis.
Results: BMP-1 tumour cell expression was elevated in liver metastases compared to invasive ductal carcinomas ($p = 0.020$). Fibulin-4 and LTBP-1 expression in tumour cells was significantly higher in intraductal carcinomas than in invasive ductal carcinomas ($p = 0.00004$ and $p = 0.0147$, respectively). Fibulin-4 peritumoral stromal expression was markedly higher in metastases than in all primary tumours ($p < 0.001$). LTBP-1 expression was also increased in metastatic tumour cells and intratumoral stroma compared to invasive ductal and lobular carcinomas ($p < 0.01$, and $p < 0.01$, respectively).
Conclusion: The elevated expression of Fibulin-4 and LTBP-1 in tumour cells of intraductal carcinomas compared to invasive ductal carcinomas suggests their potential role in maintaining the non-invasive phenotype, possibly linked to intracellular ECM accumulation before stromal release in early tumour progression. In contrast, increased Fibulin-4 and LTBP-1 stromal expression along with the upregulation of BMP-1 in metastatic tumour cells in liver metastases supports their involvement in TGF-β–mediated ECM remodelling and tumour–stroma interaction that facilitates invasion and distant spread.

Funding: This study was supported by TUBITAK project no: 118S378

PS-01-004

Comparison of clinicopathological characteristics between HER2-ultralow and HER2-null in triple-negative breast cancer

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Background & Objectives: Triple-negative breast cancer (TNBC) is a breast carcinoma subtype that has been shown to have poorer outcomes, mainly owing to the limited treatment options available. In the current context, low human epidermal growth factor receptor 2 (HER2) expression is of interest as a useful biomarker for the treatment of breast cancer with new anti-HER2 drugs. Beyond the evaluation of HER2-low, the inclusion of HER2-ultralow in the DESTINY-Breast 06 trial has further complicated HER2 detection and classification. This study aims to analyse potential clinicopathological differences between the HER2-ultralow and HER2-null groups in TNBC.
Methods: A cross-sectional descriptive study was conducted on a cohort of 146 TNBC patients with HER2-0 (IHC score 0 according to ASCO/CAP 2018 guidelines) diagnosed at our hospital between October 2021 and February 2024. Immunohistochemical expression was assessed using the anti-HER2 antibody (clone 4B5, Ventana). HER2 status was further classified into HER2-null (no staining) and HER2-ultralow (incomplete and faint/barely perceptible staining in ≤10% of tumour cells). Clinicopathological features were compared between the HER2-ultralow and HER2-null groups.
Results: Of 146 TNBC patients with HER2-0, the mean age was 53.6 years (range: 29-90 years). The histologic types in this study were invasive carcinoma no special type (NST) 89.7%; metaplastic carcinoma 8.2%; other special types 2.1%. Histological grade 3 accounts for the highest proportion (83.6%). There were 94 (64.4%) HER2-null patients, 52 (35.6%) HER2 ultra-low patients. There were no significant differences in age, histologic type, grade, lymphovascular invasion, and stromal tumour infiltrating lymphocyte (sTIL) between HER2-ultralow and HER2-null patients. Additionally, no significant differences were found in Ki67 index, AR expression, CK5/6 expression, or EGFR expression (all p> 0.05).
Conclusion: Approximately one-third of TNBC cases with HER2-0 in this study were classified as HER2-ultralow. No significant

clinicopathological differences were observed between HER2-ultralow and HER2-null patients.

PS-01-005

Decision making in breast pathology reporting: the effect of clinical relevant thresholds

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Background & Objectives: In breast cancer (BC) pathology reports, small differences around cut-off values can impact staging and consequently, clinical decision making. Several pathology variables are not very exact, leaving room for interepretation by the pathologist. Therefore, the aim of this study was to investigate pathologists' decision-making around clinically relevant cut-off values.
Methods: We performed a retrospective, nationwide analysis of primary invasive BC specimens in the Netherlands using real-world data from the National Pathology Registry. Data collection included tumour diameter and ER/PR status from patients diagnosed between 2014 and 2022.
Results: Overall, 64.099 BCs were analysed for tumour diameter. For larger tumours (>2 cm), rounding was observed to the nearest half- or whole centimeter. For smaller tumours, rounding occurred only to half-centimeters, while there was an avoidance of the 1.0 cm and 2.0 cm threshold. For ER/PR assessment, 74.502 BCs were analysed. In cases with low ER expression, rounding was observed at multiples of 5. However, around the clinically relevant cut-off value of 10% in the Netherlands, pathologists tend to semiquantify the percentage of ER and/or PR expression, by also using 9% and 11%, with a trend to classify a case as just positive (10% or 11%).
Conclusion: Pathologists take clinical cut-off values into account in their decision making process. For tumour size, they tend to avoid the 1.0 cm and 2.0 cm thresholds. For ER/PR, they tend to categorize the tumour as positive around the threshold. Futher research is needed to determine the implication of this for treatment decisions.

PS-01-006

The landscape of HER2-low breast cancer: a retrospective study

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Background & Objectives: HER2-low breast cancer, defined as IHC 1+ or 2+ with an ISH-negative result, represents a newly recognized category of breast tumours. Precise classification of HER2-low tumours is crucial for both prognosis and treatment decisions. Emerging antibody-drug conjugates provide promising therapeutic options for this patient subgroup.
Methods: From the database of the Emergency County Hospital of Timișoara, all cases of breast cancer evaluated by immunohistochemistry (IHC) for ER, PR, HER2, and Ki67, were identified. Among these, cases of HER2 1+ and HER2 2+ ISH-negative (non-amplified) tumours were selected, for which the following information was collected: patient age, the presence or absence of neoadjuvant treatment, type of specimen (core-needle biopsy, partial or radical mastectomy), histologic tumour type, hormonal receptor status (ER and PR), and Ki67 proliferation index.
Results: A total of 348 cases were collected, comprising 263 surgical resections and 85 biopsies. HER2-low tumours accounted for approximately 35.63% of all cases, with similar distributions in both specimen types. Most HER2-low tumours were diagnosed in patients over 50 years old, particularly in the 61–70 age group. Among 50 cases with a HER2 2+ score, FISH analysis revealed HER2 gene amplification in 7 cases, no amplification in 39 cases, and no available data in 4 cases, resulting in a 22% HER2 amplification rate. Within the HER2-low group, 41.41% were classified as Luminal A, 62.99% as Luminal B (HER2-negative), and 12.60% as triple-negative. Of the HER2-low cases from surgical specimens, 65.45% of patients received neoadjuvant therapy.
Conclusion: HER2-low cancers accounted for just over one-third of all breast carcinomas, a lower prevalence than that reported in the literature, predominantly affecting patients over 50 years old. Most tumours were Luminal A or B, with a minority classified as triple-negative.The prevalence of HER2-low cases in the group of tumours treated with neoadjuvant therapy was 65.45%.

PS-01-009

SUPERB – AI SUPported Evaluation of immunotherapy Response in early triple negative Breast cancer

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Background & Objectives: Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer, where immunotherapies are gaining increasing importance. Despite promising results, not all patients respond to these treatments. The collaborative project SUPERB aims to develop an AI-supported predictive biomarker that accurately forecasts the response to immunotherapy based on (sub-) visual and spatial tissue features. This will enable optimized patient stratification for personalized therapy and improve treatment efficiency.
Methods: We utilized a unique dataset of 328 digitized breast cancer core biopsy slides from the clinical neoMono trial, which investigated an innovative immunotherapy approach for TNBC patients. We developed deep-learning algorithms to analyse histopathological images and to identify predictive tissue and cell patterns. These patterns were then combined to develop the novel "AI Therapy Predictor," which can detect specific cell types, the tumour-associated immune microenvironment, and sub-visual tissue properties before therapy. The AI Therapy Predictor is then, based on these image-based biomarkers, aimed to predict neoadjuvant treatment response (i.e. pathological complete response yes/no).
Results: We completed 292,104 expert-level manual annotations for granular tissue structures and cells on 221 images for multiple tissue classes, including invasive carcinoma, in-situ and immune tissue. These were used in combination with other broader data to build deep learning algorithms for image-based biomarker detection for TNBC patients. On a holdout dataset, the accuracy for the fine-grained delineation of invasive carcinoma tissue structures within tissue images was 93.2% (specificity 99.9%, sensitivity 86.5%). Correlation of the AI Therapy Predictor with treatment response is ongoing.
Conclusion: It is expected that the AI Therapy Predictor will achieve high-precision predictions of therapy response, contributing to

improved care for TNBC patients and advancing the development of AI-assisted diagnostics in oncology.

Funding: BMBF

PS-01-010

The relationship between PIK3CA mutation and tumour immune microenvironment in hormone receptor positive (HR+)/HER2 negative breast cancer and their prognostic value

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Background & Objectives: The prognostic value of tumour-infiltrating lymphocytes (TILs) in HR+/HER2-breast cancer (BC) remains unclear. Studies have shown that genetic alterations in cancer cells can influence the tumour immune microenvironment (TME). PIK3CA gene mutations are the most common genetic alterations in HR+/HER2- BC with unknown impact on the composition of the TME.
Methods: To address this question, we enrolled 123 patients with HR+/HER2- BC with long term follow-up available. Surgical specimens were reviewed for evaluation of TILs in intratumoral (iTIL) and stromal compartments (sTIL) and for presence of stromal plasma cells (PCs). FOXP3+ cells in tumoral and stromal compartments were evaluated by immunohistochemistry on tissue microarrays. Real-time PCR was used for detection of hotspot mutations of the PIK3CA gene.
Results: BCs were luminal A (N=65) or luminal B (N=58). Genotyping PIK3CA was successful in 112 samples, and patients were divided into three groups: wild-type (N=59), exon 9 (N=20) and exon 20 mutation (N=33). Analyzed components of TME did not differ significantly between groups of patients regarding PIK3CA mutational status. Higher iFOXP3+ and sFOXP3+ were associated with lower clinical stage (P=0.039 and P=0.012) and negative nodal status (P=0.029 and P=0.047). Negative PCs were associated with luminal B phenotype (P=0.007), higher recurrence (P=0.019) and metastatic disease at diagnosis (P=0.033). Overall survival was significantly longer for patients with iTIL (P=0.039), higher iFOXP3 and sFOXP3 (P=0.021 and P=0.009) and with positive PCs (p=0.004). Disease-free survival (DFS) was significantly longer for patients with PIK3CA mutation (p=0.041), higher sTIL (p=0.019) and positive PCs (p=0.041). In multivariate analyses PCs showed prognostic value with regard to better overall (HR=0.30; 95%CI 0.11-0.81; P=0.002) and DFS (HR=0.38, 95%CI 0.19-0.78; P=0.008).
Conclusion: Our study demonstrated that FOXP3 and PCs infiltrates were associated with important clinicopathological variables and better prognosis, and also that immune TME of HR+/HER2- BCs don't differ regarding the PIK3CA mutational status.

Funding: This research was supported by Ministry of Science, Education and Youth of Republic of Croatia and Faculty of Medicine University of Rijeka, project ID: uniri-iskusni-biomed-23-202

PS-01-011

Analysis of serum immune profiles in breast carcinoma: association with clinicopathological factors and survival in a retrospective cohort

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Background & Objectives: Recent research has highlighted the crucial role of inflammation in breast cancer (BC). Consequently, recent efforts have focused on identifying biomarkers through liquid biopsies. Cytokines, chemokines, growth factors, and immune checkpoints are among the most relevant, but their serum patterns remain unclear. We aim to analyse different serum factors among BC subtypes and evaluate their association with clinicopathological features and survival.
Methods: We included a retrospective cohort of 229 invasive BC patients and 50 healthy donors. A total of 10 serum factors were measured using LEGENDplex™ panels by flow cytometry. The results were correlated with clinicopathological factors and patient survival. Statistical analysis was performed using the SPSS v.23.
Results: BC patients exhibited higher MIP-3α, IFN-γ, M-CSF, IL-9, and IL-10 and lower IL-2RA, B7.2, IL-27, IL-1β, and PD-1 (all p≤0.047). Younger patients had increased IL-9, IL-10, IFN-γ, M-CSF, and reduced IL-2RA and B7.2 (p≤0.043). IL-9 and IFN-γ were elevated in grade I (p≤0.046) and, alongside IL-10, M-CSF, B7.2, IL-27, and IL-1β, in low-proliferative tumours (p≤0.05). M-CSF correlated with lymphnode involvement and low sTILs (p≤0.029). MIP-3α and IL-27 were elevated in highly proliferative and smaller tumours (p≤0.043) respectively. Furthermore, IL-9, IFN-γ, and M-CSF were predominant in luminal tumours, while MIP-3α was higher in non-luminal subtypes (p≤0.049). Notably, elevated IL-2RA and B7.2 levels correlated with shorter overall survival -OS- (p≤0.009), while high PD-1 was linked to poor disease-free survival -DFS- (p=0.008). However, only IL-2RA and PD-1 (p≤0.013) emerged as independent factors for worse OS and DFS, respectively.
Conclusion: Our results showed that BC patients had specific serum profiles. IL-9, IL-10, IL27, and IFN-γ correlated with favourable clinicopathological features, while M-CSF and MIP-3α with aggressiveness. Moreover, IL-2RA and PD-1 emerged as independent factors for a worse prognosis.

Supported by SEAP-Proyecto Semilla; Expt-200042, Biobank-HGUA-DrB (21-154) and HUB-ICO-IDIBELL (PT17/0015/0024).

Funding: Supported by SEAP-Proyecto Semilla; Expt-200042, Biobank-HGUADrB (21-154) and HUB-ICO-IDIBELL (PT17/0015/0024)

PS-01-012

p53 status and its impact on the response to perioperative hormonal therapy in luminal breast cancer

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Background & Objectives: Perioperative hormonal therapy (pHT) is a common strategy in luminal breast cancer (BC). However, 30-40% of patients develop resistance to this therapeutic modality, leading to higher recurrence rates and worse prognosis. Alterations in p53, present

in up to 55% of luminal B tumours, may influence this response, but its role remains unclear. This study examines the relationship between p53 status and changes in oestrogen receptor (ER), progesterone receptor (PR), and Ki67 expression after pHT, aiming to assess its prognostic and therapeutic implications.
Methods: A retrospective study (January 2020 through July 2024) was conducted on 237 luminal A and B BC patients treated with pHT. Immunohistochemical ER, PR, and Ki67 expression were evaluated in core needle biopsies (CNB) and surgical specimens. p53 status was classified as wild-type (p53-wt) (1-75% positive nuclei/3+) or mutated (p53-mut) (0% or >75% positive nuclei/3+). Associations were analysed using χ^2 or Fisher's exact test.
Results: Medium/high expression of ER (98%), PR (62%), and 15% for Ki67 was found in CNB. In the surgical specimen, we observed medium/high expression of ER (92%), PR (26%), and 6% for Ki67. Among p53-wt BC, ER remained highly expressed (94%), PR was predominantly negative (39%), and Ki67 expression was reduced to <15% (69%) after pHT (all p<0.0001). Similarly, in p53-mut BC, ER was maintained (81%) (p=ns), PR was negative in 55%, and the Ki67 index dropped by 64% after treatment. However, no significant differences were found.
Conclusion: In our clinical series, we observed that p53-wt BC showed a significant reduction in the expression of PR and Ki67. However, these changes were not significant in p53-mut BC. Thus, our data suggest that p53-positive status could predict poor response to pHT and is postulated as a potential predictive biomarker.

Funding: Supported by Grants ISABIAL Expte. 2023-0140 and Expte. 2024-0314

PS-01-013
Correlation of HER2 2+ usual and unusual immunohistochemistry staining patterns with FISH results in breast carcinomas
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Background & Objectives: Apart from the usual HER2 2+ immunohistochemistry (IHC) staining patterns defined by ASCO/CAP guidelines, there are patterns that do not exactly fulfil their criteria and the guidelines are silent on whether these would merit inclusion into the HER2 2 + category. The objective of our study is to evaluate the proportion of different HER2 2+ IHC staining patterns and their correlation with FISH results.
Methods: 210 breast carcinoma core biopsies reported as HER2 2+ over a period of 1 year were studied. All cases reported as HER2 2+ were subjected to FISH analysis. HER2 2+ cytoplasmic membrane staining patterns were classified into described usual pattern and unusual staining patterns as all nondescript cases were also included in HER2 2+ category in our institute. Unusual patterns include 1) complete intense in ≤10% cells, 2) incomplete, weak to moderate in >10% cells 3) complete, weak to moderate in 10% cells 3) basolateral or basal 4) cytoplasmic granular staining. The proportion of FISH positivity was compared between the usual and unusual IHC patterns.
Results: HER2 gene amplification was seen in 34/210 (16%) cases of which 18/34 (53%) cases showed usual (complete moderate >10%) pattern and 16/34 (47%) cases showed unusual patterns (intense complete <10% - n=2 (6%), complete moderate 10% n= 8 (23%), incomplete moderate n= 6 (18%) while cases with cytoplasmic granular or basolateral staining were negative for FISH.
Conclusion: In addition to the described usual HER-2 2+ staining patterns, our study showed 4 unusual patterns. Few cases with incomplete moderate intensity and complete moderate intensity staining in 10% cells which may not be have been subjected to FISH testing if strict guidelines were followed, showed FISH positivity. Our study shows that these rare IHC pattens should be recognized and reflexed to FISH testing to avoid missing HER-2 targeted therapy in possible HER-2 amplified tumours.

PS-01-014
Exploring the transcriptomic landscape of non-metastatic axillary lymph nodes as a prognostic factor in breast cancer
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Background & Objectives: The intratumoral immune response plays an important role in breast cancer (BC) prognosis. However, limited research has explored the potential impact of the immune response within axillary lymph nodes (ALNs). Studies evaluating the immune composition of non-metastatic ALNs (ALNs-) using immunohistochemistry suggest that ALN- immune cellularity may be a prognostic factor for patient survival and relapse. Given the observed differences at the protein level, this study aims to analyse whether transcriptomic differences in ALNs- are also associated with prognosis in BC patients.
Methods: This retrospective cohort study included 18 patients diagnosed with invasive ductal BC between 2006 and 2015. Clinicopathological data were collected, and patients were followed for 10 years from diagnosis. Formalin-fixed paraffin-embedded ALN- samples were selected for RNA extraction and gene expression analysis using Human Clariom S microarrays to identify differentially expressed genes between patient groups. Bioinformatics analysis was conducted using Bioconductor in R.
Results: This study included three patient groups: Relapse (n=6), Exitus (n=6), and Alive (n=6). Bioinformatics analysis identified Butyrophilin Subfamily 3 Member A2 (*BTN3A2*) as the only gene found across all comparisons, specifically in the Relapse vs. Exitus comparison, with a log fold change (logFC) greater than 2 (logFC=2.15). Biological significance analysis revealed that *BTN3A2* is involved in over-represented biological processes related to immune response regulation (normalized enriched score (NES)=1.53) and activation (NES=1.62). However, no differentially expressed genes or biological processes were found using an adjusted p-value threshold of 0.05. Higher *BTN3A2* expression was significantly associated with a lower histological grade (p=0.013) and improved overall (p=0.042) and cancer-specific survival (p=0.017).
Conclusion: *BTN3A2* plays a role in T-cell responses in the adaptive immune response. Therefore, these findings underscore the importance of further investigating the ALN microenvironment, as immune responses within ALNs may also play an important role in BC prognosis.

Funding: This work was supported by BosomShield, a project that has received funding from Marie Skłodowska-Curie Doctoral Networks Actions (HORIZON-MSCA-2021-DN-01-01) under grant agreement 101073222. Further support was provided by SCARLET, a project funded by Proyectos Estratégicos Orientados a la Transición Ecológica

y a la Transición Digital, from the 2021 call of the Ministerio de Ciencia e Innovación, with grant number TED2021-130081B-C22 and funding from NextGenerationEU. Esther Sauras Colón was also beneficiary of a grant from the Generalitat de Catalunya (Doctorats Industrials, Pla DI, AGAUR, Grant No. 2022DI057)

PS-01-016

Long term follow-up of B3 lesions

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Background & Objectives: The B3-category encompasses a group of lesions with low potential of malignant transformation. The aim of the present study is to evaluate the evolution of B3-lesions in long term follow-up, comparing cases treated with open surgery and cases that did not undergo surgery.

Methods: A revision of 256 B3 lesions, including flat epithelial atypia (FEA), atypical ductal hyperplasia (ADH) and classical lobular neoplasia (LIN), diagnosed between January 2008 and December 2015, by VAB was performed.

Cases were subdivided as follows: "Open surgery" group (OS, 168 cases in which surgical excision followed the B3 diagnosis) and "VAB only" group (88 cases in which no further surgery was performed).

Results: Open Surgery: 25% (42/168) were upgraded to in situ/invasive carcinoma. The upgrade rate was the highest in ADH (35.71%) and in mixed lesions (23,6%).

VAB only: 9% (8/88) developed in situ/invasive carcinoma during the follow-up period (mean 12.5 years). No further events were recorded in 80/88 cases (91%).

FEA, both pure and mixed, was the most frequently occurring lesion in both groups.

Conclusion: Open Surgery: upgrade rates corresponded to the average upgrade rates reported in literature. However, the scientific literature reports a wide range of upgrade with marked inter-institutional differences, leaving the question of the optimal approach for the treatment of these lesions open for debate.

VAB only: A strict follow-up was shown to be a sufficient measure to avoid disease progression in 91% of cases; the 9% of patients that have presented with disease upgrade are currently alive and in follow-up. The results of this study suggest that open surgery can be avoided in patients with B3 lesions, and that a strict follow-up regime is sufficient in order to maintain control over the disease.

PS-01-017

Agreement analysis between manual and computational scoring of Ki-67 in breast cancer

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Background & Objectives: Pathologists traditionally assess Ki-67 through visual estimation, a method prone to variability, especially when the proliferation index is not clearly high or low. This subjectivity increases the likelihood of discrepancies in borderline cases. The gold standard for Ki-67 evaluation remains manual counting of positive and negative tumour cells, expressed as a percentage. However, this approach is time-consuming and impractical for routine clinical use. With advancements in digital pathology and AI-driven algorithms, automated quantification has become a feasible solution.

Methods: Ki-67 specimens stained with clone MIB-1 (Agilent) using the BenchMark Ultra (Roche) were selected from a slide repository to cover a clinically relevant range. Both Ki-67 and corresponding H&E slides were scanned at 20x on GenASIs HiPathPro (Applied Spectral Imaging). Three regions of interest (ROIs) per slide were digitally marked within the tumour area on the H&E images and automatically transferred to the Ki-67 images following tissue matching. Marked regions were scored by the computational algorithm to determine the Ki-67 score. Three pathologists independently assessed the same ROIs and results were statistically compared.

Results: Core biopsies from 23 breast cancer patients (age 53±13) were included, 22 with IDC and one with mucinous carcinoma. A total of 69 ROIs were analysed. The Intraclass Correlation Coefficients (ICC) between pathologist's Ki-67 assessments were 0.899, 0.902 and 0.913, comparable to the ICC between each pathologist and the computational algorithm (0.929, 0.911 and 0.929). When applying a cutoff of 30%, high agreement was observed for all data pairs with a Cohen's Kappa measure higher than 0.85 (0.87, 0.91 and 0.91 between pathologists and 0.87, 0.91 and 1.00 between pathologist and computational score).

Conclusion: Our analysis evaluates the agreement between manual and automated scoring, highlighting the potential of computational algorithm to enhance accuracy and reproducibility in Ki-67 assessment.

PS-01-018

HER2 APP, breast cancer based algorithm for precise scoring of HER2-null, ultra-low, and low expression as an alternative to ASCO/CAP visual scoring: an analysis of 422 cases

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Background & Objectives: ASCO/CAP updated breast HER2 guidance to include HER2-null [HN], HER2-Ultra-Low [HUL], and HER2-Low [HL]. Reporting HUL and HL is challenging because it requires extensive examination of specimens that are time intensive and imprecise. Artificial Intelligence [A.I.] advancements have enabled membrane staining quantification, though real-world use is unclear. This study assesses A.I.-based membrane scoring as a complement or alternative to visual scoring [VS].

Methods: 422 core biopsies of real-world, invasive breast type NOS, HER2 0 (n=225) and HER2 1+ (n=197) cases, were retrieved from 2023-2024. Original slides were anonymised, scanned at x40, and analysed with an advanced version of Visiopharm's HER2-APP, Breast Cancer algorithm [APP]. APP scored cases were stratified with updated ASCO/CAP criteria using APP derived cell membrane positivity (MP) percentages. Cases were reclassified as HN: MP=0%, HUL: MP=1–10%, and HL: MP>10%. VS was not re-evaluated.

Results: APP scores reclassified original cases into HN (n=40; 9.5%), HUL (n=122; 29%), and HL (n=260; 61.5%). From the diagnosed VS HER2 0 group (n=225), 38 (17%) persisted as HN, while the remaining were reclassified as HUL (n=116; 52%), and HL (n=71; 31%). 187 (83%) previously HER2 0 cases were reclassified as positive. In the VS HER2 1+ group,189 (96%) cases were classified as HL, 6 as HUL, and 2 as HN. The majority of HUL cases contained a MP of ≤ 5% (n=80).

Conclusion: APP precisely quantified MP, distinguishing HN, HUL, and HL. Potentially 52% of previously "negative" cases fit the HUL category, greatly increasing Trastuzumab Deruxtecan [T-DXd] eligibility. Most HUL cases had ≤ 5% MP, which is challenging for VS detection.

APP shows a promising approach for identifying these groups according to updated ASCO/CAP guidelines. Precise, unbiased MP scores may also enhance T-DXd dosing for lower toxicity and better patient outcomes. Agreement and process time analysis vs VS are needed to reassure clinical utility.

PS-01-019

Pathological characteristics of male breast cancer: a study of 81 cases in Southern Tunisia

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Background & Objectives: Male breast cancer (MBC) is a rare condition representing less than 1% of all male neoplasms. Despite the morphological resemblance to female breast cancer (FBC), MBC has different pathological characteristics. We aimed to investigate the clinico-pathological features of MBC.
Methods: This is a retrospective study of 81 cases of MBC, registered at the department of pathology of the university hospital of Sfax in Tunisia, during a period of 19 years (2006-2024).
Results: The mean age was 68 years (29-90 years). The mean tumour size was 3.4 cm (0.5-13 cm). The tumours were bifocal in 6 cases and bilateral in 2 cases. One patient had gynecomastia. Invasive carcinoma of non-specific type (ICNST) was the most common histological subtype, accounting for 87.6% of cases (n=71). The other tumours were invasive lobular carcinoma (ILC) in 3 cases, ductal carcinoma in situ in 3 cases, encapsulated papillary carcinoma in 2 cases, invasive micropapillary carcinoma in one case and angiosarcoma in another. The most common histological grade was II in 68% of cases. Node involvement was observed in 65% of cases. Paget disease was associated in 7.4% (n=6). Estrogen receptors (ER), progesterone receptors (PR) and Her2 status were positive respectively in 82.8%, 81% and 23.8%. The most frequent molecular subtype was Luminal A in 70.7%, followed by luminal B (22%), Her2 overexpressing (4.8%) and triple negative (2.5%).
Conclusion: Less than 1% of breast cancer patients are male. For MBC, The mean age at diagnosis is around 60 years, 10 years later than in women. ICNST is the predominant histological type. ILC is exceptional. Compared to the FBC, MBC is more hormonosensitive with less frequency of Her2 overexpressing. Triple negative tumours in MBC are rare. MBC seems to be more aggressive than FBC due to its discovery at an advanced stage with larger tumour size and frequent node metastases.

PS-01-020

HER2 scoring agreement for HER2-low and overexpression in breast carcinomas: comparison of HER2 status in breast carcinomas tested by four different HER2 IHC assays scored manually by pathologists and AI

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Background & Objectives: Artificial Intelligence (AI) enhances accuracy, efficiency, and consistency of HER2 IHC scoring. This study compares the interobserver accuracy of four HER2 IHC assays in breast carcinomas (BCs) between AI and pathologist assessments focusing on HER2-low and HER2 classical overexpression.
Methods: 98 human FFPE BCs from two microarrays were analysed by FISH and four different IHC assays: (1) HercepTest SK001, Agilent, (2) HercepTest GE001, Agilent, (3) PATHWAY 4B5, Roche, and (4) HER2 EP3, Sakura Finetek using 2023 ASCO/CAP guidelines. Consensus IHC results were determined by four reviewers serving as ground truth and then compared to AI from IMSTAR Dx.
Results: Initial clinical agreement from the reviewers for the HER2 IHC assays GE001, SK001, 4B5, and EP3 were 92.9%, 92.9%, 88.8%, and 87.8%, respectively, and a final clinical agreement was consolidated as ground truth. Final clinical agreement between reviewers and AI for HER2 IHC assays 4B5, GE001, EP3 and SK001 were 93.9%, 83.7%, 80.6% and 70.4%, respectively. The clinical disagreement usually occurred for HER2-low BCs. The negative predictive agreement (NPA) between reviewers and AI for HER2 IHC assays EP3, 4B5, SK001 and GE001 were 100%, 91.9%, 89.3%, and 73.1% respectively. The positive predictive agreement (PPA) for 4B5, GE001, EP3, SK001 were 97.2%, 95.7%, 73.6%, and 62.9%.
Conclusion: There is a strong NPA for EP3 and a strong PPA for 4B5 when comparing AI to the ground truth. Similarly, interobserver variability in HER2 IHC scoring across the four IHC assays was observed, with greater disagreement for the EP3 assay. The discrepancy between reviewers and AI likely stemmed from the fact that both observers and AI were primarily trained on the 4B5 assay with its specific staining profile rather than all assays. To ensure diagnostic and clinical accuracy, alternative IHC assays should be integrated into training and validation of HER2 IHC scoring algorithms, including AI.

PS-01-022

Diagnostic utility of TRPS1 immunohistochemistry in identifying breast origin: a two-year retrospective analysis

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Background & Objectives: TRPS1 has been proposed as a potential immunohistochemical marker for determining the breast origin of metastatic tumours. Accurate identification of the primary site is critical for guiding treatment strategies, making TRPS1 a valuable diagnostic tool. In this study, we aimed to share our two-year experience in evaluating the utility of the TRPS1 antibody in identifying breast origin.
Methods: Between 2022 and 2024, cases examined with the TRPS1 antibody were retrospectively reviewed. The expression of TRPS1 was assessed in various primary tumour origins, including breast, lung, gastrointestinal, gynaecological, and other malignancies. Statistical analyses were performed to determine the sensitivity, specificity, and predictive values of TRPS1 for identifying breast origin.
Results: A total of 250 cases were included in the study, of which 95% (n=238) were female and 5% (n=12) were male. The primary tumour site was the breast in 68% (n=171) of cases, while 27% (n=67) had other primary sites and, in 5% (n=12) of cases, the origin of the tumour could not be determined due to poorly differentiated tumours or insufficient tumour tissue. TRPS1 expression was positive in 66% (n=165) of cases and negative in 34% (n=85). Of the TRPS1-positive cases, 96.4% were breast cancer. Interestingly, most TRPS-1 positive non-breast cancers (83.3%, n:5) were gynaecological.
TRPS1 demonstrated a sensitivity of 93% (95% CI: 88.1%-96.3%) and a specificity of 91% (95% CI: 81.5%-96.6%) in detecting breast carcinoma. The positive and negative predictive values were 96.4% (95% CI: 92.3%-98.7%) and 83.6% (95% CI: 73.0%-91.2%), respectively.
Conclusion: TRPS1 immunohistochemistry is a highly sensitive and specific marker for differentiating breast cancer from other malignancies. Its high positive predictive value suggests that TRPS1 expression in metastatic tumours is strongly indicative of breast origin. However, it should be noted that TRPS1 positivity can also be observed in other tumours, particularly gynaecological malignancies.

PS-01-023

Aberrant expression of p53 in HR+/HER2- early breast cancer – association with luminal B/non-luminal subtypes and higher risk category in the Prosigna Assay

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Background & Objectives: Pathogenic *TP53* mutations have been associated with endocrine resistance in hormone-receptor-positive, HER2-negative early breast cancer (HR+/HER2-BC). We have validated aberrant patterns for p53 (p53abn) in immunohistochemistry (IHC) known from gynaecologic cancers as surrogate markers for mutations in BC (*Armbruster et al, Virchows Arch 2024*). The present study delineates the results of the Prosigna gene expression profile (Veracyte) in this selected group of potentially high-risk patients.

Methods: We included 199 consecutive cases of early HR+/HER2-BC from the University Women's Hospital Tuebingen from 2023-2024 analysed with the Prosigna assay (including NST and ILC, pT1 and pT2, pN0 and pN1a). p53-IHC pattern was classified into four categories: variable nuclear expression (wild-type, wt), and the aberrant patterns (p53abn) defined as overexpression, complete absence and cytoplasmic.

Results: p53abn was observed in 24 of 199 cases (12.1%) of HR+/HER2- BC. p53abn cases were distributed differently across molecular subtypes (LumA 29.2%, LumB 58.3%, HER2-enriched 4.2%, Basal-like 8.3%) compared to p53wt pattern (LumA 53.1%, LumB 45.1%, HER2-enriched 1.1%, Basal-like 1.1%) (p=0.01, Pearson-Chi-Square). A tendency towards higher risk categories for distant metastasis was computed for the p53abn group, with low/intermediate/high risk were 16.7/29.2/54.2% for p53abn vs. 33.1/30.9/36.0% for p53wt pattern.

Conclusion: p53abn was found in a significant number of HR+/HER2-early BCs and was associated with gene expression profiles enriched for LumB/non-luminal cases. The weak association with Prosigna risk categories might indicate p53 as an independent prognostic parameter. Further clinical investigations are required to show whether the systematic application of *TP53* mutational profiling or its validated surrogate marker, p53 IHC staining patterns, is able to identify patient subpopulations potentially at risk of suboptimal therapeutic efficacy from adjuvant endocrine therapy alone.

PS-01-024

Tumour-infiltrating lymphocytes in triple-negative breast cancer: What is their correlation with molecular subtypes, tumour grade, and stage?

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Background & Objectives: Tumour-infiltrating lymphocytes (TILs) are key components of the tumour microenvironment and play a crucial role in the immune response against cancer. In triple-negative breast cancer (TNBC), TILs are particularly relevant as prognostic markers. This study aims to evaluate the presence and distribution of TILs in TNBC and examine their correlation with tumour grade, tumour size, and disease stage.

Methods: This retrospective study examined 64 consecutive cases of triple-negative breast cancer (TNBC) treated surgically at CAC Batna Hospital in 2023. TNBC was defined by the absence of oestrogen receptor, progesterone receptor, and HER2 expression on immunohistochemistry. Tumour-infiltrating lymphocytes (TILs) and their volume (TILV) were assessed on haematoxylin and eosin (H&E)-stained slides according to International TILs Working Group (ITILWG) guidelines. Stromal TIL density was quantified by estimating the percentage of tumour stroma occupied by lymphocytes, excluding necrotic areas. Cases were classified into low (<10%), moderate (10–30%), and high (≥30%) TIL infiltration groups. To ensure reliability, two senior pathologists independently and blindly reviewed all evaluations.

Results: TIL analysis revealed distinct stromal (sTIL) and intratumoral (iTIL) infiltration patterns. High sTIL correlated with larger tumours (r=0.45, p=0.003) and elevated grade (35% vs. 15%, p=0.002), while iTIL increased with metastases (25% vs. 10%, p=0.005) and advanced stage (p=0.008). The strong sTIL-iTIL correlation (r=0.52, p<0.001) suggests coordinated anti-tumour immunity. Notably, iTILs showed stronger association with poor prognosis markers, potentially serving as biomarkers for metastatic risk and treatment resistance. These findings highlight the need for standardized TIL assessment protocols in clinical practice. Future studies should explore how TIL spatial distribution influences immunotherapy response and patient outcomes, particularly in aggressive tumour subtypes.

Conclusion: The evaluation of TILs in triple-negative breast cancer provides valuable insights into the antitumor immune response. This analysis is a quick, cost-effective method that can enhance clinical management by refining therapeutic strategies and optimizing treatment decisions.

PS-01-025

Phyllodes tumours of the breast: Pathologic characteristics of 81 cases, with a highlight of the diagnostic challenges

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Background & Objectives: Phyllodes tumours of the breast are neoplasms of fibroepithelial origin and are rare, with an estimated incidence rate of 2.1 per million female patients per year. They can be categorized, using their histological features, into benign, borderline or malignant. We present an analysis of 81 cases, examined in our Pathology Department over a 20-year period.

Methods: A comprehensive search was performed in our Department's database. Patients with pathology reports compatible with biopsies and excision specimens of phyllodes tumours of the breast, over the prior 20 years, were included. Reports and tissue slides were separately reviewed by a different than the initial diagnosing pathologist. For patients with a probable or definite diagnosis of phyllodes tumour of the breast, patient records were accessed to determine patient characteristics. A thorough and complete assessment of each patient's histopathologic reports followed.

Results: We identified 81 total patients. Regarding patient characteristics, all 81 (100%) were female. Mean age at diagnosis was 50.7 years (SD 14.93 years). The type of specimen was core needle biopsy for 4 patients (4.9%) and excision specimen for 77 patients (95.1%). Median tumour size was 4.4 cm (IQR 2.85 cm). Among the 71 excised, unequivocally categorized phyllodes tumours, 46 (64.8%) were classified as benign, 12 (16.9%) as borderline and 13 (18.3%) as malignant. Diagnostic challenges occurred in 6 (7.7%) cases of excision specimens. Recurrence occurred in 6 (7.7%) patients having undergone

excision. The heterogeneity in mitotic activity accounted for most of the diagnostically challenging cases.
Conclusion: Phyllodes tumours of the breast present rare, yet not uncommonly encountered tumours in surgical centres with high volume of Breast Pathology specimens. Accurate histologic categorization is important for subsequent appropriate management. Special attention is required in the categorization of cases with overlapping features.

PS-01-027
Insulin-like growth factor receptor 1: expression and prognostic significance in diabetic and non-diabetic women with breast cancer
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Background & Objectives: Aim was to investigate the correlation between expression of IGF1R and basic histopathological and immunohistochemical prognostic breast cancer parameters and to investigate the difference between diabetic and non-diabetic women. Patients with type 2 diabetes mellitus (T2DM) may have a poor prognosis due to the increased number and activity of the insulin-like growth factor receptor 1 (IGF1R) in a physiological environment of hyperglycemia
Methods: A 129 women with invasive breast cancer (stage I-III) have been diagnosed in University hospital Foča; prior surgery T2DM was diagnosed in 14 (10.8%) women. Formalin-fixed paraffin-embedded tumour samples we used for immunohistochemically staining for visualization: IGF1R, oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor (HER-2). Statistical analyse of the obtained data was performed using the SPSS version 17.0; two-sample t-test was performed. The relapse-free survival (RFS) was examined using *Kaplan-Meier* curves, and the difference between parameters was assessed by the *Log-Rank test.*
Results: Women with T2DM had significant higher tumour stage (P=0.038), number of metastatic lymph node (P=0.019), diameter (P=0.039) of breast cancer, ER expression (P=0.001) and IGF1R expression (P=0.039), as well as significant higher rate of multifocality/multicentricity (P=0.036) of breast cancer. Log-Rank test showed that T2DM (P=0.023), tumour stage (P=0.039) and HER-2 (P=0.033) were independent prognostic factors for RFS
Conclusion: Type 2 diabetes mellitus was associated with adverse outcomes because of early recurrence of breast cancer and advanced tumour and lymph node involvement stage. T2DM can induce the higher expression and increased binding capacity of IGF1R and ER, as well as preoperative multicentric or multifocal tumour growth.

PS-01-028
Assessing tumour-infiltrating lymphocytes in breast cancer: depth variability across sections, observer agreement, and prognostic implications
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Background & Objectives: Tumour-infiltrating lymphocytes (TILs) are valuable prognostic biomarkers in breast cancer (BC), particularly in triple-negative and HER2-positive subtypes. However, assessing TILs in H&E-stained slides remains challenging due to tumour heterogeneity, interobserver variability, and lack of standardized evaluation criteria. This study aimed to evaluate TILs variability between two distinct BC tumour depths, assess interobserver agreement among pathologists, and determine whether TILs variability across tumour depths influences patient outcomes.
Methods: Two pathologists independently scored stromal TILs in two sections obtained from 12 consecutive 2-µm sections, specifically selecting the 1st and 12th (24 µm apart) from 104 invasive ductal carcinoma biopsies. Both pathologists were blinded to clinical data and section order and assessed TILs (%) following International TILs Working Group guidelines. Variability in TILs percentage across depths and interobserver agreement were evaluated using the intraclass correlation coefficient (ICC). TILs percentage was categorized with a 10% cutoff for the analysis of kappa, Cox regression, and Kaplan-Meier statistics. The relation between TILs scores and survival outcomes was analysed using Cox regression and Kaplan-Meier curves for disease-free survival (DFS).
Results: The ICC for TIL differences between sections 1 and 12 was 0.950, with a kappa of 0.913, indicating excellent agreement. Interobserver variability showed an ICC of 0.878 and a kappa of 0.748, demonstrating strong agreement. For one pathologist, Cox regression showed significantly better DFS for patients with >10% TILs compared to <10% in section 1 ($p = 0.007$) and section 12 ($p = 0.039$). Kaplan-Meier analysis further confirmed this prognostic value in DFS at both depths ($p = 0.004$, $p = 0.033$). For the other pathologist, although TILs were not significantly prognostic, their value remained consistent across depths.
Conclusion: TIL assessment showed high consistency across tumour depths and between pathologists. Despite minor variability, TILs remained a reliable DFS prognostic biomarker, maintaining their prognostic value among both sections.

Funding: This work was supported by BosomShield, a project that has received funding from Marie Skłodowska-Curie Doctoral Networks Actions (HORIZON-MSCA-2021-DN-01-01) under grant agreement 101073222. Further support was provided by SCARLET, a project funded by Proyectos Estratégicos Orientados a la Transición Ecológica y a la Transición Digital, from the 2021 call of the Ministerio de Ciencia e Innovación, with grant number TED2021-130081B-C22 and funding from NextGenerationEU

PS-01-029
Prognostic impact of HER2 expression in luminal breast cancer: central analysis of the prospective randomized ABCSG 8 trial
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Background & Objectives: Data on low HER2 expression in early luminal breast cancer and its influence on survival is scarce. We investigated the impact of low HER2 expression on prognosis in postmenopausal patients with early luminal breast cancer treated within the prospective randomized ABCSG 8 trial.
Methods: HER2 immunoreactivity was assessed centrally on 2132 whole tumour slides using current ESMO guidelines. Univariable Cox regression was used to estimate a group difference for disease-free (DFS), distant recurrence-free (DRFS) and overall survival (OS). Differences of baseline clinicopathological parameters (age, grade, tumour size, lymph node status, hormone receptor status, Ki67 labelling index) between HER2 negative, ultra-low and low, respectively, were estimated by Fisher`s exact test or Wilcoxon test.
Results: 1756 (82.4%) tumours were scored as HER2 negative (score 0), 87 (4.1%) as HER2 ultra-low (score 0), 222 (10.4%) as HER2 low (score 1+), 28 (1.3%) as HER2 equivocal (score 2+) and 39 (1.8%) as HER2 positive (score 3+). Negative, ultra-low and low HER2 expression did not show a significant association with any of the above mentioned clinicopathological parameters. The median follow-up time was 10.1 years. Outcome between HER2 low and ultra-low did not show statistically significant differences (e.g., 10-year DFS = 71.9% vs. 72.8%). HER2 score 3+ was associated with a significantly worse DFS (p=0.003) and DRFS (p=0.02), but not for OS (p=0.16).
Conclusion: Within the prospective randomized ABCSG 8 trial, the rate of ultra-low and low HER2 expression was considerably lower than described in previous studies. There was no difference in the baseline characteristics between HER2 negative, HER2 ultra-low and HER2 low invasive breast carcinomas. The HER2 score was prognostic for DFS and DRFS with similar outcomes for HER2 low and HER2 ultra-low expression.

PS-01-030
Mixed breast carcinomas: collision tumour or clonal progression? An immunohistochemical and molecular study of 20 cases
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Background & Objectives: Mixed carcinomas of the breast are rare, accounting for approximately 5% of cases according to the WHO classification. The relationship between the ductal and lobular components remains poorly understood. Some authors suggest these tumours may represent a collision of two distinct neoplasms, while others propose a single tumour in which one component arises from the other.
Methods: We analysed 20 cases of mixed breast carcinomas diagnosed at our hospital over a three-year period. Each case was evaluated not only by morphological criteria but also by assessing E-cadherin expression. Immunohistochemical analysis included oestrogen receptor (ER), progesterone receptor (PR), E-cadherin, Ki-67, HER2, and p53. Additionally, PIK3CA mutations were analysed using PCR.
Results: We did not observe significant differences between the ductal and lobular components regarding ER, PR, p53, or PIK3CA status. These findings support the hypothesis that the lobular component may originate from the ductal component following specific genetic alterations, particularly the loss of E-cadherin.
Conclusion: • Our findings suggest an immunohistochemical relationship between ductal and lobular carcinoma.

- Lobular carcinoma should be diagnosed based on its characteristic morphology and complete loss of E-cadherin.
- In most cases, the lobular component appeared to arise from the ductal component following loss of E-cadherin.
- PIK3CA was the most frequently observed molecular alteration.
- p53 mutations were not identified in any case, in either component.

PS-01-031
Invasive papillary breast cancer. Approaching morphology and molecular profiling
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Background & Objectives: Invasive Papillary Carcinoma (IPC) is a rare breast cancer subtype marked by an invasive papillary structure, with fibrovascular cores covered by high epithelial cells. Since limited data are available, this study aims to investigate the molecular features of IPC.
Methods: We analysed three of five IPC cases from our archives using paraffin-embedded samples. Immunohistochemistry was performed alongside next-generation sequencing (NGS) with the Myriapod NGS Cancer Panel on an Illumina iSeq100 platform, targeting 17 genes. The largest tumour, a mass about 11 cm diameter, underwent additional analysis using scanning electron microscopy (SEM) with a Zeiss 600.
Results: SEM observation of the papillary structures, which are already well visualised by light miscroscopy, allows us to better understand the three-dimensional architecture and the connections between the vascular connective axis and the epithelial component, as well as the connective tissue with the vessel wall. In this tumour molecular analysis identified PIK3CA mutations, including a pathogenic missense variant in exon 5 (c.1035T>A, p.Asn345Lys) with an allelic frequency of 42.5%. Additionally, a PIK3CA c.1252G>A mutation in exon 8 was detected, resulting in p.Glu418Lys, classified as a missense and splice region variant with conflicting pathogenicity assessments (allelic frequency: 42.0%). No mutations were found in the other two IPC cases.
Conclusion: SEM osservation of IPCs'papillae bring us a different point of view. The depth of field emphasises the connections between epithelial and connective structures and the included blood vessels t. PIK3CA mutations, which are commonly found in various human cancers, are present in up to 40% of breast cancers and are paradoxically associated with a better prognosis (2). Although PIK3CA promotes cell proliferation and transformation in vitro (3), its presence in the large tumour is consistent with a favourable prognosis for IPCs.

PS-01-032
Is it TIME for the clinical stratification of HR+/HER2- breast cancer?
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Background & Objectives: Tumour immune microenvironment (TIME) plays a pivotal role in the prognosis and therapeutic response in triple-negative and HER2+ breast cancer (BC). Our study aimed to characterize TIME cellular composition of HR+/HER2- BC to gain insight into tumour biology.
Methods: Tissue Microarrays from 70 HR+/HER2- BC patients have been created. Imaging analysis (HALO®) was used to assess the immunohistochemical expression of immune markers (CD3, CD20, CD4, CD8, FOXP3, CD68/KP1, CD163, iNOS). Statistical analysis was performed using GraphPad Prism Software. The study was approved by the local Ethical Committee and was partially funded by Gilead Fellowship Program 2023.
Results: Both CD4+ and CD8+ tumour-infiltrating lymphocytes (TILs) were higher in tumour stroma than in the normal counterpart (P=0.0087 and P=0.0014, respectively). This was particularly significant for the FOXP3+ subpopulation, which include regulatory T cells (Treg, CD4+/FOXP3+) and activated CD8+ T cells (CD8+/FOXP3+) (P=0.0007). Interestingly, the tumour stroma was also enriched in Th1 TILs (CD4+/FOXP3-) (P=0.0096). In terms of prognosis, the metastatic tumours had less CD4+/FOXP3- TILs than the non-metastatic ones (P=0.0045). Together, tumour associated macrophages (TAMs) were polarized into M1 (pro-tumoral) and M2 (anti-tumoral) phenotypes.
Conclusion: These data suggest a complex interplay between immune cells in HR+/HER2- BC: while the presence of CD4+ and CD8+ TILs may indicate an active immune response, the enrichment of Tregs, activated CD8+ T cells and TAMs suggests a potentially dysfunctional immune response. Intriguingly, the lower levels of Th1 TILs in metastatic tumours imply that the immune environment may be less capable of mounting an effective response, and their depletion could be a marker of poor prognosis.

Funding: The study was partially funded by Gilead Fellowship Program 2023

PS-01-033
Ex-vivo confocal microscopy: a novel approach for evaluating needle breast biopsies
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Background & Objectives: Breast cancer diagnosis relies on histopathological evaluation of core needle biopsies, but conventional processing with fixation and paraffin embedding delays results. Confocal microscopy (CM) offers a rapid, non-destructive alternative for immediate tissue evaluation.
Methods: We analysed 47 ex-vivo core needle biopsies from 41 lumpectomy patients, assessing both benign and malignant tissues. Biopsies were assessed using fusion CM (Vivascope, Germany), which provides H&E-like images, and the results were compared to the gold-standard histopathological analysis.
A rapid staining protocol was applied, consisting of 30 seconds of Acridine Orange followed by 20 seconds of Fast Green, repeated twice, with intermittent saline washes, preserving sample integrity for routine processing.
One pathologist with experience in confocal imaging evaluated confocal H&E-like images for invasive carcinoma presence, histological type, percentage involvement, and in situ carcinoma. H&E stained histological sections of the biopsies were then obtained after fixation and routine processing.
Results: CM produced good-quality images allowing to identify key histological features.
The correlation between preliminary findings from confocal imaging and the final diagnosis based from H&E-stained histological sections was 89%. Five biopsies remained inconclusive under confocal imaging. The pathologist correctly identified three lobular invasive carcinomas (LIC) and one ductal carcinoma (DIC) with mucinous differentiation but misclassified two DICs as LICs. In four cases, confocal imaging raised uncertainty between inflammation and tumour, highlighting a diagnostic challenge in certain scenarios.
Of the core needle biopsies, 24 were carcinoma-positive, with 84% concordance in tumour involvement ($\geq$50% vs. <50% of the tissue), reflected by a Cohen's kappa coefficient of 0.60, indicating moderate agreement between confocal imaging and histopathology.
Conclusion: While paraffin-embedded histopathology remains the definitive diagnostic method, the use of CM offers a potential new tool for early diagnostic information. This approach could improve biopsy quality by avoiding non-representative samples and accelerate the diagnostic process, enhancing the clinical workflow without compromising accuracy.

PS-01-034
Evaluation of P63 positivity in breast carcinomas as a prognostic value
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Background & Objectives: Breast carcinoma is the most commonly diagnosed malignancy in women worldwide with a high mortality rate. P63 is an immunostain used as a myoepithelial marker in breast tumours. P63 is a transcription factor from the P53 protein family and expressed by the TP63 gene located at the chromosome 3q28. P63 positivity is reported in breast carcinomas, not otherwise specified (NOS) subtype. The pattern of P63 staining is reported as focal and weak staining. This staining pattern can be explained with possible mechanisms such as tumour progression, tumour cell transdifferentiation or early phase differentiation. Recent studies showed correlation between P63 positivity and worse prognostic outcome in HER2-positive breast carcinomas. In this study, we aim to evaluate possible correlations between P63 positivity and biomarker status/tumour grade in breast carcinomas.
Methods: This study included 118 cases of breast carcinoma diagnosed at our centre between 2020 and 2025. The relationship between P63 positivity and demographic, histopathological and biological markers was evaluated in this study. IBM SPSS 21.0 was used for statistical analysis.
Results: P63 expression was significantly associated with higher Ki-67 proliferation indices (p=0.009), with p63-positive cases showing Ki-67 values predominantly above 40%. A statistically significant correlation was observed between p63 and HER2 (CerbB2) positivity (p=0.006), and HER2 score 3 was more common in p63-positive cases (p=0.029). Additionally, p63 positivity correlated with ER negativity (p=0.044). No significant associations were found between p63 and PR status (p=0.536) or tumour grade (p=0.098).
Conclusion: Findings of this study show that p63-positive breast cancer cases are more likely to exhibit HER2 overexpression, ER negativity, and high proliferative activity (Ki-67 > %40) — all of which are associated with poor prognosis. This supports the potential role of p63 as a marker of biologically aggressive tumour behaviour.

PS-01-035

Her2/neu protein expression in primary tumour and local metastases of breast cancer

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Background & Objectives: Prognostic and predictive significance of heterogeneity of Her2/neu in primary and metastatic tumour in breast cancer stays unclear. Objective: to assess discordance rate of Her2/neu protein expression in breast cancer local metastasis compared with primary tumour.
Methods: Surgical specimens of the primary tumour and local metastases of 104 patients with breast cancer were studied. Immunohistochemistry (antibodies to Her2/neu, Ventana) was used to determine Her2/neu expression level in primary tumour and metastases. ASCO/CAP 2013 scoring system was used. Groups were formed according to the primary tumour Her2/neu expression level: group 1: 0 (61 patients), group 2: 1+ (12 patients), group 3: 2+ (19 patients), group 4: 3+ (12 patients). Frequency of Her2/neu expression changes in metastases was analysed in groups using Fisher exact probability test.
Results: In group 1 Her2/neu expression level in local metastasis and primary tumour was discordant in 19 cases of 61 (31,2%, 95% CI 20,3-44,4%), increased only. In group 2 – in 10 cases of 12 (83,3%, 95% CI 51,6-97,9%), increased in 2 of 12 (16,7%, 95% CI 2,1-48,4%), decreased in 8 of 12 (66,7%, 95% CI 34,9-90,1%), p=0,036. In group 3 – in 17 cases of 19 (89,5%, 95% CI 65,5-98,2%), increased in 1 (5,3%, 95% CI 0,3-28,1%), decreased in 16 (84,2%, 95% CI 59,5-95,8%), p<0,05. In group 4 – in 6 cases of 12 (50,0%, 95% CI 22,3-77,7%), decreased only.
Conclusion: Her2/neu expression may be discordant when breast cancer primary tumour and local metastases are compared. Discordance rate depends on the Her2/neu primary tumour expression and is highest in cases with 2+ Her2/neu level and lowest in cases without (0) expression. Among cases with discordant Her2/neu expression cases with decrease of Her2/neu level predominate.

PS-01-036

Leptomeningeal carcinomatosis is more likely to have an earlier onset in patients with an initial metastatic breast cancer

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Background & Objectives: Leptomeningeal carcinomatosis (LC) is a devastating late-stage complication occurring in few patients with breast cancer (BC). We aimed through this study to determine whether clinico-pathological features of BC at diagnosis influence the time to develop LC.
Methods: Data analysis of our cerebral-spinal-fluid (CSF) cytology database was performed in the period between 2005 and 2021, identifying 34 patients who have undergone at least one CSF-cytology-sampling in the context of suspicion of BC-LC. Amongst them, 20 patients met diagnostic criteria for LC diagnosis (positive CSF cytology and/or neuroimaging in the presence of suggestive neurological symptoms). We used Student's and Anova tests for comparisons of means.
Results: The median age of patients at the time of initial BC diagnosis was 46,5 years. The majority of patients were assigned a stage III-IV at baseline (65%) with distant metastases in 30% of cases. Fifteen patients (75%) underwent a breast surgery. Primary breast tumours were predominantly HR-positive (75%) and HER2-negative (65%). All patients developed a LC within a median interval of 37 months (≈ 3 years). Patients with a metastatic disease at baseline experienced shorter time between diagnosis of BC and LC (p<0,001) compared with non-metastatic ones. In contrast, time taken for LM to develop was much longer for patients initially treated by breast surgery, especially those having experienced a radical mastectomy (p=0,002).
Conclusion: LC represents a late complication of BC, occurring within an interval counted in years from the date of initial BC diagnosis. According to this study, patients with an initial metastatic status as well as those who were not eligible for a breast surgery showed an earlier onset of LC in comparison with their non-metastatic and operated-on counterparts, respectively.

PS-01-037

Morphological and immunohistochemical variability between high vs low-grade encapsulated papillary carcinomas

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Background & Objectives: Encapsulated papillary carcinoma (EPC) is a distinct type of breast carcinoma currently classified as an in-situ carcinoma of low to intermediate grade due to indolent nature despite lacking myoepithelial cells around the tumour periphery. However, evidence suggests there is a subset of pure EPCs that have high-grade features and should be considered invasive carcinomas with an expansile growth pattern. This study aims to define morphologic and immunohistochemical features that can distinguish high-grade EPC with potential impact on patient management.
In this retrospective study, our aim was to identify morphologic and immunohistochemical features that may be associated with histologically high grade EPCs with potential clinical implication in patient care and prognosis.
Methods: Resection specimens of pure EPCs diagnosed from 2014-24 at Toronto General Hospital were selected and their clinicopathologic features were reviewed: including patient age, tumour size, nuclear grade, Nottingham histologic grade, mitotic count, presence or absence of necrosis, presence or absence of lymphovascular space invasion and the expression of ER, PR and HER2.
Results: 31 cases of pure EPC were reviewed. The high-grade cohort (n=6) had a mean size of 2.92 cm (SD=0.93), mean mitotic count of 16.83 (SD=10.96), 33% with necrosis. 67% had strong ER expression while 20% had strong PR expression. The intermediate-grade cohort (n=25) had a mean size of 1.21 cm (SD=0.73) and mean mitotic count of 4.96 (SD=4.49), 5% with necrosis. 95% of specimens showed strong ER expression while 50% showed strong PR expression. In summary, when compared to the intermediate group, the high-grade specimens had a significantly larger overall size (p<0.05), higher rate of necrosis (p<0.05), higher mitotic count (p<0.05), and less ER expression (p<0.05).
Conclusion: Possible associated indicators of high grade EPCs include: Larger size at time of grossing, presence of necrosis, higher mitotic count and lack of ER expression.

PS-01-038

Observational study comparing current pathology practices with utilization of computational pathology algorithms for primary breast cancer diagnosis

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Background & Objectives: The increasing global burden of breast cancer, along with rising diagnostic demands and a shortage of pathologists, requires innovative solutions to improve histopathological workflows while ensuring high diagnostic accuracy. This study evaluated an AI-powered decision-support solution (Ibex Breast®) to assess its impact on workflow efficiency, diagnostic performance, and AI standalone accuracy in detecting breast cancer, invasive carcinoma, and ductal carcinoma in situ (DCIS).
Methods: The study included a cohort of 200 retrospective breast biopsies with H&E slides evaluating different subtypes (IDC, ILC, DCIS) from a pathology lab in Western Australia. The two-arm crossover study design evaluated two diagnostic workflows: a standard digital pathology workflow (Arm A) and an AI-assisted workflow (Arm B). Efficiency metrics, including pathologists' reporting time, were measured, and patient turnaround time (TAT) was assessed. Diagnostic performance, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), were compared between workflows. Standalone AI accuracy was also evaluated.
Results: The integration of AI significantly improved efficiency, reducing pathologist review times by an average of 43.5% (from 71.0 ± 47.8s/case in Arm A to 40.2 ± 28.4s in Arm B; $p < 2.2 \times 10^{-16}$). AI-assisted workflow showed high diagnostic performance compared to standard workflows, achieving 100% sensitivity and specificity for cancer and invasive carcinoma detection. The standalone AI demonstrated 100% sensitivity and specificity for cancer and invasive carcinoma, and 92.9% sensitivity for DCIS. AI integration could reduce TAT by 1.7 days for cases requiring immunohistochemistry (IHC) tests through preordering based on AI findings.
Conclusion: The AI-assisted workflow significantly enhances diagnostic efficiency and reduces patient TAT for primary diagnosis of breast cancer without compromising accuracy. By streamlining workflows, reducing pathologist workloads, and expediting case reporting, AI has the potential to address critical challenges in modern pathology, including rising workloads and pathologist shortages, ultimately improving patient outcomes.

PS-01-039
Multimodal discovery of cellular and microanatomical determinants in breast cancer metastasis
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Background & Objectives: Cancer metastasis remains one of the leading causes of cancer-related mortality following ineffective treatment. While genomic alterations and tumour-intrinsic factors are well-established drivers of metastasis, recent evidence suggests that tissue architecture and organ-specific microenvironments play an active role in shaping the metastatic process. Despite the recognition of the tumour microenvironment as a key driver of metastasis, the specific contributions of the microanatomical composition and arrangement of the metastatic site to the metastatic process remain poorly characterized.
Methods: We conducted a comprehensive analysis comprising 22 patient-derived xenografts comprising of paired primary and metastatic cancer samples across molecular subtypes. Our approach integrated 420 H&E whole slide images and 120 multiplexed imaging datasets incorporating 50 distinct markers. Following manual annotation of 120 slides, we developed a deep-learning semantic segmentation model capable of identifying vascular structures, airways, and tumour lesions in H&E slides of metastatic lung tissue. We further employed advanced spatial analysis techniques to interrogate cellular arrangements within multiplexed images to elucidate their association with metastatic potential.
Results: Our model successfully identified all microanatomical structures (vessels, airways) and tumour lesions across the entire H&E slide collection. Subsequent analyses revealed how morphological features, and spatial arrangements of microanatomical structures and tumour lesions correlate with metastatic potential and molecular subtypes. Multiplexed imaging data enabled the identification of specific molecular markers that are microanatomically dependent, and further specification of cellular heterogeneity during the process of cancer colonization in breast cancer metastasis to the lung.
Conclusion: Investigating the role of microanatomical structures in early-stage breast cancer metastasis in PDX models reveals the intricate, multi-scale nature of factors conditioning the metastatic process. The fundamental principle studied in this work, once validated in human datasets such as TCGA and METABRIC, has the potential to enable better disease prognosis and other clinical applications that would ultimately improve patient outcomes.

Funding: WWTF 10.47379/LS23067

PS-01-040
Real-world experience with the 70 gene assay for treatment decisions in ER+/HER2- invasive breast cancer
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Background & Objectives: Multigene classifiers have been established for treatment decisions in ER+/HER2- invasive breast carcinoma but these tests are expensive, in part centrally performed and have been only partially tested in prospective trials. In our certified breast units we used the EndoPredict® but recently switched to MammaPrint® (70-gene assay). Our aim is to report our first experience with the 70-gene assay with respect to prognostic groups and clinicopathological parameters.
Methods: Patients for testing are determined in tumour boards. The pathologist as ordering physician selects a representative tumour block from the surgical specimen; 10 consecutive sections are cut according to the instructions by the manufacturer and submitted within the provided kit box to central lab. Each case is registered online. The report is immediately available online after analysis (email alert). The 70-gene assay considers low-risk and high-risk carcinomas with 2 further subgroups each.
Results: During the last 14 weeks we have submitted 20 cases. Median analysis time was 7.5 days. 15 (75%) cases were classified as high-risk, 5 (25%) as low risk. Low risk cases were younger compared to high-risk cases (median age 54 versus 68 years), showed lower Ki67 labelling index (median 12.5% versus 30%) and were less frequently HER2 low (1/5 versus 13/15). No differences were found with respect to PR, tumour size and nodal status. Due to the small number of cases, we omitted the subgroup analysis. All EndoPredict® analyses were classified as high risk.
Conclusion: In real world the use of the 70-gene assay is feasible despite central analysis and recognizes a low-risk group. Low-risk carcinomas seem to be distinct from high-risk carcinomas with respect to

age, Ki67 labelling index and HER2 low frequency. In this prospective setting we will be able to report a larger cohort at the congress.

PS-01-041

Evolution the testing of the human epidermal growth factor receptor 2 (HER2) in breast cancer in Spain over the last 10 years

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Background & Objectives: Human epidermal growth factor receptor 2 (HER2) is assessed by immunohistochemistry (IHC) and in-situ hybridization (ISH). CONFIRMA-HER2 is the largest registry in Spain with information on the HER2 biomarker testing in breast cancer (BC). The aim of this study was to analyse the evolution of HER2 status over a decade within the CONFIRMA-HER2 registry.
Methods: A retrospective analysis of HER2 determinations recorded in the CONFIRMA HER2 registry of BC samples diagnosed between 2013 and 2023 in 160 hospitals across Spain. The evolution over time of the technique used to determine HER2 (IHC and ISH) and the result of the determination (HER-negative or HER-positive) was analysed.
Results: A total of 199,934 HER2 determinations recorded in the CONFIRMA-HER2 registry were analysed. The use of IHC for HER2 testing has increased over the 10 years of analysis (lowest value 93.0% in 2014 to 99.8% in 2023) while hybridizations have decreased (highest value 33.2% in 2015 to 19.5% in 2023). Overall IHC results were 35.5% IHC 0, 27.8% IHC 1+, 22.7% IHC 2+, 11.2% IHC 3+ and 2.9% invalid/non-evaluable, with the proportion of IHC 0 increasing most over time. Of the total hybridizations performed, 17.9% were amplified and 82.1% were non-amplified, with this distribution remaining fairly constant over time. After excluding invalid/non-evaluable results, 15.3% determinations were HER2-positive and 84.7% were HER2-negative over the period 2013-2023. The highest percentage of HER-positives was recorded in 2015 (18.8%) and the lowest in 2022 (16.6%). Of all determinations, 46.5% were HER2-low (IHC 1+ or IHC 2+/non-amplified ISH) with the highest percentage in 2020 (48.6%).
Conclusion: CONFIRMA-HER2 registry provides key information on the evolution of HER2 testing in Spain, a critical element in the treatment and prognosis of BC, especially in recent years with advances in HER2-targeted therapy.

PS-01-042

***CDH1* somatic mutation analysis in advanced breast cancer: correlation with clinicopathologic and molecular features**

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Background & Objectives: *CDH1* inactivation is typically correlated with loss of E-cadherin expression and often associated with lobular breast carcinomas and rarely seen in ductal carcinomas. The loss of expression of E-cadherin, a cell adhesion molecule, has been proposed to correlate with higher risk of metastasis and therefore poor prognosis. In this study, we aimed to compare *CDH1* mutated and non-mutated breast cancer with their associated clinicopathologic and genetic characteristics.
Methods: We evaluated 304 patients with metastatic/recurrent breast cancer who underwent next generation sequencing performed on an institutional custom-built hybrid capture 610-gene panel between 2021-2024. *CDH1* somatic mutation status was examined with respect to clinical, pathologic, and molecular profile including tumour mutational burden (TMB).
Results: *CDH1* somatic mutations were detected in 43 of 304 patients (14%): 40 truncation mutations (93%), 2 missense (5%) and 1 in-frame deletion (2%). *CDH1* mutated cases were all females (100%), predominately HR positive (93%), and all HER2 negative (100%). *CDH1* mutated cases were mostly lobular carcinomas (72%) and mixed ductal and lobular (IDLC) (23%), and rarely ductal (5%), as compared to *CDH1* non-mutated cases (4% lobular, 5% IDLC, and 91% ductal, $p<0.001$). Of 10 IDLC with *CDH1* mutations, 5 (50%) were multifocal, 1 (10%) bilateral, 1 (10%) stage IV with lung metastasis. TMB-high was higher in *CDH1* mutated cases (21%) than *CDH1* non-mutated (7%, $p=0.02$). Co-existing *PIK3CA* mutation was frequent in *CDH1* mutated cases (60%) as compared to *CDH1* non-mutated cases (32%, $p<0.001$). In contrast, *TP53* mutation was less frequent in *CDH1* mutated cases than those without (9% vs 49%, $p<0.001$).
Conclusion: *CDH1* mutated breast cancers were mostly ER positive, HER2 negative, lobular or IDLC, and notably predictive of multifocality. They were likely TMB-high, with co-existing *PIK3CA* mutation, and less likely *TP53* mutation. These enhanced knowledge enables strategic multidisciplinary planning in identifying targeted and immunotherapy beyond conventional treatment.

PS-02 Poster Session Digital and Computational Pathology

PS-02-001

Aging of AI caused by scanner drift can be rescued by colour calibration

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Background & Objectives: The full potential of artificial intelligence (AI) in digital pathology is limited by technical inconsistencies in scanning of whole slide images (WSIs), posing a challenge for widespread clinical application as fine-tuning algorithms for each new site is impractical. A recent study comprehensively demonstrated that standardizing intra- and inter-vendor WSI colour by calibration increases AI robustness and reliability. Further concerns exist over 'AI aging' as scanners change in colour reproduction fidelity over time, impacting AI post-validation performance and potentially compromising safety.
Methods: We employed a colour calibration technology that corrects WSIs to ground truth colour of real glass slides using ICC profiles. To assess impacts of temporal colour variation, 119 prostate cores with balanced ISUP grade distribution were scanned alongside the colour calibration slide on one scanner every 14 days for one year. The tissue colour was measured for change. Scanner-induced temporal variance on pathologist concordance and AI model performance was evaluated on a deep learning model trained on over 46,000 WSI for prostate cancer diagnosis.
Results: The RGB colour stability of the scanner degraded over even short timepoints, discernable by humans and revealing traceable events needing quality assurance that caused sudden changes. Timepoint ICC profiles recovered to stable, accurate colour resulting in better AI concordance with pathologist ISUP grading, and actual tissue did not change colour. With only scanner colour left uncontrolled, AI performance linearly regressed which ICC colour calibration rescued to intended consistency.
Conclusion: Frequent colour calibration provides a universal solution to the variation introduced by scanners drifting, making AI-based

cancer diagnostics more reliable in the real world. In future studies introducing more scanners will investigate impacting AI reliability exponentially and grade-specific rescuing of AI-aging for ISUP 2-4 is expected to have significant diagnostic impact. This study pioneers real-time quality assurance for stable and scalable performance of scanners and AI over time.

Funding: R.S. received funding from Innovate UK (Future Leaders Fellowship MR/V023314/1)

PS-02-002

Development of an automated tumour region segmentation model of prostate cancer using weak labels and in-silico data generated with a diffusion model

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Background & Objectives: Accurate segmentation of tumour regions in histopathological images using deep learning models relies heavily on training with precisely labeled datasets. However, crafting these annotations is costly and time intensive. Our work addresses this challenge by showcasing how weak labels and *in-silico* data can be used to minimize the dependency on extensive pathologist input while maintaining model accuracy.
Methods: To train a tumour epithelium segmentation model for prostate immunohistochemical (IHC) slides, we implemented a weak labelling workflow that reclassified predictions from an epithelium segmentation model into *tumour* and *normal* epithelium based on coarse tumour centre annotations from a pathologist. Thereby we generated pixel-precise weak labels. Utilizing a diffusion model, we augmented these weakly labelled images with in-silico data. For training, we generated 7,080 weak labelled patches of size 512x512pxl at 0.5µm/pxl and 4.0µm/pxl resolution from 57 whole slide images (WSIs) and evaluated the models on 86 annotated Fields-Of-View of size 500x500µm from 20 WSIs. Experiments involved training with random subsets (5%, 10%, 25%) of the original patch dataset and systematically increased in-silico data through augmentations (1x-15x). Using the H-Optimus-0 foundation model as a feature extractor, we investigated the overlap of real and in-silico data distributions in UMAPs.
Results: Our baseline tumour epithelium segmentation model achieved a Dice score of 0.91 using 100% of weakly labelled data. While accuracy remained stable using 25% of data, it decreased to 0.90 for 5% and 10% subsets. Adding 1x and 10x folds of in-silico data restored the performance to 0.91. An optimal number of augmentation rounds was identified beyond which model accuracy decreases again. UMAPs showed in-silico images reproduce real appearances while enriching training data diversity.
Conclusion: The study demonstrates the feasibility of developing highly accurate segmentation models with minimal pathology annotations (5-10% of original dataset) using weak labels and in-silico data.

PS-02-003

AI-based morphological characterization of Small Cell Lung Cancer subtyped by molecular transcriptional pattern

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Background & Objectives: Small cell lung cancer (SCLC) has recently been classified into four subtypes by their molecular transcriptional signature based on four specific proteins: ASCL1, NEUROD1, POU2F3, and YAP1. However, the possible morphological differences of these subtypes have not been examined. Hence, we aim to investigate the morphology of these subtypes by providing AI-based strategies. To the best of our knowledge, this is the first study to explore the morphological characteristics of SCLC subtypes from the computational point of view.
Methods: Here, we first perform single-cell classification to analyse the morphological features by detecting each cell and measuring their colour- and shape-related features in the regions of interest. Second, we conduct whole-slide image (WSI) classification to investigate whether these subtypes can be identified based on the visual, morphological, and spatial features of image patches. We use a weakly supervised state-of-the-art pathological image classification method, CLAM (Clustering-constrained Attention Multiple Instance Learning). Additionally, we generated heatmaps with the help of the attention mechanism to visualize the model's focus in the prediction process.
Results: The single-cell analysis shows that the geometrical features of ASCL1-positive and POU2F3-positive cases are very similar, with only small differences compared to NEUROD1-positive cases. However, the colour-related features play a more significant role than the geometric features. Furthermore, the WSI classification framework proves that the morphological differences across subtypes are distinct enough for accurate classification. The generated heatmaps highlight regions of interest to better understand the importance of specific regions within a slide. Importantly, these highlighted regions correspond well with the rough annotations provided by our pathologist, supporting the model's reliability.
Conclusion: Overall, we showcase that SCLC subtypes based on the expression of different transcription factors exhibit distinct morphological characterization.

PS-02-004

Computer-aided scoring as an objective method in the assessment of HER2 immunostaining in breast cancer with high intratumoral heterogeneity

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Background & Objectives: The interpretation of HER2 IHC in cases with elevated intra-tumoral heterogeneity may be challenging, sometimes resulting in high interobserver variability. The aim of this evaluation was to assess the usefulness of a computer-aided method for the scoring of HER2 immunostaining, particularly in specimens with high intra-tumoral heterogeneity.
Methods: Specimens stained with HER2 clone 4B5 using the BenchMark Ultra (Roche) were selected from a slide repository to include various HER2 expression levels. Both HER2 and corresponding H&E slides were scanned at 20x on GenASIs HiPathPro (Applied Spectral Imaging). Three distinct regions were digitally marked within the tumour on the H&E images and automatically transferred to the HER2 specimens following tissue matching. Three independent pathologists provided one integrative HER2 score of 0, 1+, 2+ or 3+ for the 3 marked regions analysed together. A score for the three regions and per individual region were also obtained using a computational algorithm.
Results: Core biopsies from 23 breast cancer patients (age 53±13) were included, 22 with IDC and one with mucinous carcinoma. 20 out of the 23 HER2 specimens (87%) were scored identically by the 3 pathologists and the computational algorithm (10 negative 0 or 1+, 7 equivocal 2+, and 3 positive 3+). The 3 discrepant cases were scored either 1+ or 2+ by the pathologists. In these cases, high heterogeneity

was observed across the 3 marked regions, with individual computational score per region varying between 0 and 2+. For note, the proliferation index Ki-67 for these discrepant cases was >20% while the integrative computational score across the 3 regions was 2+.
Conclusion: Manual HER2 assessment may be hampered in cases of high intra-tumoral heterogeneity, particularly when assessing HER2 low. In such cases, computational analysis emerges as a useful integrative method providing objective and reproducible scoring across heterogeneous tissue.

PS-02-005
Convolutional neural networks improve metastatic risk prediction beyond staging in early-stage melanoma using histopathological images from the population-based Dutch Early-Stage Melanoma Study (D-ESMEL)
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Background & Objectives: Current melanoma staging is insufficient to identify high risk patients of distant metastasis among stage I/II melanoma (i.e. no metastasis at diagnosis), as 41% of melanoma deaths occur among patients who were initially diagnosed at stage I/II. We aimed to develop a convolutional neural network (CNN) model using whole slide images (WSIs) from primary early-stage melanomas to improve the prediction of future distant metastasis for possible adjuvant treatment or increased surveillance.
Methods: To identify novel histopathological predictors beyond known staging predictors, we used the Dutch Early-Stage Melanoma (D-ESMEL). This study includes a discovery set with 224 matched case-control sets and a validation cohort consisting of a population-based nested case control study, including 5,558 patients with 154 unmatched case-control sets. In the discovery set each metastatic case is matched to a control on date of diagnosis, age, sex, Breslow thickness, and ulceration to identify novel prognostic factors. An end-to-end workflow was developed on the discovery set which automatically extracts relevant patches from WSIs, performs filtering, classifies patches into low and high-risk, and outputs patient-level risk predictions. The workflow is applied on the validation cohort and the CNN predictions were used to perform a weighted Cox proportional hazards (CoxPH) regression and a log likelihood test to assess the added value on top of staging in a population-based cohort.
Results: Our CNN model reached 83% sensitivity and 100% specificity in a holdout test set of the discovery set. In the validation cohort, staging alone reached a weighted C-index of 0.82. Adding our CNN's predictions on top of staging contributed significantly to the prognosis of metastasis (hazard ratio=1.24, 95% confidence interval: 1.03-1.48, $p<0.05$) and significantly improved the weighted C-index to 0.84 ($p<0.01$).
Conclusion: To our knowledge, this is the first histopathological model that adds prognostic value on top of staging for predicting distant metastasis in early-stage melanomas.

Funding: This work has been funded by the by KWF Kankerbestrijding (Dutch Cancer Society) (Grant Number: 2021-1/13470)

PS-02-006
Evaluating the performance and generalisability of a clinical-grade AI-based approach for determining MSI/dMMR status in colorectal cancer: A blinded multi-regional study
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Background & Objectives: Microsatellite instability (MSI) and mismatch repair deficiency (dMMR) testing are essential for colorectal cancer (CRC) management. Despite guidelines recommending routine testing, high costs, long turnaround times, and pathology workforce shortages limit widespread implementation. PANProfiler Colorectal (PPC) is an artificial intelligence (AI)-driven approach that determines MSI/dMMR status in minutes using only H&E-stained whole slide images (WSIs), offering a cost-effective and scalable alternative. This study evaluates PPC's performance and generalisability across diverse UK subpopulations using real-world retrospective CRC cases.
Methods: A blinded validation study was conducted using 3,576 WSIs of H&E-stained primary CRC tumours from three sites, with results compared against traditional testing methods. WSIs were sourced from St James's University Hospital (n=3,124), Wales Cancer Biobank (n=54), and Northern Ireland (NI) Biobank (n=398), with the cohorts representing England, Wales, and NI, respectively. MSI-high/dMMR prevalence across cohorts (12.5% - 20.6%) was consistent with reported UK rates. PPC provided results as *Stable* (proficient MMR or non-MSI-High), *Unstable* (dMMR or MSI-High), or *Indeterminate* (no definitive result).
Results: PPC provided a definitive result for 86.6% of cases, as measured by the test replacement rate (TRR). Overall percent agreement (OPA) ranged from 84.3% (Wales) to 94.1% (England), with an aggregated OPA of 93.8% (95% CI: 92.9% - 94.7%). Positive percent agreement (PPA) varied between 91.7% (NI) and 100.0% (Wales), with an aggregated PPA of 92.5% (95% CI: 89.5% - 94.9%). Negative percent agreement (NPA) ranged from 80.0% (Wales) to 94.3% (England), with an aggregated NPA of 94.0% (95% CI: 93.1% - 94.9%). TRR varied between 71.4% (NI) and 94.4% (Wales) across regions.
Conclusion: Using real-world retrospective data, PPC demonstrated robustness and accuracy in assessing MSI/dMMR status in CRC tumours. These findings support its wider adoption as a valuable solution for improving CRC management, highlighting its ability to generalise across diverse patient populations.

Funding: This project was (partially) funded by IUK Smart Grant 10054824

PS-02-007
Deep learning-powered scoring of ER, PR and Ki-67 across major WSI scanners using a single, generalizable cell-classification model in breast cancer
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Background & Objectives: Estrogen receptor (ER), progesterone receptor (PR), and Ki-67 are routinely examined by immunohistochemistry (IHC) to assess hormone receptor status and tumour proliferation in breast cancer. However, IHC scoring in a digital pathology setting can be hindered by variation in staining and scanning, as well as inter- and intra-reader variability, and scanner variability. To

address the aforementioned issues, we developed a deep learning-based tool to provide ER, PR, and Ki-67 scores from whole slide images (WSIs).
Methods: A deep convolutional neural network (DCNN) segmented and classified invasive carcinoma, in-situ carcinoma, cancer stroma, necrosis, and normal stroma in regions of evaluable tissue predicted by an artifact model. Another DCNN identified IHC signal-positive and -negative cancer cells. Both DCNNs were trained and evaluated using sparse annotations (N=111,622) across 14,646 WSIs. Continuous slide-level ER, PR, and Ki-67 scores were calculated using the ratio of positive cancer cells to total cells within invasive carcinoma. For model evaluation, 5-way manual pathologist slide-level scores were collected on held-out WSIs (N=1,115) for ER, PR, and Ki-67, and intra-class coefficient (ICC) values were calculated. Models were considered non-inferior to pathologists if ΔICC (the difference between model and pathologist ICCs) > -0.1.
Results: Model performance was non-inferior to manual pathologist scoring. Model ICC values were 0.91, 0.86, and 0.93, and ΔICC values were -0.05, 0.00, and -0.02 for ER, PR, and Ki-67, respectively. Model performance was generalizable across six whole slide scanners (ICC range: 0.89-0.96).
Conclusion: This tool effectively and accurately scores ER-, PR-, and Ki-67-stained WSI and is non-inferior to pathologists for this task across major digital pathology scanners. Although further evaluation is needed to understand model performance in real-world laboratories, these findings support digital IHC scoring, which has the potential to improve pathologist efficiency.

PS-02-008
The WHO Classification of tumours evidence gap map tool: a software tool supporting evidence-based decision making in tumour pathology
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Background & Objectives: Evidence-based practice improves tumour pathology research and its classification. However, identifying high quality scientific publications and research evidence gaps can be challenging. The WCT EVI MAP project funded by European Commission (HORIZON-HLTH-2021-CARE-05 grant number 101057127) aims to create a decision-making support tool by developing a software that visualises evidence gap maps (EGMs) to facilitate evidence-based decision-making and assisting in its analysis, helping researchers and healthcare professionals to identify knowledge gaps informing future research.
Methods: We developed a web application that visualises EGMs and integrates its outcomes in a searchable database of scientific publications composing the evidence-base of the WHO Classification of Tumours (WCT). Built using open-source technologies, the web application utilizes the R Shiny package (v4.3.3, v1.8.1.1) for the web interface and a MariaDB (v10.4.32), a fork of MySQL, for the database prototype. Both components have been optimized to efficiently handle user queries through a dynamic, responsive approach.
Results: The tool consists of three sections. The first is the EGM Panel, where the maps can be consulted. The second is the Dashboard, which allows users to filter articles by tumour type, tumour characteristics, and based on methodology to analyse specific areas of tumour pathology. To enhance the experience, visual figures complement specific outcomes. Finally, the EGM Creator Panel allows users to select specific findings and build new EGMs from our database based on user needs.
Conclusion: This web application constitutes a powerful tool to facilitate evidence-based decision-making in tumour pathology and its classification, significantly improving future review processes of the WCT. By providing access to EGMs, facilitating their analysis and linking them to relevant publications, this tool simplifies the identification of research gaps and pockets of low-level evidence in tumour pathology. This will promote evidence-based practice in pathology, benefiting pathologists, researchers and clinicians.

Funding: This work was supported by the European Commission [HORIZON grant number 101057127]. All partners signed a consortium agreement

PS-02-009
AI-driven microsatellite instability testing in gastric and endometrial cancers: towards reflex testing
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Background & Objectives: Microsatellite instability (MSI) testing is crucial for managing solid tumour patients, particularly for immune checkpoint inhibitor therapy. Reflex MSI testing is recommended for colorectal cancer (CRC), gastric cancer (GC), and endometrial cancer (EC), but challenges such as workload, cost, and tissue availability result in underdiagnosis. While AI models were developed for MSI testing in CRC, limited work exists for less prevalent cancers like GC and EC. This study aimed to develop AI models for MSI testing in GC and EC with strong validation performance, paving the way for clinical use of these screening methods.
Methods: AI classification models were developed to predict MSI status from digitized H&E slides in GC and EC, using independent multicentre cohorts (4 proprietary, 2 per indication, from 3 countries, N=556 patients; TCGA, N=851 patients). Foundation models (H-optimus-0) were combined with the Chowder architecture. In EC, non-tumour regions were automatically excluded during training. A "leave-one-cohort-out" validation approach was used to ensure generalizability and minimize overfitting.
Results:•**GC**: The model achieved an average AUROC of 0.934 (0.916, 0.935, 0.950) for three left-out cohorts. In cross-validation, AUROC reached 0.938 (95% CI: 0.889-0.988), with 0.909 (95% CI: 0.837-0.981) specificity at 0.800 sensitivity.
•**EC**: The model achieved an average AUROC of 0.830 (0.774, 0.820, 0.895) for three left-out cohorts. In cross-validation, AUROC reached 0.833 (95% CI: 0.755-0.911), with 0.716 (95% CI: 0.575-0.856) specificity at 0.800 sensitivity.
Conclusion: Our AI models for MSI detection in GC and EC demonstrated strong validation performance. The "leave-one-cohort-out" strategy was crucial in ensuring robust generalization for future external validation and clinical use. These models have the promise to deliver faster, cost-effective solutions, advancing toward routine reflex MSI testing for GC and EC.

Funding: This work is funded by a collaboration between Owkin and Merck (MERCK SHARP & DOHME LLC)

PS-02-010
Enhancing lymph node metastasis detection with AI: diagnostic, efficiency, and cost benefits of DeepPATH–LYDIA
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Background & Objectives: AI integration in histopathology helps ease diagnostic bottlenecks. DeepPATH-LYDIA, a CE-marked AI tool for breast, colon, lung cancer, and melanoma, highlights suspected tumour areas in lymph-node whole slide images (WSI). This evaluation measures its impact on diagnostic accuracy, workflow efficiency, and cost savings from fewer immunohistochemistry (IHC) requests.
Methods: Four histopathologists with varying experience levels independently reviewed WSIs representing macro-metastases, micro-metastases, isolated tumour cells (ITCs), and negative WSIs. Each completed two assessments—one with AI assistance and one without—separated by four weeks. Slide order and rotation were randomized to reduce bias. Diagnostic labels were compared to ground truth, while review times were recorded to assess efficiency. Time savings, along with Positive Predictive Value (PPV), Sensitivity, and False Positive Rate (FPR), were calculated. IHC savings for breast cancer and melanoma were estimated using Monte Carlo simulation, incorporating relevant diagnostic guidelines and the performance gains observed with AI assistance.
Results: A total of 105 WSIs were evaluated: 30 macro-metastatic, 30 micro-metastatic, 15 ITCs, and 30 negative. DeepPATH–LYDIA assistance improved all performance metrics. PPV increased for macro (95.2% vs. 89.8%), micro (94.3% vs. 87.9%), and ITCs (87.2% vs. 64.9%). Sensitivity also improved: macro (98.3% vs. 95.0%), micro (82.5% vs. 78.3%), and ITC (68.3% vs. 40.0%). FPR was lower with AI assistance (5.0% vs. 10.8%). Review times were reduced across all categories—up to 1.5× for macro, 2.4× for micro, 1.7× for ITC, and 2.2× for negative slides. IHC savings, tailored to breast-cancer and melanoma use-cases, reached up to €11 and €63 per case, respectively.
Conclusion: DeepPATH-LYDIA improves diagnostic accuracy, enhances efficiency, and reduces IHC costs compared to unassisted reviews, supporting its integration for AI-assistance into clinical practice for cancer staging.

PS-02-011

3D HnE: optimising nucleic acid dye penetration for 3D histology

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Background & Objectives: Histology plays a crucial role in elucidating tissue microarchitecture and diagnosing diseases. However, histology has been limited to a 2D tissue section. Recently, a new technology called 3D histology has enabled the visualisation of tissues in 3D, but 3D histology is currently limited by insufficient dye penetration. We aim to develop a staining method called 3D Haematoxylin analogue and Eosin (3D HnE) to increase the penetration depth of a nucleic acid dye.
Methods: Since 3D histology is fluorescence-based, we selected SYTOX orange, a DNA- and RNA-binding dye to mimic haematoxylin staining. The 3D histology protocol consisted of fixation, delipidation, staining and clearing. In the staining step, we used different combinations of supramolecular hosts and organic solvents. To quantify dye penetration depth, we cut the stained tissue in half and imaged the cut-face with a confocal microscope.
Results: We tested 8 supramolecular hosts and 8 organic solvents. SYTOX in water stained only the tissue edge brightly and showed the least penetration depth (70 μm). The addition of sulfobutylether-β-cyclodextrin (SBECD) improved the penetration depth to 130 μm. On top of SBECD, addition of most organic solvents further increased penetration depth, showing a synergistic effect between SBECD and organic solvents. Among organic solvents, the addition of 50% tetrahydrofuran (THF) and 50% 1-methylimidazole (1-MI) achieved the best penetration depths (600 μm, 900 μm). We also tested numerous supramolecular hosts. SBECD achieved the best penetration depth among all supramolecular hosts.
Conclusion: To the best of our knowledge, we are among the first research groups to develop a specific strategy for optimising nucleic acid dye penetration. This allows imaging of a large piece of tissue, overcoming a major limitation in 3D histology. Moreover, 3D HnE does not require trained technicians or specialised equipment, facilitating a wider adoption in biomedical research and clinical histopathology.

PS-02-012

Next generation histopathology: a 3D atlas of normal and cancer tissues

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Background & Objectives: Histopathology has traditionally been limited to 2D tissue sections, which fail to display the full 3D context of tissue microarchitecture. To overcome this, we have made advances in 3D histology by inventing the 3D Haematoxylin analogue and Eosin (3D HnE) staining method. Here, we apply 3D HnE to normal and cancer tissues to construct a 3D histological atlas.
Methods: The workflow of 3D histology was different from the traditional 2D histology. The tissue was first fixed with 4% formaldehyde. Then, the tissue was delipidated with 66% dichloromethane. The tissue was rehydrated and stained with the 3D HnE staining solutions. The tissue was then dehydrated and cleared with benzyl alcohol-benzyl benzoate. A confocal microscope or light-sheet microscope was used for imaging. ImageJ and Matlab were used for converting fluorescent images into bright-field haematoxylin and eosin (H&E) images.
Results: With the 3D histology workflow, we imaged mouse and human tissues including ileum, pancreas, spleen, lung, colon cancer and breast cancer. Interestingly, in the ileum tissue sample, we could observe the 3D transition from intestinal villi to intestinal crypt, as well as the myenteric ganglion embedded between the inner circular and outer longitudinal smooth muscle layers. In the pancreas and spleen samples, we could view the 3D distribution of tissue components, including pancreatic acini and islets, splenic red and white pulp. In the lung sample, we could visualise the 3D shape of alveoli. In the colon cancer and breast cancer samples, we could view the dysplastic glands with a distorted 3D architecture.
Conclusion: We have constructed a 3D histological atlas of normal and cancer tissues, which could serve as a valuable reference for histopathologists. 3D histology could advance the understanding of 3D tissue microarchitecture, such as the characterisation of 3D glandular morphology.

PS-02-013

Artificial intelligence prediction of clinicopathological factors and LRRC15-immunolabeled Cancer-associated-Fibroblast level in colorectal carcinoma using attention-based multiple instance learning

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Background & Objectives: Leucine-rich repeat-containing 15 (LRRC15) expression in cancer-associated fibroblasts (CAFs) correlates with poor prognosis across multiple cancer types. Traditional immunohistochemical (IHC) assessment of LRRC15 is labor-intensive, subjective, and requires specialized staining beyond routine H&E. We aimed to develop an innovative AI approach that could predict LRRC15 expression levels and key clinicopathological factors (specifically pT, pN categories) directly from H&E-stained images.
Methods: We developed a novel two-pronged approach: First, for direct LRRC15 quantification in IHC slides to generate ground truth values, we implemented a novel encoder-decoder model incorporating YOLOv8 detection on 2,980 CAF-area patches (512×512 pixels) from LRRC15-immunolabeled TMA slides. Using 50 annotated patches with bounding boxes and staining intensity scores (0-3), we created a linear-weighted H-score system (range 0-5) emphasizing higher staining intensities. Then for H&E-based prediction of pT, pN categories and LRRC15 H-score, we designed an innovative weakly supervised attention-based multiple instance learning (MIL) framework. This model was trained and tested with dataset spilt on 82 colorectal cancer cases to predict LRRC15 expression levels, muscle invasiveness (≥pT2), and nodal metastasis status (pN0 vs. pN+) directly from H&E patches without requiring IHC staining.
Results: Our dual-model system achieved remarkable performance. The encoder-decoder YOLOv8 model provided objective LRRC15 quantification with H-scores ranging from 1.0 to 2.84 (median 1.18), with 80% accuracy. The attention-based MIL model demonstrated high predictive accuracy from H&E slides alone, achieving 80% accuracy in identifying high LRRC15 expression (grade 3), 83.3% accuracy in predicting muscle invasive carcinoma (≥pT2), and 81.82% accuracy in identifying pN0 status.
Conclusion: Our innovative AI approach successfully bridges the gap between routine H&E histology and specialized biomarker assessment. The attention-based MIL framework effectively extracts predictive features from standard H&E images to simultaneously predict LRRC15 expression and critical clinicopathological factors, offering a cost-effective alternative to special staining, with potential in treatment stratification and prognostic assessment.

PS-02-014
Sparkling Science Project "DigiPath Cancer Fight" – reaching pupils through digital pathology
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Background & Objectives: Cancer remains one of the leading global health challenges, with accurate diagnosis being crucial for effective treatment. Digital pathology, enhanced by artificial intelligence (AI) and machine learning (ML), has revolutionized histopathological analysis, improving diagnostic precision and efficiency. This project aims to engage pupils in digital pathology and cancer research through interactive learning experiences. The pupils actively participate in research by generating their own datasets for training AI tools, which are then cross-evaluated by pathology experts and AI models.
Methods: In collaboration with Medical University of Graz (University Clinic of Dermatology and Venerology, D&R Institute of Pathology, and BBMRI.at), pupils (aged 12-18) from three secondary schools in Graz/Austria participate in workshops and hands-on training sessions where they learn about pathology and biobanking. Furthermore, they explore whole-slide imaging (WSI), actively use digital pathology tools (QuPath) and annotate data. Activities include working with anonymized datasets, analysing tissue samples, and applying AI-assisted diagnostic techniques. The project is funded by the ÖAD (Agency of Education and Internationalisation) and the Federal Ministry of Education, Science, and Research in Austria.
Results: Pupils gain fundamental knowledge in cancer biology and prevention, biobanking, pathology, and digital diagnostics. They actively create annotated datasets for ML algorithms. Comparative analysis between pupil-annotations, expert pathologists, and AI models provides valuable insights into the accuracy of machine-assisted diagnostics. The increased interest in medicine, science, and technology careers among participants highlights the project's educational impact.
Conclusion: This initiative successfully bridges the gap between education, research, and healthcare technology by integrating pupils into the evolving field of digital pathology. By fostering early exposure to biomedical innovation, the project enhances scientific literacy and promotes the development of future professionals in medicine, life sciences, and AI. The findings will be disseminated through scientific conferences, public outreach events, and online platforms to raise awareness of digital innovations in cancer research and diagnostics.

PS-02-015
Utilizing the report structure when extracting information from free text reports via natural language processing and an open large language model
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Background & Objectives: Free text pathology reports are still common and cannot be easily analysed to extract aggregate data. Open multi-lingual large language models (LLM), such as BERT, may be adaptable to healthcare environments, where privacy is paramount.
Methods: A code base on GitHub leveraging Hugging Face, pyTorch and BERT was used to do transfer learning on lower endoscopy biopsy specimens (LEBS). Reports were processed to extract the LEBS and a subset was labelled by two individuals with the help of rule-based string matching (RBSM). A keyword search was used to identify fragments of interest (FOIs) which were then used to train a multilayer perceptron-BERT model (MLP-LLM) and used to help classify all specimens.
Results: The cohort had 188,880 LEBS and 1,290 were labelled. The RBSM suggested that pathology specimens can be classified into three groups: GR1 (positive for X), GR2 (negative for X) and GR3 (X not mentioned), where X (e.g. "granuloma") is a term of interest. The RBSM could separate GR1/GR2 versus GR3; however, it failed on GR1 versus GR2. Thus, the labelled data was used to extract 720 FOIs geared to GR1 (134/720) versus GR2 (586/720). 15,827 of 188,880 cases were GR1+GR2. By MLP-LLM, 1,344 were GR1 and the accuracy of GR1 versus GR2 was 1494/1500 in randomly selected GR1+GR2 LEBS. Five training/validation/testing splits yielded a mean (standard deviation) accuracy of 97.6%(1.5%) in testing and 97.5%(3.1%) in a balanced GR1+GR2 set (n=268). GR1+GR2 had 2,152 unique phrases and 1,374 were singular. The 30 least common accounted for 33.0% of the GR1+GR2 cases.
Conclusion: The analysis demonstrated quantitatively the variation in free text reporting and confirmed that RBSM alone is not viable in LEBS. Understanding the inherent structure of free text reports allow them to be more accurately analysed. Transfer learning uses moderate computational resources and delivers a high accuracy with appropriate pre-processing.

PS-02-016

AI-based estimation of tumour cell percentage in NSCLC: agreement analysis and feature overview from digital pathology algorithms

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Background & Objectives: Estimation of tumour cell percentage (TC%) is a mandatory pre-analytical step before molecular testing in non-small cell lung cancer (NSCLC) yet remains poorly reproducible and imprecise when performed manually by pathologists. While tumour recognition relies on pathologist expertise, TC% quantification is a mathematical task for which the human eye is poorly suited.
Methods: This study presents the application of two artificial intelligence (AI)-based algorithms to 100 NSCLC whole-slide images scanned with a Leica GT450. These tools provide quantitative features such as total tissue area, tumour area, TC%, number of tumour and non-tumour cells, and proportions of necrosis or mucin when available. Manual TC% estimations by two pathologists were collected for comparison but not used as ground truth.
Results: Among the 100 cases, both algorithms provided interpretable results for over 90% of slides. The agreement between algorithms was high, with a mean TC% difference of 1.54% and a standard deviation of 5.71%. In contrast, inter-pathologist variability showed a mean TC% difference of 23.58% with a standard deviation of 16.51%. The average TC% provided by the AI was 24.38% (SD: 17.62%). In contrast, the average TC% estimated by the pathologists was 47.49% (SD: 26.23%), with wider discrepancies observed in samples with low tumour cellularity, potentially leading to overestimation risks.
Conclusion: These findings highlight the improved agreement and objectivity of AI tools for TC% quantification. Their implementation may help reduce variability and support consistent sample triage for molecular analysis. These tools are especially valuable for digital pathology workflows and for molecular biology platforms. A follow-up study is underway to extend this agreement analysis to other tumour types.

PS-02-017

Predicting microsatellite instability in colorectal cancer H&E-stained whole slide images with interpretable deep learning

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Background & Objectives: Microsatellite instability (MSI) is a clinically relevant biomarker for colorectal cancer with an increasing number of deep learning approaches using H&E staining for its prediction. We developed an interpretable deep learning model to predict MSI and investigated its performance in combination with tissue type analysis to quantify the amount of tissue required for accurate prediction and improve interpretability.
Methods: We used additive multiple instance learning (Add-MIL), an approach that requires only slide-level labels for training and can assign a probability to each patch (small image tile) of the whole slide image, allowing efficient evaluation of each patch's contribution to the prediction. For the approach, we used the foundational model H-optimus-0 at 1 µm/px with 224x224 px patches. The training set consisted of 1401 colorectal slides (214 MSI) from TCGA and CPTAC databases. Evaluation was performed on two external cohorts with 250 (100 MSI) and 850 (87 MSI) resection slides, respectively. To assess the tissue type, we used a publicly available segmentation model from the tia-toolbox to determine which patches predominantly contained tumour.
Results: The model achieved an area under the receiver operating characteristic (AUC) of 0.951 on the small and 0.909 on the large evaluation dataset. When limited to tumour patches (comprising 24% and 28% in the small and large cohorts, respectively), the AUC decreased slightly to 0.945 and 0.895. Using only the top 100 patches with the highest MSI scores moderately decreased performance to AUCs of 0.937 and 0.886, respectively.
Conclusion: Add-MIL yielded high performance while allowing greater insight into the results, especially when combined with tissue segmentation. Our findings demonstrate that MSI status can be determined accurately even from a limited number of informative tissue regions. Future work includes more fine-grained analyses and extending the evaluation to biopsies, where only a limited amount of material is available.

PS-02-018

Fast tissue origin classification for quality control in digital pathology with deep learning

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Background & Objectives: Digitalization of large histopathology archives requires processing and validating millions of scanned whole slide images in a limited amount of time. We aim to automatically classify the tissue origin (organ) of H&E-stained slides within one second to enable efficient quality control in digital pathology. Such rapid classification can support the detection of mislabeled slides early in the workflow.
Methods: We trained a deep learning model using thumbnails (1024×1024 pixels) from 11,579 diagnostic images from TCGA and 5,045 from CPTAC. The images were categorized into 14 classes based on the most common tissue types in TCGA: Bladder, Brain, Breast, Colorectal, Kidney, Liver, Lung, Pancreas, Prostate, Skin, Stomach, Thyroid gland, Uterus and Other (encompassing the remaining tissue types). We used a ConvNeXt-Small architecture, pretrained on ImageNet, and trained it using five-fold cross-validation with early stopping. The resulting model ensemble was evaluated on two independent external cohorts: a smaller cohort with 2,876 slides across five classes (Colorectal, Kidney, Liver, Pancreas, Prostate) and a larger cohort with 7,773 slides across all 14 classes. For evaluation, we extracted the thumbnail of the largest tissue component within each slide, identified via contrast-based thresholding.
Results: The model achieved a balanced accuracy of 93.1% on the 5-class cohort and 78.1% on the full 14-class cohort. Notably, when considering only the predictions with high confidence, 50% of the large cohort could be classified with 90% balanced accuracy. The inference time was approximately 60 milliseconds per slide using an RTX 3090 GPU.
Conclusion: Our deep learning approach demonstrates high classification performance with very low inference time, indicating its potential for real-time and cost-effective quality control in digital pathology. Future work includes expanding to more tissue types and more detailed evaluation on challenging cases such as metastases.

PS-02-019

Implementing an AI-assisted digital system in real-world practice: the IMP diagnostics experience

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Background & Objectives: Digital Pathology (DP) provides a significant opportunity to optimize workflows but its integration into clinical practice requires significant adjustments. We outline a strategic framework for implementing the Genius™ Digital System (Hologic), an AI-driven platform for cervical cancer screening, detailing the strategies employed to address real-world challenges in a high-volume pathology laboratory.
Methods: A redesigned workflow transitioned traditional analog cytology to digital. Training occurred in two stages: an initial hands-on session by Hologic, including case reviews and competency assessment, followed by internal training, to reinforce new diagnostic protocols and ensure staff proficiency (n=1300 cases; 8 participants). Routine roll-out began in May 2024, with continuous monitoring and iterative adjustments. A satisfaction survey (1-5) was conducted and workload capacity was reassessed post-implementation. Descriptive statistical analysis was performed (Microsoft®Excel®2019).
Results: IMP Diagnostics processes ≈90,000 gynaecologic cytology exams annually, scanning 90% (liquid-based). Workflow modifications included batch registration (vs. continuous daily registration), updating staining protocol, and using dedicated workstations. In the internal training set, 22 additional cases of ≥LSIL were identified using the digital system (firstly interpreted as negative in the traditional screening). Early challenges included delays in service distribution due to unexpected increase in exam volume, initial learning curve, limitations from using three workstations, and hardware issues. In response, staff schedules were revised and an extra workstation and second scanner were added. Staff satisfaction surveys showed high ratings for ease of navigation (4.8), diagnostic quality (3.9), and overall system performance (4.1), demonstrating confidence in the system. The digital platform allowed resident cytotechnicians to screen 2-3x more cases daily.
Conclusion: Our experience implementing an AI-assisted digital cytology system offers valuable insights for laboratories transitioning to DP. Our findings show improved efficiency and diagnostic accuracy. By sharing our challenges and solutions, we provide a practical framework for similar initiatives.

PS-02-020

Optimizing deep learning image analysis model training using uncertainty metrics-guided selection of regions of interest in non-small cell lung cancer

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Background & Objectives: Supervised deep learning models for analysing immunohistochemically stained histology images require high-quality annotated regions for training. However, manual selection of the regions of interest (ROIs) for annotation on histology slide images is time-consuming and subjective. This study investigates the use of uncertainty metrics to guide ROI selection, aiming to improve model performance while reducing annotation efforts during model development. We hypothesize that concentrating on annotating areas where the model exhibits lower prediction confidence (i.e., regions of high uncertainty) can improve training efficiency and model's accuracy.
Methods: We applied an existing deep learning model (baseline model) to 120 IHC-stained non-small cell lung cancer (NSCLC) slides. Based on the model's prediction errors, a pathologist selected and annotated 457 regions of interest (ROIs). Using Monte Carlo Dropout, we measured the model's uncertainty and categorized these ROIs into four groups (Q1–Q4), with Q1 representing regions of highest uncertainty. New models were trained on different subsets of this training data: all 457 ROIs, only the highest uncertainty ROIs (Q1), only the lowest uncertainty ROIs (Q4), combined high-uncertainty ROIs (Q1 and Q2), and combined low-uncertainty ROI groups (Q3 and Q4). We then compared models' performance on an independent test set of 198 ROIs from 70 slides, annotated by three independent pathologists.
Results: Models trained on high-uncertainty ROIs (baseline model+Q1, 115 ROIs) consistently outperformed those trained on lower-uncertainty regions (baseline+Q4, 113 ROIs), demonstrating a significant 12.1% improvement in predictive accuracy (F1 score 0.805 vs 0.774).
Conclusion: Uncertainty-guided ROI selection provides a promising strategy to optimize computational pathology model training, improving performance and streamlining annotation workflows. Our results suggest that incorporating uncertainty-based ROI selection enhances model learning efficacy, potentially reducing the number of ROIs that pathologists need to annotate for model development. Future work will expand the application to additional datasets and evaluate its utility beyond NSCLC.

PS-02-023

AI-assisted macroscopic assessment of lung resections: a pilot study

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Background & Objectives: The recent implementation of the NHS Lung Cancer Screening Program in the UK has resulted in a rise in early-stage diagnoses, which has subsequently increased the workload for histopathology departments and specimen complexity. Macroscopic assessment is a crucial yet time-consuming step in pathology, that requires specialised expertise to accurately identify and sample tumour areas. This study aims to develop and compare three AI-driven algorithms for analysing macro photographs of lung specimens, providing automated detection, classification, and mapping of lung tumours.
Methods: A total of 184 macro photographs were collect from 117 lung resection specimens, which included both benign and malignant cases. Each image was labelled with segmentation annotations to highlight abnormal areas, such as non-neoplastic changes, benign neoplastic lesions, and malignant neoplastic tumours. We developed, fine-tuned and tested three deep learning segmentation models, including U-Net, ConvNeXt V2 and Segment Anything Model (SAM), to identify abnormal regions, comparing their performance in detecting lung lesions on macro photographs.
Results: The fine-tuned SAM model achieved high accuracy in identifying abnormal lung regions on macro-images (F1: 0.74; Dice: 0.75), outperforming U-Net (F1: 0.17; Dice: 0.23) and ConvNeXt V2 (F1: 0.72; Dice: 0.62), indicating its potential to assist with accurate tumour sampling.
Conclusion: The Segment Anything Model demonstrates promising performance in the segmentation task, utilising data that reflects real-world variability. These findings suggest that this AI tool can streamline macroscopic assessment of lung specimens, improving the consistency in tumour sampling. Additionally, it can support pathologists in managing increasing case volumes and assist in training new junior doctors. Integrating AI into macroscopic analysis, may contribute to faster, standardised specimen processing and improved diagnostic workflows. Further validation on a larger dataset is essential to refine its clinical applicability and integration into routine practice.

PS-02-024

AI-based automatic analysis of sputum smears stained Ziehl-Neelsen used as screening tool for tuberculosis

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Background & Objectives: Tuberculosis is the main cause of death by infectious diseases world-wide. Mycobacterium tuberculosis can be identified in sputum or tissue for positive diagnosis and in screening programs especially in high incidence of tuberculosis regions.
Methods: Microscopic identification of Mycobacterium tuberculosis in Ziehl-Neelsen (ZN)-stained sputum smears is extremely time consuming, thus not entirely suitable for screening on a large number of subjects. We previously presented an algorithm able of automatic detection of Mycobacterium tuberculosis on tissue stained with ZN with very good results (specificity of 100%, sensitivity of 95.65% and accuracy of 98.33%).
We tested the performances of this algorithm on 1059 ZN-stained sputum smears as a possible tool in screening. The slides were scanned with automatic scanners Leica Aperio AT2 and GT450 40× scanning mode in one plane without Z-stacked images. The results of the algorithm were displayed as a heat-map of 32x32pixels patches in batches of different levels of confidence with an increment of 5: (95-100], (90-95], etc. Each patch could include one or more bacilli, either single or in clusters.
Results: The analysis of the positive patches reveals a good specificity (86.84%) and 100% sensitivity for patches with level of confidence over 90; the accuracy remains over 95% for all level of confidence over 80 except the class (95-100]. Problems with specificity (13.16% false positive results) are caused by peculiarities of sputum smear appearance (uneven thickness, dust contamination, lack of coverslip) but this is expected in screening. Further training of the algorithm on sputum smears will be perform to increase the specificity over 95%.
Conclusion: Even in its current form, our algorithm is suitable for screening since its results show no false negative results; in this manner the persons with highest risks to disseminate the infection are identified and further diagnosed and treated

Funding: This research was partially funded by a grant of the Ministry of Research, Innovation and Digitization, CNCS–UEFISCDI, project number PN-III-P4-PCE-2021-0546, within PNCDI III (no. PCE 109/2022)

PS-03 Poster Session Head & Neck Pathology

PS-03-001

Diagnosis of amyloidosis with minor salivary gland biopsy: case series

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Background & Objectives: The minor salivary gland biopsy (MSGB) is a sensitive and low-invasive method to diagnose amyloidosis. Another advantage of MSGB is related to distinct distribution patterns of amyloid deposits within the salivary gland in case of different types of amyloidosis. The current study describes our experience of diagnosing amyloidosis on the base of MSGB.
Methods: Retrospective study of all MSGB with the clinical suspicion of amyloidosis performed at our centre between 2023-2025. The diagnosis of amyloidosis was based on histologic evaluation of H&E MSGB slides and positivity for Congo red stain with the assessment of amyloid distribution pattern. Immunohistochemical (IHC) subtyping of amyloidosis was performed with antibodies against serum amyloid A protein, transthyretin and kappa and lambda light chains.
Results: The study included MSGB from 32 patients whose median age was 73 years old (range: 50-92). There was female predominance (18/32, 56%). In 18 cases (56%), the diagnosis of amyloidosis was confirmed; in 16 of them the amyloid was subtyped. AL amyloidosis was detected in 8 patients (53%), AA amyloidosis in 6 (40%) and wild-type transthyretin amyloidosis (ATTR) in 1 (7%). Among patients with AL amyloidosis, 6 had been previously diagnosed with monoclonal gammopathies. The underlying pathology in AA amyloidosis was determined in 3 cases and included familial mediterranean fever, chronic osteomyelitis and rheumatoid arthritis. One patient was diagnosed with AL and concurrent ATTR with MSGB and endomyocardial biopsy, respectively. Histologically, both AL and AA amyloidoses had a predominant basement membrane (BM) distribution pattern (94%) with minor vascular and interstitial patterns. In the ATTR case, nodular amyloid deposits were observed.
Conclusion: AL and AA amyloidoses were almost equally prevalent in our series without traditionally described predominance of the former. Histologically, AL and AA amyloidoses were indistinguishable, both demonstrating BM pattern that in our opinion can be overlooked mimicking salivary gland atrophy.

PS-03-002

Evaluating tumour budding in laryngeal squamous cell carcinomas: a comprehensive study of the largest Indian cohort with insights on prognostic implications and clinical outcome

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Background & Objectives: Tumour budding(TB) is a promising prognostic predictor in many carcinomas. Yet its utility and importance is underexplored in laryngeal squamous cell carcinoma (LSCC). The objectives of this study were: (1) to assess TB (tumour budding score, maximum tumour budding/hpf, total tumour budding/10 hpf) in LSCCs; (2) to investigate its association with clinical and histopathological parameters; and (3) to determine its prognostic significance.
Methods: This study is the largest Indian study on LSCC, analysing 94 cases from total laryngectomy specimens over five years.
Results: The cohort comprised 85 men and 9 women, aged 38–76 years. Most tumours (63.82%) had transglottic involvement, with 73.4% being moderately differentiated. The majority were in pT4a stage (71.27%). Nodal involvement was present in 45% of cases. Lymphovascular invasion (31.9%) and perineural invasion (38.29%) was recorded. Tumour budding was high (>10 buds/hpf) in 9.5%, moderate (5-9 buds/hpf) in 30.85%, and low (1-4 buds/hpf) in 59.57%. Significant correlations were found with N stage ($p \leq 0.01$), lymphovascular invasion ($p = 0.04$), T stage ($p = 0.02$), perineural invasion ($p = 0.02$), and lymphocytic stromal response ($p = 0.02$). These results suggest that greater tumour budding is linked to more aggressive cancer characteristics and worse prognosis.
Follow-up at six months was available for 66 patients, with 3 showing recurrence within 6 months. Higher tumour budding showed significant association with recurrence($p \leq 0.03$).
Over a period of 8 to 20 months, 10 patients developed recurrence. Of these, 6 had recurrence in the neck nodes, 2 at the operated site, and 2 at both the operated site and in the neck nodes. Additionally, 2 patients later developed lung metastasis.

Conclusion: As the largest Indian study on LSCC, this research highlights that tumour budding is an independent prognostic marker and necessitates the need to standardize the assessment of TB in larynx.

PS-03-003

Gnathic metastases: a 10-year retrospective analysis of rare bone and soft tissue malignant involvement

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Background & Objectives: Metastases to the bone and soft tissues of the jaws are extraordinarily rare, often signifying advanced-stage cancer and a poor prognosis. This study investigates the clinicopathologic features of 14 metastatic neoplasms involving the oral region and diagnosed at our institution over a decade.
Methods: We searched EPIC and COPATH for all cases signed as metastatic tumours in the past decade at Temple University. Inclusion criteria consisted of the following:
(a) Archived cases from our institution, diagnosed between 2013 and 2023, with available haematoxylin and eosin (H&E) and immunohistochemical slides.
(b) Adequate documentation of clinicopathologic characteristics of jaw metastases, along with a confirmed history of primary malignancy.
(c) Microscopic findings indicative of metastatic disease, regardless of whether the primary site was identified.
Results: A total of 14 cases of oral metastases were identified, comprising 4 cases (29%) in men and 10 cases (71%) in women, with a median age of 69 years (range: 43–89 years).

- **Anatomic location:** 2 cases (14.2%) involved the oral soft tissues, 7 cases (50%) occurred in the posterior mandible, 3 cases (21.4%) in the anterior mandible, and 2 cases (14.2%) in the maxilla.
- **Clinical associations:** 4 cases (28.5%) were linked to extraction sites, and 4 cases were initially misdiagnosed as pyogenic granuloma.
- **Primary sites:** The most common primary site was the breast (n = 5, 35.7%), followed by cases with an unknown primary origin (n = 5, 35.7%). Other identified primary sites included kidney (n = 1, 7.1%), colon (n = 1, 7.1%), lung (n = 1, 7.1%), and thyroid (n = 1, 7.1%).

Conclusion: Metastases in the jaws are exceedingly rare, representing 1% of tumours in this area. Greater awareness in the differential diagnosis is essential, as these lesions often mimic inflammatory, reactive, or benign processes, and, sometimes, may represent the first clinical manifestation of an occult malignancy.

PS-03-004

Mucin-rich salivary duct carcinoma: a distinct subtype or a new entity? Insights from transcriptomic analysis

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Background & Objectives: Mucin-rich salivary duct carcinoma (SDC) is a rare and poorly characterized subtype of SDC. Conventional SDC shares molecular features with breast carcinoma, but the transcriptomic profile of mucin-rich SDC remains unclear. Given its distinct histopathological features, we aimed to explore the molecular characteristics of mucin-rich SDC through transcriptomic analysis and compare it with conventional SDC and pulmonary adenocarcinoma to better understand its classification.
Methods: We analysed three cases of mucin-rich SDC diagnosed in the parotid gland and palate. Immunohistochemistry (IHC) and molecular analysis, including next-generation sequencing (NGS), were performed. Whole Exome RNA sequencing and targeted transcriptomic profiling were conducted to assess gene expression patterns and clustering among mucin-rich SDC in comparison to conventional SDC and pulmonary adenocarcinoma. Hierarchical clustering analysis was performed to determine molecular similarities.
Results: All three cases demonstrated positive expression of CK7 and HER2, with variable expression of additional markers such as EMA and androgen receptors. Mutational analysis identified alterations, including KRAS (G13D) and PIK3CA (H1047R), among others. Transcriptomic profiling revealed that mucin-rich SDC cases clustered with pulmonary adenocarcinomas rather than with conventional SDC of the salivary glands. This molecular distinction suggests a different oncogenic pathway and possible implications for classification.
Conclusion: Mucin-rich SDC exhibits a transcriptomic profile that is more closely related to pulmonary adenocarcinoma than to conventional SDC. These findings suggest that mucin-rich SDC may represent a distinct molecular entity with potential diagnostic implications. Further studies with larger cohorts are needed to validate these observations and refine the classification of mucin-rich SDC.

PS-03-005

Prognostic impact of immune phenotype in oral squamous cell carcinoma

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Background & Objectives: In oral squamous cell carcinoma (OSCC), the current tumour-node-metastasis staging system fails to reliably identify high-risk patients, and potential biomarkers improving the risk, prognostic, and predictive stratification of OSCC are sought. Due to the importance of the tumour immune microenvironment in the development and progression of cancer, here we investigated the prognostic impact of the immune phenotype in OSCC.
Methods: The study included 119 OSCC patients treated by curative surgery. Densities of stromal and intra-tumoral tumour-infiltrating lymphocytes (TILs) were evaluated according to guidelines of the International Immune-Oncology Biomarker Working Group in haematoxylin and eosin-stained slides. Based on the extent and spatial distribution of TILs, the tumours were classified as immune-excluded, immune-inflamed, and immune-desert, immune phenotypes were correlated with clinicopathological parameters, and their prognostic significance was investigated. Survival analyses for disease-free, disease-specific, and overall survival were performed by the Kaplan-Meier method, and the prognostic value of immune phenotypes was assessed by Cox regression models.
Results: Immune-desert and immune-inflamed phenotypes significantly correlated with lymph node metastasis, higher stage and grade, infiltrative pattern of invasion, and perineural invasion. A significantly higher incidence of local recurrence was demonstrated in patients with immune-inflamed phenotype versus excluded-phenotype. In Kaplan-Meier analysis, the most prevalent immune-excluded phenotype displayed significantly better disease-free, disease-specific,

and overall survival, in contrast to shorter survival rates for immune-desert and immune-inflamed OSCC. Cox regression analyses showed an independent negative prognostic impact of both immune-desert and immune-inflamed phenotypes compared to immune-excluded OSCC, in all measured clinical endpoints including disease-free, disease-specific, and overall survival.
Conclusion: Our findings support that the histological evaluation of tumour immune phenotype might provide significant information on OSCC hazard discrimination, prognostication, and treatment decisions. The study identified the immune-desert and immune-inflamed OSCC phenotypes associated with worse prognosis reflecting the lack of pre-existing anti-tumour immunity or immunosuppressive tumour immune microenvironment.

Funding: Supported by the Ministry of Health, Czech Republic – conceptual development of research organization (FNOl, 00098892) and the Internal Grant Agency of Masaryk Univerzity (MUNI/A/1621/2024)

PS-03-006
Liquid biopsy in saliva: MMP-2, MMP-9, and TIMP-2 as potential biomarkers for oral squamous cell carcinoma
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Background & Objectives: Oral squamous cell carcinoma (OSCC) is a prevalent malignancy with a significant global burden. Early detection remains challenging. Matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) are associated with tumour invasion and metastasis. This study aimed to evaluate the diagnostic utility of salivary MMP-2, MMP-9, and TIMP-2 as potential non-invasive biomarkers for OSCC.
Methods: An observational cross-sectional study was conducted including 60 patients with histologically confirmed OSCC and 30 age- and sex-matched controls from the HEADSpace/Interchange Colombian cohort. Saliva and serum samples were collected to quantify biomarker levels using ELISA. Generic MMP activity in saliva was measured via fluorescence-based assays. Tissue microarrays were constructed from paraffin-embedded tumour blocks, and protein expression was evaluated by immunohistochemistry (IHC).
Results: MMP-9 and MMP-2 concentrations were significantly elevated in saliva from OSCC patients compared to controls (MMP-9: 936.47 ng/ml vs. 13.16 ng/ml; MMP-2: 79.93 ng/ml vs. 2.06 ng/ml; both $p<0.005$). Serum analysis confirmed increased MMP-9 levels (656.92 ng/ml). Salivary MMP activity was higher in the case group (134.86 RFU ±13.19) compared to controls (66.66 RFU ±14.66; $p>0.05$). IHC demonstrated significantly higher expression of MMP-9, MMP-2, and TIMP-2 in tumour tissues than in normal mucosa ($p<0.005$).
Salivary MMP-9 showed strong diagnostic performance (Sensitivity = 0.817, 1-Specificity = 0.133), as did MMP-2 (Sensitivity = 0.717, 1-Specificity = 0.367). Among tissue markers, TIMP-2 demonstrated the best performance (Sensitivity = 1.00, 1-Specificity = 0.00).
Conclusion: Salivary concentrations of MMP-2 and MMP-9 are significantly increased in OSCC patients, supporting their use as potential diagnostic biomarkers. These findings were consistent with serum levels, MMP activity, and IHC expression. Further studies are warranted to assess the prognostic value of these biomarkers in relation to recurrence, metastasis, and patient survival.

PS-03-008
MTAP loss correlates with favourable prognosis in HPV-independent, p16-negative oropharyngeal squamous cell carcinoma
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Background & Objectives: HPV-independent oropharyngeal squamous cell carcinoma (OPSCC) is an aggressive cancer, but molecular prognostic stratification has not been established. Deletion of *CDKN2A* (encoding p16) is a common genetic event in HPV-independent OPSCC. Homozygous deletion of *CDKN2A* is recognized as a poor prognostic factor in various tumours such as gliomas, and MTAP immunostaining serves as a surrogate marker for it. In addition, since MTAP is related to the methionine salvage pathway, various cancer cell lines with *MTAP* deletion are reported to exhibit increased sensitivity to the pyrimidine analog 5-fluorouracil (5-FU). In this study, we aimed to clarify the prognostic impact of expressions and homozygous deletions of *CDKN2A* (*p16*) and *MTAP* in OPSCC.
Methods: We examined *CDKN2A* (*p16*) and *MTAP* in 177 cases of OPSCC (106 HPV-positive, 71 HPV-negative), using immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH).
Results: MTAP loss by IHC was observed in 25.3% (16/63) of HPV-negative/p16-negative OPSCCs, and FISH confirmed the homozygous deletions of both *CDKN2A* and *MTAP*. All HPV-negative/p16-positive OPSCCs (n=8) and HPV-positive OPSCCs (n=106) did not show MTAP deficiency. The prognosis of HPV-negative/MTAP loss group (n=16) was significantly better than that of HPV-negative/MTAP-retained group (n=47), and was as favourable as HPV-positive group (n=106). Moreover, a similar trend was confirmed in HPV-negative OPSCC patients treated with pyrimidine-based chemotherapy (n=46).

Conclusion: These findings suggest that MTAP deficiency is closely associated with homozygous deletions of *CDKN2A* and *MTAP* in HPV-negative/p16-negative OPSCC. Furthermore, MTAP loss may be a favourable prognostic factor in HPV-negative OPSCC and this paradoxical phenomenon might be explained by the enhanced treatment efficacy to chemotherapy with pyrimidine analogs.

PS-03-009
Clinicopathological spectrum of salivary gland myoepithelial carcinoma of the head and neck region
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Background & Objectives: Myoepithelial carcinoma (MECA) is a rare salivary gland tumour accounting for 0.1-0.45% of salivary gland neoplasms. MECA often arises from pleomorphic adenomas and exhibits aggressive behaviour with high recurrence and metastasis rates. Diagnosing MECA is challenging due to its histological overlap with benign and other malignant tumours.
This study aims to evaluate clinical and histological features and immunohistochemical profile of MECA, distinguish de novo cases from those arising in pleomorphic adenomas.
Methods: MECA cases of the head and neck region diagnosed at our institute from January 2014 to December 2023 were retrieved and reviewed. Clinical details were obtained from electronic medical records.
Results: A total of 58 cases (36 males, 22 females; M:F = 1.6:1) were analysed, with age range 14-80 years (mean 52.2 and median 51 years).

Minor salivary glands were more commonly involved as compared to major salivary glands (1.3:1), although the parotid gland was the most frequent site (34.5%). Tumours displayed lobulated and expansile invasion patterns Diverse cell morphologies were noted, predominantly epithelioid, followed by plasmacytoid, clear cell and spindle cell morphology, in a myxoid and/or hyalinised stroma. Architectural patterns included solid, nested, cord-like, and trabecular, with 63.8% showing a combination of these patterns.
Pre-existing pleomorphic adenoma was found in 24.1% of cases (8 in major and 6 in minor salivary glands). Immunohistochemistry confirmed myoepithelial differentiation, with SOX10 (86.4% cases) and S100 (87.8% cases) as reliable markers. Poorer recurrence-free survival (RFS) was linked to presence of necrosis ($p = 0.002$), invasive growth patterns ($p = 0.023$), mitotic index >4/10 HPFs ($p = 0.028$), and Mib1 proliferation index >6% ($p = 0.05$).
Conclusion: This is the largest series of MECA of head and neck region in Indian continent. Our study shows that presence of necrosis, infiltrative invasion, and high Mib1 proliferation are key predictors of poor outcomes in MECA.

PS-03-010
Superselective intra-arterial chemotherapy for p16+ oropharyngeal cancer: long-term outcomes
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Background & Objectives: Despite being accessible for visual examination, the incidence of oropharyngeal cancer continues to rise. Improving treatment efficacy for these patients remains a critical challenge. The aim of this study was to analyse long-term outcomes in patients with oropharyngeal cancer p16+ treated selective intra-arterial chemotherapy and chemoembolization in combination 3D conformal radiation therapy (RT).
Methods: The study included patients with stage III (T1-3N0-1M0) and IVa (T2-4N1-3M0) p16+ squamous cell carcinoma. The exclusion criterion was the presence of distant metastases. Patients were divided into two groups: I comprised 28 patients stage III– 9; IVa – 19. Treatment protocol for Group I involved superselective volume-controlled intra-arterial chemotherapy (SIAC) using an original modified PF regimen. Intra-arterial infusion of cisplatin (100 mg/m²) and 5-fluorouracil (250 mg/m²). Supplemented with daily intravenous 5-fluorouracil (750 mg/m²). Infusion duration: 45–60 minutes. Final: intratumoral vessel injection of cisplatin concentrate (10 mL). After SIAC in parallel RT is performed daily (70 Gy/35 fr). SIAC was repeated every 21 days (3–4 cycles). Group II included 28 patients: stage III– 16; IVa– 12. Treatment: PF regimen in parallel RT is performed daily (70 Gy/35 fr).
Results: The technical success - 100%. In Group I positive tumour response was observed 24 hours after SIAC. Overall response rate 100% in Group I (SSIAC + chemoradiotherapy); 72% in Group II (PF + RT) ($p < 0.01$). No statistically significant difference in adverse events was observed between the two groups. Median survival 25 months in Group II; 81% survival rate in I at 25 months ($p < 0.01$). 7-year survival: 58% - Group I; 36% - II.
Conclusion: This study demonstrates a significant improvement in 7-year survival for patients with p16+ oropharyngeal cancer when SIAC is incorporated into the chemoradiotherapy regimen. SIAC technique proved highly effective, with superior long-term outcomes compared to PF.

PS-03-011
Incidental thyroid carcinoma: assessing prevalence and subtype reporting practices at an Irish tertiary hospital
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Background & Objectives: Incidental thyroid carcinoma (ITC) can be diagnosed postoperatively in thyroid specimens removed for benign conditions, where preoperative imaging and cytology are benign or indeterminate. This audit assesses the prevalence, histopathological features, and subtype reporting practices of ITC against the Royal College of Pathologists (RCPath) Thyroid Cancer Reporting Dataset (2023).
Methods: All thyroidectomy specimens (2020-2024) were identified using SNOMED coding. Demographic and histopathological data were collected from electronic patient records and crosschecked with laboratory reporting databases. ITC case data was reviewed, focusing on tumour prevalence, histological subtype reporting, and pathological staging compliance with RCPath (2023) guidelines.
Results: ITC was identified in 7% (n=47) of 666 thyroidectomy specimens. Patients had a mean age of 52.4 years, and 74.5% were female. The predominant indications for surgery were thyroid nodules (45%) and symptomatic goitre (38%). Tumours were predominantly small, with a mean size of 6mm (range 0.2-45mm). AJCC staging revealed the majority of cases were pT1a (85%), followed by pT1b (8%) and pT3a (5%). The most frequent histological subtypes were classic PTC (32%) and follicular PTC (30%). Initially, 32% (n=15) of cases lacked documented PTC subtype. Following introduction of RCPath (2023) guidelines – which recommends replacing the term "papillary microcarcinoma" in favour of PTC and explicit subtyping – only 8% (n=4) did not have subtype documented. High-grade features and lymphovascular invasion were rare, observed in just 2% and 4% of cases respectively.
Conclusion: This audit demonstrates a notable prevalence (7%) of ITC in patients undergoing thyroidectomy for benign conditions. Implementation of RCPath (2023) guidelines significantly improved subtype reporting compliance. Future steps include periodic re-audits, extending the audit timeframe, and assessing ITC prevalence and clinical outcomes in an Irish population through a retrospective cohort study.

PS-03-012
Optimizing intraoperative frozen section diagnosis in laryngeal surgery: navigating the challenge of small specimen size in voice preservation
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Background & Objectives: Intraoperative consultation (frozen sections, FS) is essential in guiding surgical management of laryngeal lesions. In voice-preservation surgeries, where biopsies are small, data on FS performance and diagnostic discordance are limited. This study reviews our institutional experience to assess diagnostic accuracy and identify causes of discordance in small biopsy specimens from voice-preserving procedures.
Methods: We reviewed pathology archives for FS specimens obtained by laryngologists between October 2022 and February 2025. Of 83 FS samples from 63 patients, 10 were excluded (7 extralaryngeal, 3

missing slides). Concordance was defined as a perfect FS-to-permanent diagnosis match; any upgrade or downgrade (e.g., dysplasia to carcinoma) was considered discordant. Causes of discordance were categorized as block sampling error, interpretative differences, contextual discordance, or ancillary testing needs. Clinical and demographic data were collected.

Results: Among 76 FS samples, the primary purpose was diagnosis (82.9%) or margin assessment (17.1%). Most biopsies (72.3%) measured ≤0.4 cm, with a median of 0.3 cm and two fragments per sample. Concordance between FS and final diagnoses was 65.8%. Upgrades and downgrades occurred in 25.0% and 5.3% of cases, respectively. Discordance was attributed to combined sampling and contextual issues (30.4%), sampling alone (21.7%), interpretative differences (17.4%), contextual discordance alone (13.0%), ancillary testing (13.0%), and contextual issues with ancillary needs (4.3%). FS sensitivity and specificity for neoplasm or dysplasia were 80%, with positive and negative predictive values of 95.2% and 44.4%.

Conclusion: FS remains a valuable tool in voice-preserving surgery, with high positive predictive value and low interpretative error. However, small biopsy size challenges diagnostic certainty. Block sampling—linked to over half of discordant cases—may reflect efforts to preserve tissue for permanent sections. Improved communication between surgeons and pathologists is key to balancing diagnostic accuracy with voice preservation.

PS-03-013

The role of glucose transporter type 1 expression in the pathogenesis of oral cancer

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Background & Objectives: The upregulation of hypoxia-associated genes, such as glucose transporter type 1 (GLUT-1), plays a key role in the pathogenesis of Oral Squamous Cell Carcinoma (OSCC), with increased expression correlating with greater tumour aggressiveness. This study aims to evaluate the gene expression profile of GLUT-1 in OSCC and correlate its expression patterns with the clinical and pathological data of affected individuals.

Methods: Fresh OSCC samples (n=36) and healthy gingival tissue (control samples) were collected from oncology referral hospitals in Espírito Santo, Brazil. Real-time reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was performed to assess GLUT-1 gene expression. Total RNA was extracted, treated, and synthesized into cDNA for RT-qPCR analysis using SYBR green dye. Clinical and pathological data were obtained from histopathological reports and medical records. GLUT-1 expression levels and their correlation with the clinicopathological profile were analysed using Student's t-test. Gene expression was assessed using the comparative method ($2^{-\Delta\Delta CT}$). This study was approved by the Research Ethics Committee of the Integrated Health Care Centre, Vitória-ES (Process No. 318/2011) and by the National Research Ethics Commission (Approval No. 681/2011).

Results: GLUT-1 mRNA expression showed a 38.89% increase in OSCC samples compared to healthy gingival control tissues. Moreover, significantly higher GLUT-1 expression was observed in early-stage OSCC (I/II) compared to advanced stages (III/IV) ($p < 0.05$).

Conclusion: These findings highlight the potential of GLUT-1 as a biomarker for early OSCC lesions, suggesting its possible use for early diagnosis. Further research is urgently needed to validate these findings and explore additional clinical implications.

PS-03-014

Prognostic value of tumour-infiltrating lymphocytes and the expression of PLK1 in oral squamous cell carcinoma

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Background & Objectives: Oral squamous cell carcinoma (OSCC) patients display heterogeneous clinical behaviour and are often diagnosed at advanced stages, leading to a worse prognosis. Therefore, analysing the dynamics among immune response through the assessment of tumour-infiltrating lymphocytes (TIL) and tumour progression, evaluated by the biomarker Polo-like kinase 1 (PLK1), can serve as essential tools for aiding in the recurrence and prognosis of the disease. This study aims to evaluate TIL and PLK1 expression profile and their association with the clinical and pathological features of OSCC patients.

Methods: TIL was analysed in haematoxylin and eosin staining according to Marsh et al. (2011). PLK1 expression by immunohistochemistry was evaluated in 109 paraffinized tissue samples representative of adjacent epithelium, dysplasia and OSCC. PLK1 gene expression was analysed by qRT-PCR in frozen tumour fragments (n=21) and serum samples (n=30), being 17, before treatment initiation and 13, after treatment. Clinical and pathological data were obtained from histopathological reports and medical records. The Chi-Square and Fisher's Exact tests were used to establish an association between the clinicopathological profile with TIL density and PLK1 expression.

Results: Low TIL density was associated with larger tumours (T3/T4) ($p = 0.001$) and advanced stages (III/IV) ($p = 0.011$), while high TIL density correlated with smaller tumours (T1/T2) ($p = 0.001$) and early stages (I/II) ($p = 0.01$). The analysis of PLK1 expression in the segments showed a correlation between the adjacent epithelium pairs and the dysplasia and tumour regions ($p<0.001$). High PLK1 expression was associated ($p<0.001$) with the variables T3/4 tumour size, lymph node metastasis and stage III/IV.

Conclusion: These findings suggest that TIL density and PLK1 expression may serve as valuable biomarkers for understanding tumour development and progression in OSCC.

PS-03-016

Parameters associated with lymph node metastasis in papillary thyroid carcinoma

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Background & Objectives: Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer. Among patients with PTC 30 to 80% develop lymph node metastasis, prompting the routine practice of prophylactic lymph node dissection. Factors associated with the development of lymph node metastases (LNM) remain

poorly understood. The aim of this study was to identify the association between demographic and pathological factors and the occurrence of lymph node metastases in PTC.
Methods: This was a descriptive and retrospective study focused on cases of PTC patients operated in the otolaryngology department of the Habib Thameur hospital and whose resection specimens were analysed in the pathology department of the same hospital between 2020 and 2024. Pathology reports were reviewed for clinical and histological data.
Results: A total of 179 cases were included. The mean age of patients was 48.3 years [12-87], and the sex ratio was 0.22. Tumour size more than 1 cm was seen in 92 patients (51.4%). LNM were identified in 50 cases (27.9%). Male gender, Age<40, bilaterality, multifocality, the presence of vascular invasion and extrathyroidal extension of the tumour were statistically significantly associated with LNM (all $p<0.05$). A tumour size over 1 cm was not statistically significantly associated with LNM. In multiple logistic regression analysis, only the presence of vascular invasion was identified as an independent risk factor for LNM (OR 32, $p=0.02$).
Conclusion: Male gender, age < 40 years, bilaterality, vascular invasion and the existence of extrathyroidal invasion are features associated with a high risk of lymph node metastasis in PTC. Vascular invasion was found to be an independent risk factor for LNM in PTC. Further studies on larger samples are necessary to identify additional factors that may contribute to predicting LNM in these patients.

PS-04 Poster Session Molecular Pathology

PS-04-001
A mass spectrometry pipeline for amyloid typing in Belgium

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Background & Objectives: Accurate typing of amyloidosis deposits is crucial for patient management. Immunohistochemistry remains the standard method but lacks specificity. We present a diagnostic pipeline integrating laser capture microdissection (LCM) of amyloid with liquid chromatography-tandem mass spectrometry (LC-MS/MS). The workflow is being validated by extensive retrospective analysis of amyloid-containing tissue.
Methods: Sixty archived myocardial biopsies, 83 renal biopsies and 100 samples from various other organs were analysed. Amyloid-rich regions were identified on Congo red-stained slides after which LCM was performed. Approximately 60,000 µm² of amyloid was collected per sample into Eppendorf tubes. Protein extraction occurred in a buffer containing 5% sodium dodecyl sulfate (SDS), along with ultrasonication and heat incubation to reverse formaldehyde crosslinks. Proteins were purified using S-trap columns, digested with trypsin, and peptides were analysed using a sensitive timsTOF SCP mass spectrometer using data-independent acquisition (DIA). Proteins were identified from the mass spectral data using DIA-NN software. A custom-built software tool is used to generate reports, integrating protein abundance calculations and visualizations in R.
Results: On samples that could be typed by immunohistochemistry, the concordance rate with MS-based typing was 87%, in line with literature. Importantly, our pipeline allows to type an additional number of patients that could not be typed through immunohistochemistry. Ongoing intra- and inter-run assessments are used to optimize reproducibility. Collaborations across Europe are set up for external validation of the pipeline. Turnaround time is around two months, with ongoing efforts to streamline processing for faster clinical applicability.
Conclusion: Our MS-based pipeline has clear potential for diagnostic use when immunohistochemistry is inconclusive, providing precise amyloid typing via LCM and LC-MS/MS analysis. Further validation and optimization will enhance diagnostic accuracy and reduce turnaround time to meet clinical demands. Our goal is to implement this workflow as a routine diagnostic service in Belgium.

Funding: VIB-Grand Challenges GC04-C04

PS-04-002
First results of liquid biopsy analysis with OncomineTM Precision Assay GX pan

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Background & Objectives: Tissue biopsy is considered the conventional source for molecular pathological analysis. However, there may be barriers to obtaining a tissue sample, such as inaccessible tissue due to the significant procedural risk associated with biopsy, making it less suitable for continuous monitoring of disease progression. Liquid biopsy, circulating cell free/ tumour nucleic acid, as it contains the tumour-specific mutations, offers a potent solution for detection of resistance mutations and follow up of the patients.
Methods: The Genexus Purification System was used to isolate total cell free nucleic acid from 124 liquid biopsy samples of 122 patients and quantification was completed with the onboard quantitation assay and sequenced on the GenexusTM Integrated Sequencer using OncomineTM Precision Assay GX panel. This panel covers 78 variants across 50 key genes.
Results: Based on histological or clinical data our patient cohort was grouped into 4 categories lung (n=98), colorectal (n=11), breast (n=9) and other (n=2). Six cases had no prior histological diagnosis. In 40% of the samples we did not find any clinically relevant mutation. In 39 samples we found clinically relevant EGFR mutations, in 13 samples KRAS, in 3 samples NRAS and in 8 samples BRAF mutation. In 5 breast cancer samples we found ESR1 resistance mutation and in 2 samples targetable AKT1 mutation. In one sample RET mutation, in one sample HER2 mutation and in one sample BRAF-MKRN1 fusion was detected. In a patient`s two samples, after previous ALK positive lung adenocarcinoma, ALK resistancy mutation was observed.
Conclusion: Liquid biopsyis gaining ground in the routine diagnostics. Compared to standard tissue based examination it's less invasive and easy to repeat. The available settings today based on liquid biopsy are screening for minimal residual disease after surgery, monitoring tumour recurrence and therapy efficacy and based on our results effectively detecting tumour-specific mutations.

PS-04-003
Breast cancer characterization via LA-REIMS: exploring a novel mass spectrometry-based diagnostic approach

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Background & Objectives: This study evaluates the feasibility of Laser-Assisted Rapid Evaporation Ionization Mass Spectrometry (LA-REIMS) for distinguishing breast cancer subtypes and normal tissue based on lipidomic signatures. While mass spectrometry (MS) with chromatography is the gold standard for lipid metabolism analysis,

LA-REIMS enables real-time lipidomic profiling, potentially supporting intraoperative decision-making. By integrating spatial data, LA-REIMS findings can be directly compared with H&E-stained slides, linking molecular signatures to histopathology.
Methods: Frozen tissue from 41 breast cancer cases, 34 normal tissues, and five benign tumours was analysed. All patients underwent primary surgery at Semmelweis University. Histological subtypes included 28 no special type (NST), five invasive lobular carcinoma (ILC), and eight others. Molecular subtypes comprised 10 Luminal A, 15 Luminal B1, 2 Luminal B2, 4 HER2, and 9 TNBC. Tissue slices (10–20 µm) were analysed with LA-REIMS at 75 µm resolution, and data were processed using linear discriminant analysis and cross-validation.
Results: Through multistep optimization, the laser focal length was set at 36.7 mm. Preliminary analysis of 20 cancer cases (25,064 scans) and 16 normal samples (7,312 scans) demonstrated 87.88% accuracy excluding outliers and 87.57% including outliers in distinguishing tumours from normal tissue. To differentiate ER-positive (12 cases) and ER-negative (8 cases) tumours, we analysed 13,663 scans (ER-positive) and 11,401 scans (ER-negative), achieving 75.76% accuracy excluding outliers and 73.93% including outliers. Finally, we differentiated grade 3 tumours (14 cases, 5,976 spectra) from grade 1 and 2 cases (6 cases, 23,563 spectra) with 76.60% accuracy excluding outliers and 68.82% including outliers.
Conclusion: Our preliminary findings show promising results, suggesting that LA-REIMS could aid real-time tumour classification and molecular subtyping. We aim to expand our dataset, improving accuracy across molecular subtypes and identifying key differentiation markers. Final results may contribute to biomarker discovery, enhancing personalized treatment, risk stratification, and intraoperative decision-making in breast cancer management.

PS-04-004
Somatic BRCA1/2 mutation analysis in breast cancer patients
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Background & Objectives: BRCA1/2 germline mutations are well-documented in breast cancer, present in approximately 5-10% of cases, and serve as predictive mutation for PARP inhibitor therapy. We performed a large number of somatic BRCA tests at our Institute, which provided valuable information about the distribution of somatic BRCA mutations among different breast tumour subtypes and the ratio of somatic to germline mutations.
Methods: We analysed 805 breast cancer patients from 2019 to 2024 at the National Institute of Oncology. Tumours were classified into intrinsic subtypes based on immunohistochemical studies. DNA extraction was performed using the Maxwell RSC system, tumour cell content was above 10% in every case. Next-generation sequencing (NGS) assays, including the Oncomine BRCA Research Assay and the Oncomine Comprehensive Assay v3 (Thermo Fisher), were used for somatic BRCA mutation analysis. Germline data were obtained from the Department of Molecular Genetics, where genetic analysis was performed using the Illumina TruSeq Hereditary Cancer Panel.
Results: Among the intrinsic subtypes, 36% were triple-negative, 32% Luminal A, 29% Luminal B, and 3% HER2-enriched. Somatic BRCA1/2 testing in 805 patients revealed 115 (14%) pathogenic variants and 8 variants of unknown significance. Mutations comprised 50.4% BRCA1 and 48.7% BRCA2 alterations, with one case exhibiting mutations in both genes. Germline testing was available in 92 patients, within 39 pathogenic variants were identified. Germline mutations were more likely to occur at somatic allele frequencies above 50%. The triple-negative subtype exhibited the highest frequency of both somatic and germline mutations.
Conclusion: Our studies have enabled the identification of patients for whom germline BRCA1/2 mutation analysis is indicated. Ongoing research suggests that patients with somatic BRCA1/2 mutations may soon be eligible for PARP inhibitor treatment. Our data show that somatic BRCA mutations occur 3.5 times more frequently than germline mutations.

PS-04-005
Comparison of molecular alterations in uterine endometrioid carcinomas and serous carcinomas: an *in-silico* study
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Background & Objectives: Uterine serous carcinomas exhibited frequent *TP53* mutations, extensive copy number alterations, minimal DNA methylation changes. In contrast, most uterine endometrioid carcinomas exhibited frequent mutations in *PTEN, CTNNB1, PIK3CA, ARID1A* and *KRAS*, minimal copy number alterations or *TP53* mutations.
Methods: Genomic alterations, mRNA expressions, protein expressions and DNA methylation in uterine endometriod carcinoma (n=399) and uterine serous carcinoma (n=109) in the Uterine Corpus Endometrial Carcinoma (TCGA, PanCancer Atlas) data set were compared from Cbioportal, open access, public genomic bioinformatics database (https://www.cbioportal.org). In the comparison, $p<0.05$ and $q<0.05$ were considered statistically significant.
Results: The most common mutations in endometrioid carcinomas were *PTEN* (82%), ARID1A (54.4%), *PIK3CA* (53.6%), *TTN* (43.8%), *PIK3R1* (36.3%), *CTNNB1* (33.5%), *KMT2D* (32%), *CTCF* (31.4%), *MUC16* (31.2%), *RYR2* (28.4%), while *TP53* (88%), *PPP2R1A* (37%), *PIK3CA* (37%), *FBXW7* (24.1%), *TTN* (23.1%), *ARHGAP35* (18.5%), *CHD4* (17.6%), *CSMD3* (13%), *FLG* (13%), *MUC16* (13%) in serous carcinomas. Among these genes, *TP53, PTEN, ARID1A, PIK3R1, CTNNB1, CTCF, PPP2R1A, TTN,* and *RYR2* mutations were significantly different between the two groups ($p<0.05$, $q<0.05$). *SRARP, LINCO2418, ELAPOR1, ERMN, and TFF3* mRNA expressions were the highest significance in endometrioid carcinomas, whereas *WNT7A, L1CAM, SLC6A12, FIGNL2* mRNA expressions were the highest significance in serous carcinomas ($p<0.05$, $q<0.05$). DNA methylation levels of *DOK5, ADARB2, SYT6, KCNB2*, and *PRKCDBP* were the highest significance in endometrioid carcinomas and *BEST3, C1orf64, FM24B, TNFSF18, KRT1* DNA methylation levels were the highest significance in serous carcinomas ($p<0.05$, $q<0.05$). Overall survival and disease free survival were significantly different between the two groups ($p<0.05$, $q<0.05$).
Conclusion: In this *in-silico* study, significant differences were found between the two groups in terms of 2505 genomic alterations, 10757 mRNA expressions, 3350 DNA methylation rates and 85 protein expressions. It was concluded that the epigenetic mechanism was also effective among the molecular changes between uterine endometrioid carcinomas and serous carcinomas.

PS-04-006
Validation of TruSight oncology 500 HRD for homologous recombination deficiency testing in ovarian cancer
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Background & Objectives: Homologous Recombination Deficiency (HRD) is a crucial biomarker in oncology, indicating impaired DNA double-strand break repair and serving as a predictive marker for PARP inhibitor therapy in ovarian cancer. The Myriad myChoice® CDx test

determines HRD status by analysing genomic instability markers, classifying a Genomic Instability Score (GIS) ≥42 as HRD-positive. Previously, HRD testing was only available through Myriad. However, a collaboration with Illumina led to the development of TruSight Oncology 500 HRD (TSO500 HRD), integrating comprehensive genomic profiling with HRD assessment.
Methods: This study validated TSO500 HRD against Myriad myChoice® CDx using 20 ovarian cancer patient samples with known GIS scores. Three samples underwent repeated testing to assess repeatability, robustness, sensitivity, and detection limits
Results: Correlation analysis showed $R^2 = 0.97$, Negative Percent Agreement (NPA) = 100%, Positive Predictive Value (PPV) = 87.5%, and Overall Percent Agreement (OPA) = 95%. The test variation ranged from -9 to +7, with 85% of samples fluctuating between -5 to +5, aligning with manufacturer expectations. One sample near the threshold (GIS ≥42) shifted HRD status, consistent with expected variability.
A sample with tumour content below the recommended 32% limit demonstrated sensitivity in a quality control parameter, highlighting the importance of tumour percentage evaluation. The test also showed robustness across varying DNA input levels, with samples near the minimum (40 ng) displaying no increased variation.
Conclusion: These findings confirm TSO500 HRD delivers comparable performance to Myriad myChoice® CDx, supporting its implementation for routine HRD testing, reducing turnaround times, and improving treatment decisions in ovarian cancer.

PS-04-007
NTRK1 gene fusions are frequent in juvenile xanthogranuloma
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Background & Objectives: Juvenile xanthogranuloma (JXG) is a rare form of non-Langerhans cell histiocytosis. The most common known gene mutations affect the mitogen-activated protein (MAP) kinase and phosphoinositide 3-kinase (PI3K) signalling pathways. We diagnosed and treated a case of congenital JXG in a premature newborn from a dicygotic twin pregnancy with subdermal infiltrates on the chest, hepatosplenomegaly, ascites, pancytopenia, and petechiae on the abdomen and extremities. Next-generation sequencing of tissue from a subdermal infiltrate revealed a tropomyosin 3::neurotrophic tyrosine kinase receptor (*TPM3*::*NTRK1*) gene fusion. Therefore, a retrospective analysis of 34 additional non-Langerhans cell histiocytoses (16 JXG, 3 adult xanthogranuloma and 1 benign cephalic histiocytosis, both clinical subtypes of JXG, as well as 13 Rosai-Dorfman and 1 Erdheim-Chester disease) for *NTRK*1, 2 and 3 alterations was performed.
Methods: Formalin-fixed, paraffin-embedded (FFPE) non-Langerhans cell histiocytoses (non-LCH) tissues were stained for TRK A, B and C expression using a pan-TRK rabbit monoclonal antibody (clone EPR17341; Ventana Medical Systems). Additionally, fluorescence in situ hybridization (FISH) with NTRK1 and NTRK3 gene probes was performed. Furthermore, DNA and RNA were isolated from non-LCH FFPE tissues and sequenced with a 161 gene panel (Oncomine Comprehensive Assay v3, Thermo Fisher Scientific).
Results: This study revealed an *NTRK1* gene fusion in five JXGs and one adult xanthogranuloma. In conclusion, NTRK1 gene fusions are common in JXG (6/21; 28.6% in our series). This finding places JXG in the category of proliferative diseases with one of the highest frequencies of *NTRK* gene rearrangements.
Conclusion: Therefore, *NTRK* gene fusions should be included in a gene panel test for difficult-to-treat JXG. Given the potential of NTRK gene fusions as a therapeutic target, *NTRK* inhibitors may represent a novel effective treatment for JXG with a challenging clinical course.

PS-04-008
External quality assessment for *FGFR3* testing in urothelial / bladder cancer
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Background & Objectives: Bladder cancer is the ninth most commonly diagnosed cancer worldwide with both incidence and mortality rates increasing, urothelial carcinoma is the most common sub-type. FGFR Kinase Inhibitors were approved by the European Medicines Agency (EMA) in 2024 for treatment of metastatic urothelial carcinoma patients with susceptible *FGFR3* variants. We have piloted a global external quality assessment (EQA) scheme for urothelial / bladder cancer *FGFR3* testing to assure quality of diagnostic services.
Methods: A survey was sent to over 2000 molecular pathology laboratories and thirty were selected to participate in the pilot EQA. Three formalin fixed paraffin embedded (FFPE) samples with mock clinical referrals were sent for *FGFR3* small variant or fusion testing and laboratories were instructed to use their routine test methodologies. Anonymised clinical reports were returned and assessed for *FGFR3* genotyping accuracy, result interpretation in the context of therapy, and clerical accuracy.
Results: The survey was completed by 67 laboratories from 20 countries, with the highest applications from France and Italy. Of the applicants, 87% (58/67) performed targeted NGS, 7% (5/67) performed RT-PCR and 6% (4/67) used other methods for FGFR analysis.
Of the 30 laboratories selected to participate in the pilot EQA, 27 returned results. Overall, the standard of genotyping was high. Three laboratories reported false positive results (3/27, 11.1%), with an overall error rate of 3.9% (3/77 reports). There was some variation in nomenclature used for reporting of the fusion; 33% (9/27) laboratories did not use internationally recognised nomenclature.
Conclusion: Evidence from EQA shows that the introduction of a new test is usually accompanied by a high diagnostic error rate. This pilot EQA indicated that genotyping accuracy was good but there are improvements to be made for laboratories performing *FGFR3* testing for Urothelial cancer, and that there is a need for harmonisation, particularly in reporting of fusions.

PS-04-009
Clinicopathologic and molecular analysis of brain metastases highlights genomic discordance with primary tumours
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Background & Objectives: Brain metastases are the most common malignant tumours of the central nervous system and exhibit diverse biological behaviours. Molecular heterogeneity between primary tumours and their corresponding brain metastases remains poorly understood. This study aimed to investigate the clinicopathologic features and molecular profiles of brain metastases, focusing on discordance in variant status between primary tumours and matched brain metastases.
Methods: We retrospectively reviewed 394 cases of brain metastases surgically resected at a single university-affiliated hospital. Clinicopathologic data were collected, and molecular analyses, including

Next-Generation Sequencing (NGS), Sanger sequencing, real-time PCR, and fluorescence in situ hybridization, were performed on both primary tumours and corresponding brain metastases.
Results: Of the 394 patients, 203 (51.5%) were male and 191 (48.5%) were female, with a median age of 59 years. The most common primary tumour sites were the lung (47.2%), breast (15.0%), colorectum (8.8%), and kidney (5.8%). In lung cancer cases (n=186), *EGFR* variants were identified in 50.0% of primary tumours and 54.4% of brain metastases, while *ALK* fusions and *KRAS* variants were detected in 9.6% and 15.2% of primaries and in 10.6% and 9.8% of brain metastases, respectively. NGS revealed *EGFR* and *TP53* variants (24.3% each) as the most frequent alterations in primary lung tumours, whereas *EGFR* variants (18.0%), *TP53* variants (16.0%), and *MET* alteration (6.0%) predominated in brain metastases. Among 57 paired lung cancer cases, variant discordance was observed in 30%, mainly due to the emergence of additional *EGFR* T790M variants (39%). In colorectal cancer brain metastases, *KRAS* variants were detected in 57% of primary tumours and 60% of brain metastases.
Conclusion: Our findings demonstrate notable molecular discordance between primary tumours and their matched brain metastases, particularly involving *EGFR* variants. Molecular profiling of brain metastases is essential for accurate therapeutic guidance and may influence clinical outcomes.

PS-04-010

Development and validation of digital PCR TaqMan multiplex assays as a tool for liquid biopsy *ESR1* mutations detection

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Background & Objectives: *ESR1* mutations are key biomarkers of resistance to endocrine therapies in breast cancer. The development of novel selective oestrogen receptor (ER) degrader treatments for ER+, HER2- advanced or metastatic breast cancer with *ESR1* mutations necessitates highly sensitive detection methods. This is crucial for cancer research focused on detecting emerging therapeutic resistance in liquid biopsy samples. While sequencing can detect *ESR1* mutations, digital PCR (dPCR) offers a more affordable alternative with a simplified workflow and rapid turnaround time, suitable for frequent testing or resistance detection. We designed and assessed three multiplex assays for dPCR analysis of the eight most common *ESR1* mutations, covering over 85% of cases.
Methods: Assays were designed to detect *ESR1* mutations: E380Q, L536H, L536P, L536R, Y537C, Y537N, Y537S, and D538G in three multiplex panels. Performance was evaluated for analytical specificity, analytical sensitivity, limit of blank, and linearity. Testing included contrived liquid biopsy specimens using plasma with synthetic mutant DNA spike-in. Cell-free DNA was isolated using MagMAX™ Cell-Free DNA Isolation Kit. dPCR was performed on Absolute Q™ instrument (Thermo Fisher Scientific).
Results: For all 3 multiplexes the assays demonstrated >99.9% analytical specificity for respective mutations at 5000 copies/µl. Analytical sensitivity reached an allelic frequency of 0.1% with 500-1000 copies/µl of wild type template for all 8 mutations tested. The limit of blank, established using the wild-type template, was below the sensitivity threshold at 0.3 copies/µl. In contrived plasma samples, 10 copies of mutant DNA were detectable per ml of plasma for the 8 *ESR1* mutations included in the panels.
Conclusion: Our newly developed dPCR multiplex assays for research use only on the Absolute Q instrument accurately detect *ESR1* mutations down to an allelic frequency of 0.1%. This rapid detection technique capable of detecting 8 mutations in only 3 PCR reactions is particularly suitable for analysing liquid biopsy material in cancer research.

PS-04-011

Molecular analysis of endometrial carcinoma using next generation sequencing

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Background & Objectives: The molecular classification of endometrial carcinoma has recently been included in the latest FIGO 2023 clinicopathological staging classification. Its implementation requires the use of immunohistochemical and molecular techniques. This classification differentiates four groups: POLE-mutated, P53-mutated, microsatellite instability (MSI), and no specific alterations. Specific and discriminatory markers allows for the "Histo-Molecular" classification of endometrial carcinoma, which has gained widespread acceptance ("ProMisE classifier"). Here, we applied next generation sequencing for a proper molecular classification of endometrial carcinoma samples based on the latest criteria.
Methods: A total of 113 endometrial carcinoma patients, aged between 30 and 88 were studied. The tumour types included 29 endometrioid G1, 30 endometrioid G2, 22 endometrioid G3, 16 serous papillary, 8 clear cells, 4 carcinosarcomas, and 4 mixed with a high-grade component, all collected between 1996 and 2003. A custom panel of nineteen genes was designed (ThermoFisher Scientific™) and Ion GeneStudio S5 System was used to sequence DNA extracted from frozen tumour samples of our centre's Biobank. Bioinformatics analysis was performed on the Ion Reporter™ Software 5.18 platform (ThermoFisher Scientific™).
Results: Genetic variants were most frequently found in PTEN, followed by PIK3CA, ARID1A, TP53, KRAS, and CTNNB1. Copy number alterations were observed in PIK3CA, BRCA2, BRCA1, and ERBB2. Low-grade tumours exhibited a higher number of alterations in PTEN, PIK3CA, ARID1A, KRAS, PIK3R1, CTNNB1, and FGFR2, while high-grade tumours showed more alterations in TP53 and PPP2R1A. A total of 23 POLE mutations were detected in 14 samples, of which seven (6.19%) were pathogenic variants. The remaining mutations are not classified as pathogenic/likely pathogenic.
Conclusion: Next generation sequencing is a useful tool for the molecular classification of endometrial carcinoma. The most important targets (TP53 and POLE), as well as microsatellite instability genes, are covered by this technology.

Funding: This study was supported by grants from Fundación Canaria Instituto de Investigación Sanitaria de Canarias (FIISC) through the project PIFIISC22/01 and Fundación MAPFRE Canarias and Fundación DISA

PS-04-012

Implementation of the oncomine precision assay panel for the study of non-small cell lung cancer biomarkers. A tertiary hospital experience

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Background & Objectives: The development of drugs targeting specific mutations has made molecular diagnosis a necessity in the clinical routine for non-small cell lung cancer (NSCLC). Clinical guidelines recommend next-generation sequencing (NGS) panels for biomarker analysis. Our Pathology Department has incorporated the Oncomine Precision Assay (OPA, ThermoFisher®) into the molecular diagnosis routine of non-squamous NSCLC.
Methods: A total of 236 paraffin-embedded non-squamous NSCLC samples were sequenced between September 2023 and December 2024. Nucleic acids were extracted using the RecoverAll™ Multi-Sample RNA/DNA kit (ThermoFisher®). The most relevant genetic alterations identified using the OPA panel are presented.
Results: Among the 236 samples of non-squamous NSCLC, 190 (80.5%) were altered. Single nucleotide variants (SNVs) were detected in 169 cases (89%), being *TP53* (32.7%), *KRAS* (30.9%) and *EGFR* (14.7%) the most altered genes. *TP53* mutations were spread throughout exons included in the panel (5 to 8) and R278L/W/Q and R273L/H were the most common variants. *EGFR* most detected alterations were EX19del and L858R. *KRAS* mutations were found mostly in exon 2 (89.5%), being G12C the most prevalent variant. 27 cases (14%) presented copy number variations in *FGFR3, ERBB2, EGFR, KRAS* and *MET*. RNA was altered in 19 cases (10%), being *MET* exon14 skipping (3.7%) and *ALK* fusion (2.6%) the most common alterations.
Conclusion: The OPA panel is useful for the molecular diagnosis of non-squamous NSCLC. Alterations in driver genes were found in 80.5% of the patients. *TP53, KRAS*, and *EGFR* variants respresent 78.3% of these alterations. *TP53* SNVs were widely distributed, with R278L/WQ and R273L/H being the most frequent; EX19del and L858R variants represented the 84% of *EGFR* variants; and the 89.5% of *KRAS* variants were found in exon 2. *FGFR3* and *ERBB2* were the most amplified genes. Finally, 10% of the samples bore RNA alterations, being *MET* exon14 skipping the most frequent, followed by *ALK* fusion.

PS-04-013

A pilot study on the epigenomic profiling of neuroendocrine neoplasms of the lung

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Background & Objectives: Neuroendocrine neoplasms (NEN) of the lung have very different therapeutic approaches and outcomes. Thereby, differentiation of typical carcinoids (NET) and small cell lung carcinomas (NEC) can be challenging. Consequently, the accurate identification and classification of NENs in the lung are of paramount importance for the provision of high-quality patient care. The objective of this study was to perform epigenomic profiling of NETs and NECs of the lung to identify distinct epigenomic signatures.
Methods: In this pilot study, we performed epigenome-wide methylation analysis on 16 NENs, with 8 NETs and 8 NECs. Utilizing the Illumina Infinium EPIC bead chip array, we were able to interrogate more than 850,000 methylation-sensitive CpG sites in parallel. Subsequent computational analyses were then performed to identify differentially methylated genes.
Results: A computational analysis revealed that there were distinct epigenomic differences in NETs compared with NECs. Differential methylation analysis revealed distinct differences in the DNA-methylation landscape. At specific genomic loci, a substantial variation in the degree of methylation was observed.
Conclusion: In summary, the findings of this pilot study demonstrate that DNA methylation profiling enables to differentiate epigenomic profiles of NETs and NECs of the lung. These findings have the potential to serve as valuable markers in future classification of NENs of the lung.

PS-04-014

Analysis of 35 liquid biopsy samples from stage 3 and 4 newly diagnosed lung cancer patients using Pillar Biosciences OncoReveal™ Core and Fusion Next Generation Sequencing panels

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Background & Objectives: We report on the implementation of the Pillar Biosciences Next Generation Sequencing (NGS) platform in our department for the molecular profiling (single nucleotide variants, insertions and deletions, copy number variations, microsatellite instability and fusion detection) of circulating tumour nucleic acid extracted from liquid biopsies from advanced lung cancers in parallel with FFPE sample assessment. We are also performing an in-house comparison to existing standard of care testing.
Methods: We collected whole blood in either Streck or Paxgene tubes from 35 patients; cell-free total nucleic acid (cf-TNA) was extracted from 5ml plasma using the QIAamp Nucleic Acid extraction kit; cf-DNA quantity, quality and integrity was assessed by Qubit and Tapestation, 10-30ng of input DNA/RNA was used in conjunction with the Pillar Biosciences OncoRevealTM Core and Fusion Liquid Biopsy (LBx) NGS kit to create libraries for sequencing. The Pillar NGS panels use SLIMPamp® (stem-loop inhibition mediated amplification) amplicon-based technology providing targeted analysis of 104 genes. NGS library preparation workflow took 12 hours to complete, with Fusion and Core samples prepared in parallel. Sequencing of libraries was performed using paired-end read length of 121bp (2x121) and two indexing reads of 8 cycles each. This was sequenced on the Ilumina NextSeq 550 platform to a depth of 33,000x and 200,000x for DNA and RNA respectively. Data analysis was performed using Pillar Biosciences' PiVAT® automated secondary bioinformatics software with tertiary analysis.
Results: Tissue and plasma testing results for the targetable driver alterations were highly concordant. All patients tested also had assessment with another validated assay. A detailed comparison analysis is ongoing at the time of submission of this abstract.
Conclusion: We show here that we successfully implemented a NGS panel for ctDNA analysis in routine practice. We are initiating the use for other tumour types such as advanced breast carcinomas as well.

PS-04-015

NGS-based liquid biopsy for ESR1 hotspot mutations in breast cancer: development and clinical experience

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Background & Objectives: A new treatment has been approved for patients with oestrogen receptor-positive (ER+) breast cancer harbouring ESR1 hotspot mutations, whose disease has progressed after prior therapies. Ongoing studies are also advancing additional drugs targeting these mutations, which drive resistance to endocrine therapy. Liquid biopsy, a minimally invasive method analysing circulating tumour DNA (ctDNA), is the recommended approach for detecting ESR1 mutations. Here, we describe the development, validation, and use of a new in-house next-generation sequencing (NGS)-based liquid

biopsy assay for identifying ESR1 hotspot mutations to enable precise, personalized treatments.
Methods: Primers with Ion Torrent adaptors were designed to cover ESR1 hotspot mutation regions. Validation included eight G-blocks oligos with the hotspot mutations and two wild-type (WT) G-blocks. Additionally, cfDNA was extracted from five WT plasma samples. For the clinical study, blood was collected in EDTA tubes, and plasma was separated within an hour. cfDNA was extracted from 4 mL of plasma and sequenced on an Ion Torrent S5 machine with >20,000 reads per amplicon.
Results: Validation achieved 100% coverage uniformity. The WT noise level was 0.0019%±0.0023, and the detection limit was set to 0.2%. Sequencing of diluted Gblocks at 2% and 0.5% showed 100% agreement with expected results. In a clinical cohort of 87 patients, ESR1 hotspot mutations were detected in 21 cases (24%), with an average allele frequency of 3.36%±5.16. Among these, 15 patients had one mutation, and six had multiple.
Conclusions We developed a reliable, cost-effective assay for ESR1 hotspot detection via liquid biopsy. Clinical results align with previous findings, though improved patient filtering could enhance detection rates.
Conclusion: We developed a reliable, cost-effective assay for ESR1 hotspot detection via liquid biopsy. Clinical results align with previous findings, though improved patient filtering could enhance detection rates.

Funding: Stemline Israel

PS-04-016
Ultra-fast detection of hotspot mutations in cell-sparce supernatants from Transbronchial Needle Aspiration (TBNA): proof of concept and comparison to tissue-based Next-generation Sequencing (NGS)
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Background & Objectives: Molecular testing is essential in non-small cell lung cancer (NSCLC), with tissue-based next-generation sequencing (NGS) as the gold standard. However, traditional sample processing, including formalin fixation, paraffin embedding, and DNA isolation, requires 2–3 days, and tissue scarcity can limit molecular studies. This study evaluated the feasibility of small-panel NGS-based mutation detection using cell-sparse DNA from the supernatant of transbronchial needle aspiration (TBNA) samples, comparing results to standard tissue-based NGS.
Methods: DNA was extracted from TBNA supernatants and 37 samples were subjected to small-panel NGS (AmpliSeq for Illumina Cancer HotSpot v2). The impact of sample storage length and conditions on DNA integrity as well as sequencing quality, were assessed. Results were compared to standard tissue-based NGS from the respective patients.
Results: 37 samples were examined. In under 80% of cases, pathological mutations were detected, despite low overall DNA content. Supernatants stored in saline showed superior DNA amplification and sequencing results, while prolonged formalin storage (>2 months) led to severe degradation and test failures. Shorter storage durations were associated with improved sequencing quality.
Conclusion: Small-panel NGS on TBNA supernatants enables ultra-fast mutation detection and offers a potential alternative when tissue is scarce. Avoiding prolonged formalin exposure significantly improves DNA integrity and sequencing success. This method could complement or replace tissue-based molecular testing in NSCLC diagnostics.

PS-04-017
Digital spatial profiling of tumour budding in head and neck cancer
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Background & Objectives: Tumour budding, defined as clusters of up to four tumour cells dissociated from the tumour bulk, is an adverse prognostic factor in head and neck squamous cell carcinoma (HNSCC). We leveraged spatial transcriptomics to investigate the underlying gene expression patterns by both intertumoral (bulk of budding vs non-budding tumours) and intratumoral (tumour buds vs bulk) comparisons.
Methods: FFPE tissue sections from 24 budding and 19 non-budding HPV-negative HNSCC (TUM-HNSCC cohort) were analysed using the DSP whole transcriptome atlas (NanoString Technologies, Inc.). Regions of interest were selected to include tumour buds, as well as bulk of budding and non-budding tumours, with separate compartmental analysis for tumour and stroma cells. Differential gene expression analyses identified budding-specific signatures and a tumour budding score (TBS) was derived from consistently overexpressed genes in tumour buds. The TBS was applied to bulk-RNAseq data from the Cancer Genome Atlas (TCGA-HNSC) and drug response data of SCC cell lines from the PRISM lab (PRISM-SCC).
Results: In TUM-HNSCC, the intertumoral comparison revealed 11 tumoral and 5 stromal differentially expressed genes (DEGs), while the intratumoral comparison identified 379 tumoral and 10 stromal DEGs. The sets of tumoral DEGs were enriched by functions in epithelial-mesenchymal transition, coagulation, and others. The TBS, consisting of a 28-gene signature, distinguished tumour buds from all other spatial compartments with an AUC of 0.97 (p=1e-12). In TCGA-HNSC, the TBS successfully separated budding from non-budding tumours (AUC=0.8, p=6e-09) and correlated with poor overall survival (HR = 1.5, p=0.02). In PRISM-SCC, TBS predicted the response to MEK-inhibitors.
Conclusion: Spatial transcriptomics was feasible from HNSCC FFPE tissues and revealed tumour buds-specific transcriptional programs. The TBS separated tumour buds from other tumour regions, distinguished budding from non-budding tumours in bulk-RNAseq data, predicted prognosis, and could help identify therapeutic vulnerabilities.

PS-04-018
Clinical impact and therapeutic implications of the discordance between immunochemical and molecular tests for the diagnostic definition of microsatellite instability in endometrial cancer
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Background & Objectives: To investigate the discordance between immunohistochemistry (IHC) and molecular testing in endometrial cancer (EC) to better identify patients with microsatellite instability (MSI) or stability (MSS), considering the extended utility of molecular profiling for risk stratification, therapeutic decision making and enrolment in clinical trials.

Methods: Molecular profiling of 122 patients with EC collected at Gravina Hospital (Caltagirone, Italy) was routinely performed with Targeted Next Generation Sequencing (T-NGS), IHC and Bethesda panel for microsatellite instability polymerase chain reaction (MSI-PCR) analyses, using both surgical and biopsy specimens. The Pentaplex panel with melting analysis was performed in discordant cases for MSI and deficit of mismatch repair system (dMMR) , while the methylation test was performed to identify Lynch syndrome in cases of MSI/dMMR with loss of MLH1.
Results: All cases were successfully genotyped and the molecular risk stratification data of the patients matched the literature. For MSI identification, 101 (83%) cases were classified concordantly (68% MSS/pMMR; 32% MSI/dMMR), while 21 (17%) cases had discordant results showing an ambiguous phenotype and/or genotype, with correct reclassification by a third method or retesting (16/21). Finally, in 5 (4%) cases, the data were inconclusive as the IHC staining was abnormal without MSI status, leading to difficult classification. These cases had a low rate of MLH1 promoter methylation or genetic mutations in hereditary cancer predispositions.

Conclusion: Our study confirms the possibility of routinely applying molecular classification in patients with EC to ensure correct clinical and therapeutic management. The determination of MSI remains a complicated issue where the rules used for colorectal cancer are not always optimal for EC. The use of appropriate molecular methods, such as the use of an expert team for IHC analysis, is essential for correct MSI identification in EC patients who may benefit from immunotherapy or are carriers of mutations predisposing to a hereditary genetic syndrome.

PS-04-019

Molecular profiling of lung cancer and colorectal carcinoma: mutation prevalence, clinical characteristics and diagnostic timelines: a single-centre study

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Background & Objectives: Molecular profiling plays a crucial role in the personalized management of non-small cell lung carcinoma (NSCLC) and colorectal carcinoma (CRC). This study examines the prevalence of *EGFR*/*KRAS*/*BRAF* mutations in NSCLC, as well as *KRAS*/*NRAS*/*BRAF* mutations and microsatellite instability (MSI) status in CRC, in a major academic centre in Greece. Special focus was placed on diagnostic turnaround times (TAT) to identify barriers to timely clinical decision-making.
Methods: Molecular (qPCR) and MSI (immunohistochemistry) testing data from NSCLC and CRC cases diagnosed at our institution in 2024 were collected. Clinical and pathologic data, including diagnosis date, date of test request and date of result availability, were analysed.
Results: In total, 192 patients with NSCLC and 200 with CRC were identified. Mutations were detected in 32% of NSCLC (45% in non-squamous and 6% in squamous histologies) and 58% of CRC cases. The detected frequencies for NSCLC were 4,6% for *EGFR*, 26% for *KRAS* and 1,6% for *BRAF*, and for CRC 44,5% for *KRAS*, 4,5% for *NRAS* and 10% for *BRAF*. MSI-H prevalence (7.5%) correlated with *BRAF* mutations ($p<0.001$). The median time intervals for NSCLC and CRC, respectively, were: 19 and 37 days from diagnosis to test request, 8 and 7 days from request to molecular results and 28 and 44 days from diagnosis to molecular results. Median time from diagnosis to request was shorter in metastatic tumours and biopsies (compared to primary tumours and resections), though still over 25 days for CRC, with no difference in request-to-result time based on specimen type or origin.
Conclusion: The findings support the implementation of reflex molecular testing to expedite result availability and therapy decisions for each NSCLC and CRC case. The low EGFR mutation rate that was observed in our study may reflect population-specific factors or potential limitations of the testing methodology used.

PS-04-020

Comparison of immune-checkpoint inhibitor therapy efficacy according to the predictive marker tests, microsatellite instability (MSI) and mismatch-repair deficiency (dMMR), used for patient selection

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Background & Objectives: International guideline recommendations consider immunohistochemistry (IHC) for dMMR or molecular techniques (PCR, NGS) for MSI-high determination equal, although there are scattered reports contradicting to this presumption. Here we aimed to analyse if the efficacy of ICI (immune-checkpoint inhibitor) therapies is influenced by the diagnostic method based on patient selection.
Methods: In this multi-centre retrospective analysis, we have directly compared 84 anti-PD1 immune-checkpoint inhibitor treated patients' OS (overall survival) and PFS (progression free survival) according to the qualifying diagnostic method: four MMR protein IHC or Pentaplex MSI-PCR. 35 patients were diagnosed with MMR IHC and 49 with MSI PCR tests. 30 male and 54 female patients were involved in the study and 62 patients had colorectal cancer. The mean age of the patients was 68 years ±9 years, and 67±10 years for the colorectal part of the cohort. The follow-up was set for four years. (SE-RKEB37/2024).
Results: For the entire cohort, the PFS of the MSI group at 48 month was 52.6% as compared to the 59.5% of the dMMR group. Concerning OS, at 48 months 72.4% of MSI patients were alive compared to 69.9% of the dMMR group. The Kaplan-Meier analysis did not show significant differences neither in PFS ($p=0.751$) nor in OS ($p=0.454$). This analysis was repeated for the colorectal cancer subcohort ($n=62$). At 48 months, the PFS of MSI patients was 57.0% compared to 71.5% of the dMMR group. At 48 months, the OS of the colorectal cancer patients was 77.9% for the MSI group and 75.5% for the dMMR group. The Kaplan-Meier analysis again, did not demonstrate significant differences, neither in PFS ($p=0.757$) nor in OS ($p=0.529$).
Conclusion: Our study demonstrated that the therapeutic efficacy of the anti-PD1 antibodies in cancer patients is independent from the predictive markers used for patient selection (MSI-PCR, MMR-IHC).

PS-04-021

ITGB1-driven chondrogenic differentiation in mesenchymal stem cell-like populations of pleomorphic adenomas

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Background & Objectives: Pleomorphic adenomas (PAs) are the most common salivary gland tumours, characterized by high recurrence and potential malignant transformation. Chondroid metaplasia, a hallmark of PAs, involves tumour cells with mesenchymal stem cell (MSC)-like properties enabling chondrogenic differentiation. Integrins, particularly ITGB1, mediate cell-ECM interactions and are crucial in differentiation. ITGB1 regulates mesenchymal cell condensation, a critical step in chondrogenesis. However, its role in PA chondroid metaplasia is not well understood. This study aimed to identify MSC-like subpopulations in PAs and investigate the role of ITGB1 in chondrogenic differentiation, elucidating the mechanisms underlying chondroid metaplasia.
Methods: We performed spatial transcriptomics on PA tissues to analyse gene expression within chondroid metaplasia regions and their surrounding microenvironment. PA primary cell lines were induced to undergo chondrogenic differentiation using differentiation media. RT-qPCR and immunostaining validated gene and protein expression dynamics during chondrogenic induction. Lentiviral knockdown of SOX transcription factors assessed their roles in nodule formation and early differentiation. Single-cell RNA sequencing was employed to characterize PA cellular composition, identifying ITGB1-high populations with enhanced chondrogenic potential and distinct transcriptomic profiles.
Results: Spatial analysis showed chondrogenic marker expression in chondroid regions, as well as in the mesenchymal cluster surrounding the chondroid region, indicating a supportive niche for differentiation. PA cells formed condensations and expressed SOX transcription factors, crucial for chondrogenesis and cellular organization. SOX4 and SOX9 knockdown inhibited effective nodule formation, highlighting their importance in condensation and early differentiation. Immunostaining confirmed ITGB1 expression in myoepithelial cells, and anti-ITGB1 antibodies affected nodule formation by regulating migration, adhesion, and cell-matrix interactions. ITGB1-high populations exhibited upregulated chondrogenic factors and enhanced ECM remodelling, suggesting higher chondrogenic potential.
Conclusion: ITGB1 is a critical regulator of chondrogenesis in PAs, promoting MSC-like differentiation and enhancing chondrogenic potential, highlighting its central role in chondroid metaplasia and the progression of chondroid differentiation.

PS-04-022

Sensitive, fast and cost-effective FLT3-ITD measurable residual disease monitoring using Oxford Nanopore MinIon devices

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Background & Objectives: Measurable residual disease (MRD) monitoring is essential during treatment of acute myeloid leukaemia (AML). NGS assays for FLT3-ITD MRD frequently rely on Illumina long read technology from MiSeq or NextSeq instruments which present high consumables costs, large batch effects, long run times and are limited in maximum detectable ITD length.
Methods: DNA was extracted from peripheral blood and bone marrow samples of patients with FLT3-ITD mutated AML on Promega Maxwell RSC. A wetlab and bioinformatics procedure was established using Oxford Nanopore MinIon and the getITD tool (https://github.com/tjblaette/getitd) to detect MRD.
Results: PCR primers spanning Exons 14-15 of the FLT3 gene were adapted with an 2x8bp dual sample barcode. Amplification using 200ng DNA in triplicates in a 50µl volume yielded consistent results and ascertained sensitivity down to 0,005 % allelic frequency. Amplification on primary AML samples with FLT3-ITD confirmed by fragment analysis created the expected 329 bp band on Tapestation. Sequencing of up to 9 PCR products on an Oxford Nanopore MinIon device yielded approximately 20mio reads in 20hrs with no restriction on ITD length. After basecalling, barcode splitting and removal of low quality reads each PCR reaction yielded 600-800k individual reads. Flow cells could be re-used after up to two days to perform a second run with similar quality and yield. The getITD software was modified for faster search and adapted to Nanopore reads. Limiting dilution of FLT3-ITD positive material demonstrated linearity of measurement down to 50 fragments. getITD was able to detect FLT3-ITD in all initial AML samples (5/5) and in 6/10 post-transplant remission samples. The assay showed superior sensitivity to gold-standard fragment analysis and reaches comparable sensitivity when compared to NPM1 qPCR in patients with FLT3 and NPM1 co-mutation.
Conclusion: Oxford Nanopore sequencing presents a fast, unrestricted and cost-effective solution to low volume, quick turnaround FLT3-ITD MRD detection in AML patients.

PS-04-023

Inter-laboratory variability in DNA yield and quality – results from the 2024 DNA extraction from formalin fixed paraffin embedded (FFPE) tissue EQA

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Background & Objectives: Efficiency of DNA extraction and the resulting quality of the DNA can have major implications for downstream testing. The benchmarking of the quality and quantity of DNA extracted between laboratories provides a mechanism to determine the proficiency of the extraction process. GenQA provides a DNA extraction from FFPE tissue external quality assessment (EQA).
Methods: Participating laboratories were provided with tissue from the same source (3 different cases) and were required to extract DNA using routine extraction methodology and return to GenQA for analysis. The quantity of DNA extracted was determined using digital PCR and volume of DNA, and the quality was assessed using the mean peak size in base pairs (bp) by tapestation.
Results: The yield of DNA extracted was variable. Four laboratories were within the top 10% of mass extracted for 2 out of 3 samples. Five laboratories were in the lower 10% for extracted mass in 2 out of 3 samples, and 1 laboratory was in the lower 10% for all three samples. The mass of DNA extracted from the lung tissue sample ranged from 0.21µg to 4.48µg, endometrial tissue from 0.34µg to 10.96µg and uterine tissue sample from 0.82µg to 12.04µg. The mean bp size varied across the different samples, laboratories and methods. The average mean peak size for the lung sample was 1165bp, for endometrial sample was 609bp and the uterine sample was 1062bp. The lower mean peak for the endometrial sample is indicative of a poorer initial FFPE tissue sample, which may be due to ischemia, or conditions during the fixation process.
Conclusion: The variability of mass and quality of DNA extracted by participants demonstrates the need for improvement and standardisation of extraction protocols. This is pertinent for the increase in more advanced technologies into routine practice which require DNA of high quality.

PS-04-024

Validation of a comprehensive genomic profiling liquid biopsy profiling assay, retrospective analysis of biomarker yield and clinical utilization

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Background & Objectives: Since 2023, comprehensive genomic profiling (CGP) of cell-free DNA is offered at the Department of Pathology of the Vienna General Hospital using the AmoyDx® Comprehensive Assay. At establishment, the intent was to provide diagnostic support for patients where a tissue biopsy was impossible or otherwise unavailable. Here, we describe our experience, including technical performance, biomarker yield, retrospective assessment of clinical utilization, and a browser-based software to assist in reporting and archiving of results.
Methods: The AmoyDx® Comprehensive Assay was performed using cfDNA prepared from plasma according to manufacturer's specifications. A browser-based software for annotation, reporting, interpretation and archiving of the AmoyDx analysis output was developed using R Statistics. Retrospective biomarker analysis included 411 samples, whereas clinical analysis was restricted to 126 consecutive patients. Retrospective biomarker analysis was performed using Cancer Genome Interpreter, whereas clinical data was assessed by review of hospital and prescription records.
Results: Regarding small variants, using optimized filtering criteria and reference standards at 0.5% variant allele fraction (VAF), the assay achieved an analytical sensitivity of 98%, with a limit of blank of 0.05% VAF across representative positions. We identified actionable biomarkers in 40.8% of cases, with documented clinical decision support through testing in 11.7%. In 4.7% of cases, the test identified actionable alterations that were followed by documented specific therapy. Biomarker yield and documented indication, acknowledgement and utilisation of the report showed considerable variability between submitting institutions.
Conclusion: The hard-coded filtering criteria of the AmoyDx® pipeline should be challenged for optimal sensitivity. While the assay detects biomarkers and/or confirmed decision support in a relevant number of cases, inconsistent clinical documentation limits confident retrospective assessment of its true clinical usefulness. We propose that in non-profit institutions, novel and expensive tests such as liquid biopsy-based CGP should be coupled to a prospective study design to accurately monitor clinical utility.

PS-04-025
Assessing the quality of molecular tumour boards
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Background & Objectives: Comprehensive genomic testing for solid tumours requires discussion and interpretation of complex results in multi-disciplinary molecular tumour board meetings. There is a need to look at the quality of output from such meetings as it play a critical role in the reporting of accurate genomic testing.
Methods: Participants were provided with a mock non-small cell lung cancer clinical case, genomic test results for multiple genes, and clinical details of the patient. They were requested to discuss the case in their usual molecular tumour board and submit the work up performed prior to the discussion including classification of the variants found, the outcome of the discussion in the tumour board and the report which would be produced. Results were benchmarked with those of the other participating centres with input from a clinical oncologist and clinical scientists.
Results: Eight centres submitted results for this study. The majority of laboratories submitted work up for the case which included classification of the variants provided. All eight centres identified the same *RET* fusion as being of the highest clinical significance and recognised that inhibitors are available which target the variant. However, due to local differences in approvals and reimbursement of associated treatments the recommendations were variable.
In addition to the main actionable variant the case also included details of other variants which could potentially have clinical implications, the discussion of these was more variable between participating centres.
Conclusion: The returns demonstrate the differences in the outcome of molecular tumour boards which may reflect local approvals for precision medicines. In order for high quality reporting and best outcomes for patients there is a need for harmonisation and education which can be facilitated through external quality assessment.

PS-04-028
AI-driven automation of biomarker and NGS report analysis: advancing quality monitoring in pathology
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Background & Objectives: Standardized biomarker reporting is critical for precision oncology, yet pathology laboratories face challenges in structuring diagnostic data. The Spanish Society of Pathology (SEAP) has developed national quality programs (e.g., ConfirmaHER2, LungPath), but manual data entry limits efficiency and completeness. This study evaluates C-LAB®, an AI-powered platform, for automating biomarker data extraction and standardization within SEAP's Quality Program and a national Next-Generation Sequencing (NGS) harmonization initiative.
Methods: A multi-centre study was conducted across 51 hospitals: 7 for pathology report automation and 44 for NGS analysis. C-LAB® processed 11,199 pathology reports (5,376 breast, 5,823 lung cancer) and 258 NGS reports. The platform extracted structured data on sample characteristics, testing methodologies (IHC, FISH, qPCR, NGS), biomarker results, and genomic alterations.
Results: Pathology report analysis: C-LAB® achieved 92.22% accuracy and a 93.33% F1-score in biomarker extraction, reducing processing time by 90% compared to manual entry. Real-time analysis enabled biomarker quality monitoring, with key positivity rates identified in breast (such as HER2, ER, PR, PD-L1) and lung (such as EGFR, ALK, ROS1, PD-L1, NTRK, RET, MET, KRAS) cancers.
NGS report analysis: NGS report analysis revealed variability in reporting practices: while 87.6% of reports listed tested genes and 81.7% included interpretations, only 34.1% provided therapeutic recommendations, and 5.8% mentioned clinical trial options, highlighting a gap in structured reporting. The most frequently identified biomarkers were: EGFR, ALK, MET and KRAS.
Conclusion: C-LAB® revolutionizes biomarker data management by automating extraction and standardization in SEAP's Quality Program and NGS harmonization. It enhances efficiency, accuracy, and benchmarking across centres, overcoming manual data entry challenges. Future expansion aims to integrate more specialties, cancer types, and clinical data, advancing precision medicine and healthcare accessibility.

PS-05 Poster Session Cytopathology

PS-05-001
Vitreous cytology: comprehensive assessment and diagnostic utility in neoplastic and non-neoplastic disorders
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Background & Objectives: Cytologic evaluation of the vitreous is a reliable method for diagnosing various pathologies, including infections, hematolymphoid malignancies, and metastases. Given the limited and viscous nature of vitreous, we outline our approach to vitreous cytology.
Methods: Vitreous aspiration fluid, typically gelatinous, is initially processed by centrifuging at 1000 rpm for 20 minutes (NF200). The

resulting pellet is then processed (Cellspin, THARMAC) at 500 rpm for 15 minutes, generating up to 10 slides. Two slides are air-dried for May-Grunwald Giemsa staining, and two are placed in alcohol for Papanicolaou staining. Additional slides are reserved for histochemical stains and immunohistochemistry. On most occasions, subsequent saline wash fluid of the vitreous chamber is submitted separately by the clinicians. If clinically relevant, 5 ml is sent for flow cytometry, and the remainder follows the same processing. Cell blocks are created when possible.
Results: To validate our approach, 16 vitreous samples were collected from 15 patients (median age 56 years, M:F ratio 1:1.14). Immunohistochemistry was performed on 9 samples: 5 using cytospin slides, 3 with cell blocks, and 1 with both. Histochemical stains (GMS and iron stain) were used in 2 cases to detect hyphae and hemosiderin, respectively. Flow cytometry was conducted on 12 samples. Diagnoses included high-grade lymphoma (n=5), fungal endophthalmitis (n=1), subacute haemorrhage (n=1), and reactive or benign hematolymphoid cells (n=6), with flow cytometry supporting the findings. From the same patient, n=2 samples required further evaluation (T-cell clonality studies) for definitive diagnosis. In n=1 case, the sample was deemed insufficient for evaluation due to scarcity and low cellularity.
Conclusion: Vitreous cytology, supported by ancillary studies such as histochemistry, immunohistochemistry, and flow cytometry, provides a valuable and reliable diagnostic tool for both neoplastic and non-neoplastic conditions.

PS-05-002
Sensitive next generation sequencing evaluation of routine EUS-FNA smears from solid pancreatic lesions: a pilot study
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Background & Objectives: Pancreatic ductal adenocarcinoma is a highly heterogeneous and diverse disease, characterized by a pronounced desmoplastic microenvironment. This often results in limited cell yield from endoscopic ultrasound(EUS)-guided fine needle aspirations (FNA) or biopsies (FNB) of these lesions, hindering cytomorphological evaluation. Sensitive next generation sequencing analysis (NGS) analysis with Unique Molecular Identifiers (UMI-NGS) might overcome this limit of material.
Methods: Forty EUS-derived FNA smears from solid pancreatic leasions were retrospectively analysed.
UMI-NGS was performed on all samples. In addition, when enough material was available NGS with a pan-cancer diagnostic panel was performed. The results of both cytology and NGS analyses were compared with the definitive diagnosis obtained after surgery or follow-up and pan-cancer diagnostic panel of follow-up material when available.
Results: Molecular analysis using UMI-NGS was successful in 70% of samples (28/40), while only 5 of those samples yielded NGS results with the pan-cancer diagnostic panel. In 19 of 20 samples that were morphologically classified as malignancy, UMI-NGS detected mutations that supported the diagnosis of malignancy. UMI-NGS showed KRAS mutations in 2 of the 7 samples that were morphologically classified as 'negative for malignancy (benign)' both revealed to be benign in the follow-up. In 2 of the 5 samples initially diagnosed as "suspect malignant," UMI-NGS found mutations that led to reclassification as malignant.
Conclusion: UMI-NGS demonstrated to be reliable in detecting mutations in cytological smears of pancreatic lesions and much more sensitive than NGS without UMIs. Samples classified cytologically as non-diagnostic, benign, or atypical were found to either contain insufficient material for UMI-NGS or to contain no tumour. Consequently, repeated sampling can be considered in these cases.
Based on these results, we propose the implementation of a workflow incorporating UMI-NGS into clinical pathology to improve diagnostic accuracy for solid pancreatic lesions.

PS-05-003
Deep learning for lymphoma diagnosis: a cytology-based study using digitized lymph node imprints
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Background & Objectives: Lymphoma diagnosis through cytology remains a complex task due to inter-observer variability and the inherent subjectivity of manual evaluation. This study explores the potential of deep learning models to improve lymphoma detection from digitized lymph node cytological imprints.
Methods: Using a dataset of 148 annotated slides from Caen University Hospital, Normandy, we systematically evaluated three segmentation architectures: U-Net, U-Net++, and DeepLabV3+. Annotations were initially performed by a pathology resident and subsequently reviewed and refined by an expert pathologist to ensure accuracy and consistency.
Results: Quantitative results showed that U-Net achieved the highest accuracy (0.7563) and Dice score (0.7586), while U-Net++ demonstrated superior sensitivity (0.9405), making it particularly effective for detecting malignant regions. DeepLabV3+ exhibited strong boundary detection capabilities, despite lower overall performance. Expert pathologists assessed the clinical relevance of model outputs, revealing that U-Net++ provided the most interpretable segmentations for diagnostic use.
Conclusion: These findings highlight the potential of AI-assisted cytology to enhance diagnostic accuracy, particularly for less experienced pathologists. By integrating automated segmentation models with expert validation, deep learning can help standardize lymphoma diagnosis, reduce diagnostic variability, and improve patient management. Future work will focus on expanding datasets, refining classification of lymphoma subtypes, and optimizing model interpretability for clinical deployment.

PS-05-004
A comparison of SDHB immunostain on cytological and histological specimens for gastrointestinal stromal tumours
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Background & Objectives: Gastrointestinal stromal tumour (GIST) is the most common mesenchymal neoplasm of the gastrointestinal tract. Most GISTs are associated with known molecular genetics pathways, making biomarker testing critical for guiding treatment. While over 80% GISTs are driven by activating *KIT* or *PDGFRA* mutations that respond to tyrosine-kinase receptor inhibitors (TKRI), succinate dehydrogenase (SDH)-deficient GIST accounts for approximately 5%-10% and largely resistant to TKRI. Germline testing is recommended for all SDH-deficient GISTs. Currently, SDH subunit B (SDHB) immunohistochemistry is used as a surrogate marker for SDH deficiency, typically performed

on surgical resection specimens. However, initial tissue sampling of GISTs is often obtained by endoscopic ultrasound–guided fine-needle aspiration (EUS-FNA). Therefore, this study aimed to investigate the feasibility of testing SDHB on cell blocks derived from cytological specimens.
Methods: Paired cytological (FNA) and histological (resection) specimens from 33 GISTs were immunohistochemically examined for SDHB expression. The status (retention or loss), pattern (focal, patchy or diffuse), and intensity (weak, moderate or strong) of the stains were assessed by a cytopathologist and a GI pathologist independently for all the specimens.
Results: Three cases were SDHB deficient, while 30 cases retained SDHB. The concordance rate for SDHB status (retention or loss) between cytology and histology was 100%. While the patterns of staining had no significant difference (p=0.105), the staining intensity in cytological specimens (3 weak, 11 moderate, and 16 strong) was stronger compared to histological specimens (14 weak, 9 moderate and 7 strong) (p = 0.004). Three histological specimens showed focal very weak staining which could be easily overlooked.
Conclusion: We have shown a 100% concordance rate between SDHB immunostain performed on cell blocks of cytological specimens and formalin-fixed paraffin-embedded histological specimens. Using cytological specimens for SDHB staining could potentially have a lower rate of false-negatives compared to histological specimens.

PS-05-005
From smear to diagnosis: the role of ancillary techniques in lymph node fine-needle cytology
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Background & Objectives: Diagnostic accuracy of lymph node fine-needle aspiration cytology (LN-FNAC) relies on proper management of diagnostic material and ancillary techniques (AT). AT play a crucial role in diagnosing LN-FNAC in reactive processes, Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), and metastases. While the role of AT in LN-FNAC has been extensively highlighted, their actual impact on diagnostic accuracy remains underexplored in the literature. This study aims to analyse the impact of AT on the diagnostic accuracy of LN-FNAC.
Methods: A retrospective analysis was conducted on 452 LN-FNAC samples, retrieved from the database of the Pathology Department at the University Hospital of Salerno (Italy). AT were applied in 187 cases. All these cases were reclassified according to the Sydney System, initially without AT and subsequently with AT information. The impact of AT on diagnoses was categorized as follows: "non-contributory", for cases where AT yielded inadequate results; "confirmed", when AT confirmed the initial diagnosis; "improved", when AT further refined the diagnosis, and "allowed", when AT enabled a diagnosis that could not have been reached without AT.
Results: A comparison of diagnostic categories before and after applying AT revealed a significant impact on the final diagnosis. The analysis showed the following results: AT **confirmed** the FNAC diagnosis in 19.79% of cases (n = 37/187); AT **improved** the FNAC diagnosis in 36.36% of cases (n = 68/187); AT **allowed** a diagnosis that otherwise could not have been made in 37.97% of cases (n = 71/187); and AT was **non-contributory** in 5.88% of cases (n = 11/187).
Conclusion: This analysis shows that AT refined diagnoses in nearly 95% of cases, showing either improvement, confirmation, or completely new diagnosis made possible by AT. These findings highlight the importance of utilizing and incorporating AT in the LN-FNAC to achieve more precise and reliable diagnoses, ultimately enhancing patient management and outcomes.

PS-05-006
Diagnostic utility of the third edition of The Bethesda system for reporting thyroid cytopathology with emphasis on the grey zone categories
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Background & Objectives: The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) establishes a standardized and category-based framework for reporting thyroid fine-needle aspiration (FNA) for the purpose of management. Challenges persist in accurately categorizing grey zone Non-Diagnostic (ND) and Atypia of Undetermined Significance (AUS) cases. We risk stratified thyroid FNA cases as per the 3rd edition TBSRTC and analysed the Risk Of Malignancy (ROM) for these newer suggested subcategories.
Methods: This study retrospectively reviewed 1597 thyroid FNAs from January 2019 to December 2023. Cases diagnosed as ND and AUS were sub-categorized according to the 3rd edition of TBSRTC and the ROM for each subcategory was calculated.
Results: Of the 1597 cases, 185 (11.6%) cases were ND, with predominant sub-category being others, among which the most common sub-group was blood only (67.6%). The risk of malignancy (ROM) among ND cases was 7.6%. ROM for cyst fluid was 14.3%, and for the others subcategory, it was 8.2%. AUS category constituted 147 cases (9.2%), with ROM of 12.5%. Within the AUS subcategories, Under AUS category, ROM was higher for the subcategory nuclear atypia (14.0%) than the subcategory others (12.1%).
Conclusion: The study highlights the challenges and importance of refined subcategorization in the TBSRTC, 3rd edition, and its role in enhancing diagnostic accuracy of the grey zone categories and further guiding patient management in thyroid nodules. Subcategorization may provide more precise risk stratification and therapeutic decisions.

PS-05-007
Application of telepathology for rapid on-site evaluation of touch imprint cytology in CT-guided percutaneous transthoracic core needle biopsy of pulmonary nodules: the experience of our multidisciplinary thoracic tumour board
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Background & Objectives: Lung cancer remains the leading cause of cancer-related mortality, with most cases diagnosed at advanced stages, requiring minimally invasive tissue sampling for diagnosis and molecular profiling. To maintain the high quality of these small samples, the most effective technique is rapid on-site evaluation (ROSE). However, the shortage of pathologists and frequent logistical challenges make this technique difficult to implement. The application of Telepathology can resolve these critical issues. This study evaluates the

implementation of telepathology for ROSE using touch imprint cytology (TIC) during CT-guided percutaneous transthoracic core needle biopsy (CNB) of pulmonary nodules.
Methods: We conducted prospectively from September 2024 to January 2025, the study involved 50 patients with lung nodules, analysed with CNB, and TIC samples evaluated either on-site or remotely via telecytology using a fully remote-controlled microscope system (OCUS®). TIC was performed by various operators, including pathologists, radiologists, and trained assistants.
Results: The evaluation showed that 86% of TICs were diagnostically adequate, with full concordance between on-site and remote evaluations. The average scan area of 11x9.75 mm required approximately 140 seconds for telecytology assessment, with the total adequacy evaluation time averaging 160 seconds per case. Histological analysis confirmed non-small cell lung cancer (NSCLC) as the most frequent diagnosis. The study highlighted telecytology's diagnostic accuracy and effectiveness in overcoming logistical challenges, especially the actual "shortage" of pathologists and the physical distance between radiology and pathology departments. Moreover, the results demonstrated the feasibility of involving trained non-pathologists in TIC preparation without compromising slide quality.
Conclusion: Telepathology allowed optimal use of pathologists' time, avoiding unnecessary delays in diagnosis. While scanning time remains a limitation, it did not impact procedural success or specimen quality. The findings support the integration of telecytology-based ROSE in routine practice, particularly in resource-limited settings, with implications for improved workflow efficiency and diagnostic performance.

PS-05-008
High-risk HPV prevalence and distribution in cervical cancer screening: biomarker-based approach with extended genotyping, cytology, and p16/Ki67 dual staining
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Background & Objectives: The prevalence of high-risk human papillomavirus (HR-HPV) in cytology combined with p16/Ki67 status using limited and two types of extended HPV genotyping has not yet been described.
Methods: A total of 32,724 screening tests results between 2015-2024 were retrieved, including HR-HPV testing, cytology and p16/Ki67. For HPV limited genotyping the Abbott RealTime High Risk HPV molecular assay was performed. For HPV extended genotyping two assays were used: Alinity m HR HPV and BD Onclarity HPV Assay. Immunoprofile assessment was performed by a qualified and experienced gynaecological cytopathologist. All cytology samples were assessed based on the Bethesda 2014 system. The analysed results were categorized and trends in age-specific, cytology-specific, and p16/Ki67-specific HR-HPV prevalence and distribution were observed, and differences between limited and extended genotyping were examined. Statistical methods included chi-square and McNemar's tests for study groups comparisons.
Results: The overall HR-HPV-positivity rate was 15.0%. HR-HPV prevalence in the limited genotyping group was 13.9%, in extended genotyping 1 (17.8%), in extended genotyping 2 (17.2%), with a statistically significant difference in the proportions of positive/negative cases ($p<0.0001$). No statistically significant difference was observed between extended genotyping groups ($p=0.706$). Extended genotyping group 1: the highest p16/Ki67-positivity was observed for HR-HPV 33/58 (100.0%) and 31 (58.8%), while the lowest was for HR-HPV 45 (18.2%), 18 (25.0%) and 59/56/66 (28.9%). Extended genotyping group 2: the highest p16/Ki67-positivity was observed for HR-HPV 16 (66.7%) and 31/33/52/58 (58.8%).
Conclusion: These findings, derived from analysis of 10-year of HPV-based screening test results, may contribute to cervical cancer prevention, thereby introducing a novel capability for optimizing national screening programs. A combined approach integrating new biomarker-based diagnostic technologies could support decision-making processes and help healthcare providers make more informed decisions about patient care.

PS-05-009
Usefullnes of PLAG1 and HMGA2 immunohistochemistry in salivary gland cytology
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Background & Objectives: Although the pleomorphic adenoma gene (PLAG1) and high-mobility group AT-hook 2 (HMGA2) immunohistochemical stains represent rearrangements in pleomorphic adenoma, there are studies in the literature showing that they can also stain in other salivary gland tumours. In this study, we investigated the contribution of PLAG1 and HMGA2 immunohistochemical staining in differentiating salivary gland tumours in cytology specimens.
Methods: A total of 64 cell blocks of salivary gland FNAC were included in the study. They were prepared using the Thin Prep liquid-based cytology method. All cytologies had histopathologic follow-up; 41 pleomorphic adenomas (PA), 6 Warthin tumours (WT), 4 mucoepidermoid carcinomas (MEC), 1 adenoid cystic carcinoma (AdCC), 2 basal cell adenoma/adenocarcinoma (BCA/BCAC), 2 acinic cell carcinomas (ACC), 2 epithelial myoepithelial carcinoma (EMC), 2 salivary duct carcinoma (SDC), 1 myoepithelioma and 3 carcinoma ex pleomorphic adenoma. Nuclear staining was considered positive for both antibodies.
Results: In the cell blocks, positive staining for PLAG1 was detected in 24 tumours (21 PA, 1 BCA/BCAC, 1 ACC, and 1 carcinoma ex PA) and for HMGA2 in 13 tumours (12 PA and 1 carcinoma ex PA). PLAG1 had a specificity of 86.9%, a sensitivity of 51.22% and an accuracy of 64% in differentiating PA, while for HMGA2 these rates were 95.6%, 29.2% and 51.6%, respectively. In the combination of PLAG1 or HMGA2, specificity was 82.6%, sensitivity was 73.17% and accuracy was 75.5%.
Conclusion: In salivary gland cytology, PLAG1 and HMGA2 have high specificity and low sensitivity for pleomorphic adenoma. Better results are obtained when both are used together.

Funding: Gaziantep University Scientific Research Projects Management Unit

PS-05-010
Intraoperative sentinel lymph node cytology of breast cancer patients following primary systemic therapy
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Background & Objectives: The axillary lymph node status is the most important prognostic factor for breast cancer patients even following primary systemic therapy (PST). The surgical treatment of axilla has been changed, and based on new indications, intraoperative sentinel lymph node assessment recommended a smaller subgroup of patients. At the same time, PST causes several cytopathological regression changes in lymph nodes (cytopathic effects, decreased

cellularity, fibrosis and necrosis) that could potentially affect the diagnosis of intraoperative lymph node cytology.
Methods: In our study we investigated 439 patients' intraoperative sentinel lymph node cytology. Two groups were created. The non-PST group, in which patients had sentinel lymph node biopsy (SNLB) and intraoperative cytology without preoperative treatment, and PST group in which, patients had SNLB and intraoperative cytology after PST. The intraoperative results were compared with histology as the gold standard, and sensitivity, specificity and accuracy were determined in both groups.
Results: The sensitivity of the non-PST group was: 86,08%, the specificity: 100% and the accuracy: 91,39%. Of the PST group the sensitivity was: 57,14%, the specificity: 99,55% and the accuracy: 88,44%.
The intraoperative cytology findings of the non-PST group were, as we previously seen, but in the PST group we saw various cytological appearance depending on changes caused by PST.
The cellularity of the smears was variable due to intranodal fibrosis and decreasing number of lymphocytes. Foamy macrophages and reactive fibroblasts appeared more frequently. The tumour cells were in small clusters or as single cells and showed variable cytopathic changes, like bizarre nuclei and hyperchromasia. These cytological changes were appropriate with the well-defined histological subgroups of regression patterns.
Conclusion: The low cellularity, the reactive fibroblasts and the single cell pattern can cause differential diagnostic challenge for cytopathologists. For the future intraoperative cytologic evaluation of sentinel lymph nodes remain a reliable tool in the management of breast cancer patients.

PS-05-011
Malignancy risk in category III (AUS) of the 3rd edition of Bethesda System for Thyroid Cytopathology: a study of cyto-histopathological correlation
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Background & Objectives: The 2023 revision of the Bethesda System for Reporting Thyroid Cytopathology redefined the category of Atypia of Undetermined Significance (AUS) into AUS-Nuclear and AUS-Other to reflect its heterogeneity. This study evaluates the malignancy risk for each subcategory based on histologic correlation.
Methods: A retrospective analysis was conducted on thyroid fine-needle aspiration cases diagnosed as AUS, between January 2023 and January 2025 in the Department of Pathology. Among 763 AUS cases, 110 with available resection specimens were selected for histologic correlation. These cases were further subcategorized into AUS-Nuclear and AUS-Other (architectural or oncocytic atypia). The malignancy rates for each category were determined based on final histopathological diagnoses, which included non-neoplastic disease, benign neoplasm, low-risk neoplasm and malignant neoplasm.
Results: Of the 110 AUS cases, 40 were classified as AUS-Nuclear, 32 as AUS-Other (architectural atypia), and 38 as AUS-Other (oncocytic atypia). The overall risk of malignancy for the AUS category was 16.4%, with a negative predictive value of 83.6%. The malignancy rates for each subcategory were: 30.0% (12/40) for AUS-Nuclear, including 9 papillary carcinomas, 1 oncocytic carcinoma, 1 poorly differentiated carcinoma, and 1 medullary carcinoma; 9.4% (3/32) for AUS-Other (architectural atypia), including 1 oncocytic carcinoma, 2 trabecular hyalinizing tumours and 1 NIFTP; and 7.9% (3/38) for AUS-Other (oncocytic atypia), including 1 papillary carcinoma, 1 oncocytic carcinoma, and 1 follicular carcinoma.
Conclusion: Consistent with the recent literature, AUS-Nuclear carries the highest malignancy risk, reinforcing its clinical significance. In contrast, AUS-Other subcategories exhibit lower malignancy rates, suggesting that a more conservative approach may be appropriate. These findings highlight the need for refined risk stratification within the Bethesda System to optimize the clinical management of thyroid nodules.

PS-05-012
Comparison of diagnostic yield between percutaneous ultrasound-guided fine needle aspiration and core needle biopsy in solid pancreatic lesions
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Background & Objectives: Since most pancreatic malignancies are inoperable at diagnosis, small samples are essential for confirmation of diagnosis and molecular analysis. Our study compares the diagnostic yield of cytology and histology samples from percutaneous ultrasound-guided fine needle aspiration (US-FNA) and core needle biopsy (US-CNB) in solid pancreatic lesions.
Methods: We retrospectively reviewed patients who underwent US-FNA or US-CNB for solid pancreatic lesions at Hacettepe University Hospital between 2022 and 2024 using an electronic database. Two authors analysed cytology/pathology reports and classified the diagnostic outcomes for each technique as inadequate, benign, atypical, suspicious for malignancy (SM), or malignant.
Results: Overall, 136 cases were identified. After exclusion of 12 cases with cystic lesions, a total of 124 cases of 113 patients were reviewed. There were 63 FNA cases from 57 patients (mean age 62.3), and 61 CNB cases from 56 patients (mean age 60.3). Cell block was available for review in 37 (58.7%) FNA cases. In the US-FNA group, 43 cases were diagnosed as malignant, 3 as SM, 6 as atypical, 3 as benign, and 8 as inadequate. In the US-CNB group, 44 cases were diagnosed as malignant, 2 as SM, 7 as atypical, 5 as benign, and 3 as inadequate. There were no false positive diagnoses. The definitive diagnosis of malignancy was achieved 68.2% and 72.1% of cases in US-FNA and US-CNB, respectively (Fisher's exact test: p=0.697). The overall adequacy rate of US-FNA and US-CNB was 87.3% and 95%, respectively, indicating no statistically significant difference (Fisher's exact test: p=0.206).
Conclusion: Our study demonstrates that while US-CNB showed a slightly higher diagnostic yield for malignancy and overall adequacy rate compared to US-FNA, the differences were not statistically significant. These findings suggest that both methods can be reliably used for diagnosis with technique selection depending on patient-specific factors, lesion characteristics, and institutional expertise.

PS-05-013
Opportunistic cervical cancer screening using liquid-based cytology: insights from a tertiary care centre
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Background & Objectives: Cervical screening is a reliable method for early detection, with opportunistic screening for hospital patients serving as a key approach. Additionally, ensuring consistency in interpreting cytology results is essential for diagnostic accuracy and quality patient care. This study aims to review the Liquid-Based Cytology (LBC) cervical smears across age groups, clinical presentations, and per speculum findings, focusing on epithelial cell abnormalities and inter-observer variability.
Methods: Comprehensive clinical data and LBC smears from January 2018 to December 2023 were retrieved from departmental

archives. All smears were interpreted based on the 2014 Bethesda System. Three observers with varying levels of experience in reporting LBC smears conducted the reviews.
Results: Of the 13,754 cases, the most common age group was the fourth decade, accounting for 36.8% of women. The inadequacy rate was just 0.43%. 94.2% of smears were reported as Negative for Intraepithelial Lesion or Malignancy (NILM), with inflammatory changes in 91.1%. Epithelial cell abnormalities were seen in 5.72% cases, with Low grade squamous intraepithelial lesion (LSIL) accounting for 44.19%, ASC-US (28.48%), HSIL (11.11%), and squamous cell carcinoma (3.96%)cases. Glandular lesions were 0.77% AGC and 0.13% Adenocarcinoma. Upon review, 19.16% of initially diagnosed NILM cases were reclassified as low-grade epithelial abnormalities. The highest agreement was observed in the LSIL category, followed by ASC-US, with a statistically significant Kappa statistic of 0.501, indicating moderate agreement between observers. Agreement in more severe categories like HSIL and SCC was more consistent, with a Kappa statistic of 0.323 indicating fair agreement.
Conclusion: Opportunistic cervical screening offers an alternative method in absence of a robust population based mass screening program. It enhances detecting premalignant and malignant cervical lesions efficiently. In our study, epithelial cell abnormality rate was 5.72%. Addressing inter-observer variability is also crucial for optimizing screening programs and improving patient care in tertiary healthcare settings.

PS-05-014
Cytomorphological analysis and histologic correlation of salivary gland neoplasms of uncertain malignant potential (SUMP) category in salivary gland fine needle aspirations: a liquid-based cytology experience
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Background & Objectives: The Milan System for Reporting Salivary Gland Cytology (MSRSGC) categorizes neoplastic lesions into "benign neoplasia" and "salivary gland neoplasm of uncertain malignant potential (SUMP)". SUMP includes both benign and malignant neoplasms, with an average malignancy risk of 26%. This study compares SUMP cases with tissue diagnoses, focusing on cytomorphological and background features.
Methods: Salivary gland fine-needle aspiration (SGFNA) cases reported from 2018 to 2025 using liquid-based cytology were documented. SUMP cases were classified by cell morphology, background and matrix features. Tissue biopsy diagnoses for SUMPs were also documented.
Results: Of 596 cases, 167(28%) were non-diagnostic, 54(9%) non-neoplastic, 42(7%) atypia of uncertain significance (AUS), 192(32%) benign neoplasms, 70(12%) SUMP, 20(3%) suspicious for malignancy, and 51(9%) malignant. Parotid tumours were the most common (58[82.9%]). Epithelial/myoepithelial, basaloid, oncocytic, and spindle cell morphologies were observed in 36(51.4 %), 16(22.9 %), 15(21.4 %), and 3(4.3 %), respectively. Fibrillary matrix appeared in 27/42(64.3%) with matrix features, dark/hyaline matrix in 13(31%), and minimal matrix in 2(4.8%). Background features included lymphoid (4/11[36.4%]), mucoid (4[36.4%]), cystic (2[18.2%]), and granular (1[9.1%]). Among 43(61.4%) cases with tissue follow-up, 8(18.6%) were malignant. In SUMP, the risks of malignancy (ROM) and neoplasia (RON) were 18.6% and 100%, respectively. The dark/hyaline matrix type was more frequent in malignant cases (66.7%;p=0.059). No significant association was found between cell morphology and malignancy (p=0.259). The presence of matrix was higher in malignant cases (75%;p=0.434). Background features had no relationship with malignancy (p=0.574).
Conclusion: This study supports the existing literature, showing a low malignancy risk in SUMP cases. While evaluating the background and matrix in liquid-based cytology samples is challenging, it is feasible. The study has advantages, such as being single-centreed, using consistent preparation technique, and having all cases evaluated by a cytopathologist. However, limitations include a low number of cases and a high number without tissue follow-up.

PS-05-015
Results from the second round of a HPV-based opportunistic cervical cancer screening program in Barcelona, Spain
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Background & Objectives: In 2018, a HPV-based opportunistic cervical cancer screening program started for women aged 30–70 in an area of Barcelona. Beginning in 2021, it expanded sequentially to consecutive age groups, culminating in 2023 with full coverage through primary HPV testing. We aim to report HPV, cytology, and biopsy findings from the first year of the second round of screening.
Methods: Women 30 to 70 y.o. attended in public primary care centres and due for cervical cancer screening were offered to perform a HPV test. High-risk-HPV (hrHPV) detection is performed by Cobas-HPV Test (Roche). Cytologies are evaluated after any positive hrHPV test by cytotechnologists using ThinPrep cytology and Imager assisted screening (Hologic).
Results: A total of 6,540 women (≥30 years) were screened with hrHPV testing. The hrHPV positivity rate was 14.8%, declining with age (from 23.7% in 30–35 years to 7.4% in ≥65 years), a trend consistent with the previous phase. HPV16 and/or HPV18 were detected in 25.9% of hrHPV-positive tests (3.8% of all screened women), compared to 24.3% in the earlier phase. Among 966 smears, 48.4% were ≥ASCUS (52.7% in younger vs. 41.7% in older women), a slight drop from 53.5% previously. By genotype, 68.8% of abnormal cytologies were associated with hrHPV no-16/18, 24.8% with HPV16, 6.0% with HPV18, and 0.4% with both, consistent with previous findings. Colposcopic evaluation led to biopsies in 283 women, with results of: 0.4% insufficient, 23.0% normal, 44.3% LSIL, 31.1% CIN2+ (1.3% of all women screened).
Conclusion: During the first year of the second round of HPV-based screening, the overall hrHPV positivity rate was 14.3%, with a considerable number of abnormal cytologies in triage, though fewer than previous phase that did not yet include all older age groups under HPV screening. hrHPV positivity accounted for 3.8% of screened patients, but only 1.3% had CIN2+ lesions.

PS-05-016
Detection of high-grade serous carcinoma cells in PAP smears: evidence of tumour cell migration from the fallopian tube
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Background & Objectives: High-grade serous carcinoma (HGSC) of the ovary/fallopian tube has poor survival rates, largely due to

late-stage diagnosis. While the fallopian tube is widely recognized as the primary site of origin, the presence of tumour cells in the lower genital tract remains underexplored. This study aimed to assess the frequency of HGSC cells in PAP smears and to investigate their potential migration via the tubal lumen.
Methods: This retrospective study re-evaluated archival fallopian tube specimens and PAP smears from HGSC patients. Immunostaining for p53 and Ki-67 was performed when tumour cells or precursor lesions were not initially detected. A control group of PAP smears from breast cancer patients was included to validate specificity. All patients had undergone hysterectomy, ensuring that other glandular lesions of the cervix and corpus were histologically excluded. Samples were collected between 2008 and 2025 from the archives of the Institute of Pathology at the Cantonal Hospital of St.Gallen.
Results: Tumour cells were detected in multiple PAP smears, with a mean PAP-to-adnexectomy interval of five months. In one particular case, tumour cells were present nearly two years before surgery but not recognized as HGSC at the time. In several cases, tumour cells in PAP smears were initially misclassified as atypical glandular cells (AGC-N). In contrast, all PAP smears from the control group remained negative. Re-evaluation of fallopian tube specimens of HGSC patients revealed numerous precursor lesions and free-floating tumour cells among the fimbriae.
Conclusion: Our findings suggest a potential role for cytological screening in the early diagnosis of HGSC of the ovary/fallopian tube. The presence of HGSC cells in PAP smears provides further evidence of the intraluminal spread of carcinoma cells via fallopian tubes and uterine cavity. Further research is needed to assess its diagnostic utility and impact on risk stratification.

Funding: Our study is supported by grants from the Research Committee of the Cantonal Hospital St. Gallen (grant number MD 24/12), the Cancer League Eastern Switzerland (grant number 2024-05), and the Manja Gideon Foundation (no grant number)

PS-05-017

Comparison and classification of liver cytopathology and histopathology in light of the WHO reporting system for liver cytology

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Background & Objectives: Although many organs have established cytological classification systems, liver cytopathology still lacks standardization. This study aims to reclassify liver cytology reports from our institution and determine the risk of malignancy (ROM) for each category.
Methods: Cytology reports and corresponding tru-cut biopsies performed at our institution between 2017 and 2024 were retrospectively reviewed. Cases were categorized based on demographic, radiological, and clinical follow-up(CFU) data. Cytological diagnoses were classified into five categories: I – Non-diagnostic;II – Benign;III – Atypical;IV – Suspicious for malignancy;and V – Malignant. ROM was assessed using both histopathological findings and final clinical follow-up.
Results: The study included a total of 438 cases, of which 238 (54.3%) were female (F/M ratio: 1.2 /1). The mean age was 61.24 years. Malignant lesions were classified as either primary or metastatic. Histopathological evaluation of tru-cut biopsies revealed that 118 cases (26.9%) were benign, and 320 cases (73.1%) were malignant. According to CFU, 66 cases (15.1%) were considered benign, and 372 (84.8%) were malignant. The concordance rate between cytological and histopathological diagnoses was 74.4%, while the concordance between cytological diagnosis and CFU was 82.9%.
The ROM based on histopathological outcomes for each cytological category was as follows: Category I, 66.6%; Category II, 44.4%; Category III, 77.7%; Category IV, 90.1%; and Category V, 83.8%. Based on CFU, ROM was calculated as follows: Category I, 73.3%; Category II, 52.9%; Category III, 88.8%; Category IV, 96%; and Category V, 100%. No statistically significant difference was observed between cytological and tru-cut biopsy diagnoses with respect to CFU correlation ($p = 0.127$).
Conclusion: Liver FNA demonstrates diagnostic accuracy comparable to tru-cut biopsy and is particularly useful for differentiating benign from malignant lesions. The relatively high ROM in the benign category may reflect both limitations in targeted biopsy and the absence of standardized definitions in current classification systems. Clarifying these uncertainties is essential for better clinical decision-making.

PS-05-018

Multiplexed cry-immunostaining: application in a routine cytopathology laboratory to minimize sample wastage

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Background & Objectives: Multiplex cryo-immunostaining with the X-ZELL platform enables up to 8 markers on a single slide, addressing multi-slide staining challenges in cytopathology. However, X-ZELL's cytospin preparation and fixation protocols differ from routine methods. This study evaluated whether routinely prepared cytospins provide comparable immunomorphological preservation and compatibility with X-ZELL's cryo-immunostaining protocol.
Methods: Mini lymphoma (CD45/CD3/CD20/DAPI) and mini carcinoma (EpCAM/CK7/CK20/DAPI) multiplex immunostaining panels were established. FNAB and effusion samples were analysed within three days of collection. Two preparation methods were compared: (1) the validated X-ZELL protocol (X-ZELL slides, cytofuge, cryofixation, and cryostaining) and (2) a standard method using Superfrost Plus slides (Epredia), cytocentrifuge (Shendon), and 4°C methanol fixation, followed by X-ZELL cryofixation and cryostaining. Single-marker ICC staining served as a control. Slides were evaluated blindly by an immunofluorescence specialist and a cytopathologist. Results were provided descriptively.
Results: Ten cases were included: 7 FNAB (5 lymphomas, 2 reactive) with the lymphoma panel, as well as 2 FNAB and 1 effusion case (adenocarcinomas) with the carcinoma panel. No significant difference in the percentage of evaluated cells was found between X-ZELL and routinely prepared cytospins, except for CD20 in one sample, with results comparable to ICC controls. X-ZELL cytospins demonstrated superior morphology and staining intensity without background staining, while routinely prepared cytospins showed slightly weaker intensity, particularly for dim fluorophores like CD20-APC (allophycocyanin) in the lymphoma panel. In the carcinoma panel, FNAB samples showed strong staining for cytoplasmic markers (CK7), while membrane markers (EpCAM) showed weaker intensity linked to loss of nuclear morphology. Effusion samples showed superior intensity for both markers in both methods.
Conclusion: The X-ZELL platform can be applied to routinely prepared cytopathology samples, particularly for effusions. For FNAB samples, improvements can be made by using X-ZELL slides, ice-cold methanol, and avoiding dim channels for critical markers to enhance staining consistency.

PS-06 Poster Session Dermatopathology

PS-06-001
Effect of PRMT1 and ZEB1 expression on survival in patients diagnosed with Kaposi Sarcoma

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Background & Objectives: Kaposi sarcoma (KS) is a tumour originating from vascular endothelial cells, typically occurring in immunocompromised individuals. The clinical course is highly variable; it progresses slowly in some patients, while in others, it may follow an aggressive course. In recent years, transcription factors associated with epithelial-mesenchymal transition, such as PRMT1 and ZEB1, have attracted attention due to their effects on cancer cell invasion and metastasis. However, the role and prognostic significance of PRMT1 and ZEB1 in KS are not fully understood. This study aims to investigate the possible effects of PRMT1 and ZEB1 expression on the clinical course of KS by analysing the intensity and percentage of their expression in KS biopsies.
Methods: We selected paraffin blocks from 92 biopsies of 70 patients diagnosed with KS and HHV-8 positive between 2011 and 2021. PRMT1 and ZEB1 antibodies were applied, with positive controls. Overall survival data were retrieved from the Hospital Information Management System and Medulla System, determining if patients were alive as of March 2025.
Results: A total of 92 biopsies from 70 patients with a median age of 66.8 (29-93) were included in the study. Cox regression multivariate analysis showed significant survival differences associated with PRMT1 expression percentage (p=0.03) and ZEB1 expression percentage (p=0.01). Patients with high PRMT1 and ZEB1 expression percentages had longer survival compared to those with low expression. This suggests that PRMT1 and ZEB1 could serve as biomarkers associated with a good prognosis.
Conclusion: Our findings suggest that PRMT1 and ZEB1 expression could be considered prognostic markers in Kaposi sarcoma, with high expression levels independently contributing to improved overall survival. However, no significant relationship was found between the intensity of PRMT1 and ZEB1 expression and survival. These results indicate that PRMT1 and ZEB1 may play a role in KS progression, and further studies in larger patient cohorts are needed.

PS-06-002
PRAME expression in mammary and extramammary Paget's disease

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Background & Objectives: PRAME (PReferentially-expressed Antigen in MElanoma) is a testis-cancer antigen that has been extensively studied for the diagnosis of ambiguous melanocytic neoplasms, as it is preferentially expressed in melanomas compared with benign lesions. In normal skin, PRAME is expressed in the cytoplasm of sebocytes, apocrine sweat glands and in a subset of cells of eccrine gland secretory coils. Accordingly, PRAME is expressed by the majority of sebaceous tumours and less frequently (ca. 20%) by tumours and hyperplasias of sweat glands. Mammary (MPD) and extramammary (EMPD) Paget's disease are apocrine adenocarcinomas with epidermal involvement. So far, very few data exist on the expression of PRAME in MPD and EMPD.
Methods: We investigated the immunohistochemical expression of PRAME in 33 cases of Paget's disease (13 MPD, 20 *in situ* or invasive EMPD), using the ERP20330 antibody and an automated immunohistochemistry stainer device (Ventana). Sebaceous and/or apocrine glands present in each section served as positive internal controls.
Results: All 13 cases of MPD (from female patients) expressed PRAME to various degrees (strongly in 10 cases and weakly in 3 cases). In most cases, both the intraepidermal Paget cells and the underlying breast carcinomas were PRAME-positive. Among the 20 cases (12 women) of EMPD (6 vulvar, 5 perianal, 9 other), 12 cases were strongly PRAME-positive, 5 cases showed weak immunoreactivity, and 3 cases were negative. The expression of PRAME was nuclear and/or cytoplasmic, both in MPD and EMPD cases.
Conclusion: These results expand the spectrum of cutaneous epithelial/glandular malignancies expressing PRAME, and should be known when using this antigen as a diagnostic immunohistochemical biomarker. Studies are ongoing to assess the utility in differentiating primary (cutaneous) from secondary (associated with underlying malignancies) EMPD, and the potential prognostic or predictive value of PRAME expression on MPD, as has been recently suggested for breast carcinomas.

PS-06-003
PRAME expression in Spitz nevus and Atypical Spitz tumour in children

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Background & Objectives: PRAME (Preferentially expressed Antigen in Melanoma) expression is well documented in cutaneous melanomas, but knowledge of its expression pattern in Spitz nevi and Atypical Spitz tumours is limited.
Methods: We performed a detailed microscopic reexamination of the original haematoxylin and eosin slides from 33 paediatric patients aged 1 to 18 years. A total of 28 Spitz nevi and 5 Atypical Spitz tumours were included in the study. PRAME immunohistochemistry was performed on all samples. Cases were classified on a scale from 0 (no expression) to 4+ (>75% positive melanocytic nuclei).
Results: The majority (23/28) of the Spitz nevi analysed were completely negative for PRAME. Only 7.14% (2/28) of Spitz nevi showed a 2+ heterogeneous immunoreactivity in 50% of melanocytes from both the junctional and dermal components. Three Spitz nevi (10.71%) showed weak nuclear positivity in less than 25% of melanocytes (1+). Only one (1/5) Atypical Spitz tumour from a 4-year-old patient showed faint nuclear PRAME expression corresponding to a 1+ score. Non-specific, diffuse, membranous, and cytoplasmic PRAME positivity was observed in normal sebocytes from all samples.
Conclusion: PRAME expression is not limited to malignant melanocytic tumours; Spitz nevi and Atypical Spitz tumours can infrequently express PRAME in a heterogeneous pattern. A constant membranous and cytoplasmic positivity in sebocytes was identified. PRAME should be interpreted carefully in the context of histomorphological findings.

PS-06-004
Immunofluorescence: is fresh tissue necessary?

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Background & Objectives: Direct immunofluorescence(DIF) is a technique allowing the visualization of a specific protein in tissue sections by binding a specific antibody conjugated with a fluorescent dye.

The sample can be processed fresh or transported in Michel's solution. This complicated process demands significant time and attention, and when fresh is difficult for senior scientists given staffing constraints. Workforce shortages in Ireland have created wide gaps in scientific support staff, causing significant disruption to laboratory processes and workflow. When received in Michel's, samples can be batched and the lengthy process completed in tandem, saving the senior scientists valuable time.
The objective was to prove the equivalence of tissue in Michel's solution to fresh tissue.
Methods: Retrospective single centre audit of skin samples analysed by DIF in Galway University Hospital(GUH) from 2021-2023. Biopsies were studied which had been sent either fresh or in Michel's solution. The 100 most recent cases from GUH were the fresh group. The 100 most recent cases from Sligo University Hospital were the Michel's group.
Results: Sligo 2021-2023: 28 cases showed positive staining. 99 of 100 had a positive internal control and 98 of 100 had a negative internal control.
Galway 2023: 32 cases showed positive staining. 100 of 100 had a positive internal control and 99 of 100 had a negative internal control.
Conclusion: 32 of 100 fresh samples from GUH tested positive for at least one immunofluorescence stain(2023). 28 of 100 samples in Michel's solution from SUH tested positive for at least one immunofluorescence stain(2021-2023). This audit demonstrates the efficacy of Michel's solution as a transport medium for skin samples sent for immunofluorescence.
Tissue in Michel's remains as diagnostically accurate as fresh tissue and can be reliably used for specimens for DIF. Following completion of this audit, dermatologists have begun sending samples in Michel's solution.

PS-06-005
Clinicopathologic analysis of overall survival rates for cutaneous melanoma in Turkey
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Background & Objectives: The current study aimed to investigate the clinicopathological prognostic factors of melanoma in a country with low incidence rates, primarily among individuals with low-risk cutaneous phototypes.
Methods: The study analysed 233 cases of invasive and micro-invasive primary cutaneous melanoma (CM) pathologically diagnosed at a tertiary university hospital between January 2008 and March 2020.
Results: A total of 233 patients were included in the study, comprising 103 females and 130 males. The average age at diagnosis was 57 years, with a median age of 59 years (ranging from 1 to 95 years). The overall survival (OS) rates at 1, 2, 5, and 10 years were 92%, 84%, 70%, and 62%, respectively. Favorable prognostic factors identified included female gender, nevus-associated melanoma, solar elastosis, the presence of tumour-infiltrating lymphocytes (TILs), melanoma thickness of 1 mm or less, Clark level below III, and microinvasive melanoma. When comparing patients who survived for less than 5 years with those who survived for 5 years or more, interesting associations with 5-year survival status emerged, particularly relating to ulceration, TILs, and mitotic rate values with different cut-off levels.
Conclusion: A Cox multiple regression model indicated that gender, Breslow thickness, surgical margin, TILs, lymphovascular invasion (LVI), pN status, and age at diagnosis were independent predictors of overall survival. We have significant predictors of survival. We can even predict some molecular features of cutaneous melanoma using light microscopy.

PS-06-006
Pigmentation in melanoma: what it means and its importance
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Background & Objectives: A recent study conducted in Germany found that pigmented melanomas have a better prognosis than non-pigmented melanomas. Our research, which was carried out in 2020 as part of a pathology graduation thesis in Turkey, aims to share some intriguing findings regarding the relationship between pigmentation and histopathological prognostic factors. We believe these insights will enhance the understanding of melanoma's phenotype, the deadliest form of skin cancer originating from melanocytes.
Methods: We statistically analysed 122 metastatic melanoma cases and 233 primary cutaneous melanoma cases with Chi-Square or Fisher's test according to pigmentation association with histopathologic variables.
Results: In primary cutaneous melanoma cases, pigmentation was associated with histopathologic subtype (Low cumulative sun-damage melanoma/superficial spreading melanoma is the most frequently pigmented subtype) ($p<0.001$), location of melanoma ($p=0.023$) (extremity and trunk were the two most frequent location for pigmented melanoma), melanoma related to a nevus ($p=0.037$, nevus-associated melanomas were more frequently pigmented than de novo melanomas), lower pT stage ($p=0.018$) (pT1 cases dramatically were frequent in pigmented melanomas), absence of lymphovascular invasion (LVI) ($p=0.017$), BRAF-mutation status ($p=0.011$), absence of ulceration ($p<0.001$), Clark level ($p=0.038$, pigmented melanomas were mostly Clark levels II or III), skin appendages involvement ($p=0.013$), regression status ($p=0.005$), presence of radial growth phase (RGP) ($p<0.001$, 170 cases with RGP were also pigmented), mitotic rate ($p=0.013$) (Cases with zero mitoses were all pigmented).
Conclusion: According to some of these (such as the absence of LVI) and previous results, pigmentation may also have an immunologic role in response to melanoma. These findings open new possibilities for understanding and potentially treating melanoma, offering hope for improved patient outcomes.

PS-06-007
Major histocompatibility complex class I (MHC-I) and β2-microglobulin loss are common tumour progression events in cutaneous melanoma, a tertiary institutional experience
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Background & Objectives: Cutaneous melanoma(CM) is one of the most "immunogenic" tumours, avoiding immune surveillance. The PD-1/PD-L1 axis is a prototypical immune escape mechanism adopted by neoplastic cells. However, regarding CM, different scoring systems exist for PD-L1 expression assessment such as combined positive score(CPS), and melanoma scoring system(MEL) which make interpretation a matter of debate. The effectiveness of immunotherapy with PD-1/PD-L1 inhibitors is also varied among studies, indicating alternative cytotoxic dysregulation pathway also contributes to tumour escaping. Among those, down-regulation of major histocompatibility complex class-I(MHC-I) is the most frequent one. This phenomenon is well documented in many carcinomas, and haematological malignancies, but has rarely been addressed in melanomas. We questioned

the possible mechanism for MHC-I suppression, notably the synthesis of the β2-microglobulin subunit of MHC-I. These potential cellular alterations triggered our interest to correlate between CPS and MEL scores and identify the MHC-I, and β2-microglobulin status in CMs.
Methods: We collected 25 advanced, CMs, with average follow-up period 71 months. Eleven cases with nodal metastasis were also included. We evaluated CPS and MEL scores by PD-L1(clone 22C3) immunohistochemistry(IHC) and performed correlation analysis between these 2 systems. We carried-out IHC for MHC-I and β2-microglobulin to evaluate the signal loss in percentage in primary/metastatic tumours. Furthermore, we also correlated MHC-I loss and tumour-infiltrating lymphocyte(TIL).
Results: We found a strong correlation between CPS and MEL score. Twenty-one cases(84%) of primary tumour showed significant HMC-I(>25%) loss, largely in the invasive regions associated with decreased TIL(r: - 0.44) and concurrent loss of β2-microglobulin. Significant further loss of MHC-I in metastatic tumours was also observed(p: 0.0017).
Conclusion: CPS and MEL has high concordance and can be used interchangeably in CMs. Concurrent MHC-I and β2-microglobulin loss is a common tumour-progression event in CMs, which may contribute to treatment failure. Our data points out that MHC-I could serve as a potential biomarker in CMs.

PS-06-008

LEF1 expression in melanocytic tumours cannot accurately predict *CTNNB1* mutational status acting as a potential pitfall in combined lesions

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Background & Objectives: Majority of melanocytic lesions develop along a genetic spectrum, progressing from a nevus to melanoma. Melanocytomas represent an intermediate category of tumours that lay within that spectrum and are characterized by additional genetic alterations, which can occasionally alter their phenotype. Currently, the three categories of melanocytomas, recognized by WHO, are pigmented epithelioid melanocytomas (PEMs), BAP1 inactivated melanocytomas (BIMs), and WNT-activated melanocytomas (WAMs). Among them, WAMs represent an under-recognized entity, which can occasionally be misinterpreted as other biphenotypic pigmented lesions or as melanomas. LEF1 was recently suggested as a marker of increased utility in the diagnosis of WAMs against other histologic mimics.
Methods: In this study, we analysed the expression of LEF1 in a series of 55 melanocytic tumours, including 10 Spitz nevi, 16 blue nevi, 9 common nevi, 1 clonal nevus, 10 melanomas of various subtypes, 7 WAMs and 2 PEMs. Beta-catenin expression was also assessed in all biphenotypic cases. Furthermore, molecular analysis was performed for the identification of *CTNNB1* mutations in all cases that were LEF1 positive.
Results: Thirty-seven (37) out of 55 cases displayed LEF1 positivity independent of *CTNNB1* mutational status. Specifically, LEF1 nuclear expression was present in 6/10 (60%) Spitz nevi, 5/16 (31%) blue nevi (4/5 combined BN, 0/5 dendritic BN and 1/6 cellular BN), 9/9 (100%) common nevi, 0/1 clonal nevus, 10/10 melanomas (100%), 7/7 (100%) WAMs and 0/2 PEMs. Subsequent examination for *CTNNB1* exon 3 mutations did not reveal any alterations. Beta-catenin was positive in all WAM cases (7/7) and displayed a normal membranous staining pattern in the remaining combined lesions examined.
Conclusion: These data suggest that LEF1 expression should be interpreted with caution in ambiguous pigmented and/or combined melanocytic lesions, where beta-catenin expression cannot be easily assessed. Therefore, we suggest that LEF1 positivity should be assessed in conjunction with beta-catenin or with a *CTNNB1* molecular confirmation.

PS-06-009

Trans- and dedifferentiated primary and metastatic melanoma: the challenging diagnosis and diagnostic significance of PRAME staining

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Background & Objectives: In primary, or more commonly, metastatic cases of malignant melanoma (MM) there may be a complete loss of melanocytic markers with the acquisition of signs of heterologous differentiation in some cases. This phenomenon may cause diagnostic difficulties. Here we present six cases of MM with signs of dedifferentiation (n=3) or de-/transdifferentiation (n=3).
Methods: In each case immunohistochemistry (IHC) was performed with S100, SOX-10, Melan A, HMB45, in four cases with PRAME. Molecular analysis for BRAF mutations using direct sequencing of exon 15 was performed in five case.
Results: Our study included one primary dedifferentiated and five metastatic de-/transdifferentiated cases of MM (M – 3, F – 3, aged 43 to 63 years, median – 61.5). Primary dedifferentiated neoplasm had small focus with retained melanocytic expression and epithelioid/rhabdoid morphology, dedifferentiated component had spindle cell morphology. Two metastatic dedifferentiated cases with unknown primary site located in axillary area, had epithelioid/rhabdoid morphology and were totally negative for melanocytic markers. In one case there was diffuse PRAME expression. Three metastatic cases with total or subtotal loss of melanocytic markers expression showed heterologous differentiation (right upper arm – 1, inguinal lymph node – 2): pleomorphic leiomyosarcoma, (Desmin+, SMA-, Myogenin/MyoD1-, melanoctyc markers-, PRAME weakly+), fibrosarcoma-like tumour with immature cartilaginous islands (SOX-10+ in cartilaginous component, PRAME+, S100/Melan A/HMB45-), spindle cell rhabdomyosarcoma with focal rhabdoid morphology and osteoproduction, (Desmin+, Myogenin/MyoD1+/-, H3K27Me-, S100/Melan A focal+, HMB45 single cells+, PRAME+). In the first two cases, the primary site was known with confirmed skin MM. BRAF mutation was detected in all dedifferentiated cases.
Conclusion: Awareness of de-/transdifferentiation phenomenon is important for making accurate diagnosis of MM. MM may have various types of heterologous differentiation and IHC for PRAME can be useful in difficult cases, but it should be considered in the context of clinical history, morphology and immunophenotype, as other high-grade sarcoma may also show postive expression.

PS-06-010

Distribution of IL-17-positive cells and IgG4-positive plasma cells in patients with bullous dermatoses

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Background & Objectives: Bullous dermatoses are a group of autoimmune-mediated diseases affected squamous epithelia, such as the skin and oral mucosa. The aim of our study is to investigate the relation between different subtypes of immune cells and the development of bullous pemphigoid and pemphigus vulgaris patients.
Methods: We investigated 24 patients with bullous pemphigoid (BP) and 14 with pemphigus vulgaris (PV) with antibodies against IL-17 and IgG4 by immunohistochemistry. The correlation between density of markers-positive cells, morphological and clinicolaboratory data were evaluated.
Results: We found infiltration by IL-17-positive cells and IgG4-positive plasma cells in all studied specimens. IL-17-positive cells could be found in all cases, with a median number of 28.4 cells/mm^2 (SD±3.92) and IgG4-positive plasma cells with median number of 16.9 cells/mm^2 (SD±2.2). Comparing the density of the two types of cells, we found that IL-17-positive cells are significantly more in comparison with IgG4-positive plasma cells (p=0.013, t-test). There was a tendency - in patients with BP there was a greater number of IL-17-positive cells compared with PV (x2=3.44, p=0.098). No significant results was found between and other clinicopathological parameters.
Conclusion: Based on the IHC findings and the comparison of the data, we suggest that there is a strong relationship between the activation of both immune cell populations in bullous dermatoses and the severity of the disease.

Funding: This research was funded by the Bulgarian Ministry of Education and Science (MES) in the frames of the Bulgarian National Recovery and Resilience Plan, Component "Innovative Bulgaria", Project No. BG-RRP-2.004-0006-C02, "Development of research and innovation at Trakia University in service of health and sustainable well-being"

PS-06-011

The value of peritumoral lymphocyte infiltration in progression-free survival (PFS) of NRAS, TERT and CHEK2 mutant melanoma

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Background & Objectives: The presence of tumour infiltrating lymphocytes (TIL) is a favourable prognostic factor in cutaneous melanoma. However, TIL infiltration in *NRAS*, *TERT* and *CHEK2* Stage I and II mutant melanoma is still controversial. The current study's objective have been to compare the *NRAS*, *TERT* and *CHEK2* mutation status with peritumoral lymphocytic infiltration and PFS in Stage I and II melanoma.
Methods: Altogether, 118 patients who underwent melanoma surgical treatment at the Riga East University Hospital at the stage IA-IIC were retrospectively enrolled in the study. *TERT* and CHEK2 mutational status was assessed by NGS testing. The *Qiagen* pan-cancer-multimodal panel gene kit was used (Cat. No. / ID: 334942). *NRAS* mutations was assessed by digital droplet PCR (ddPCR) using *NRAS Q61* (#12001006) and *NRAS G12/G13* (#12001627) Screening Assays (*Bio-Rad*, USA) as per the manufacturer's instructions.
Results: Patients with *TERT* mutation had significant worse PFS compared to *TERT* wild melanoma (HR=13.8, 95 % C.I = 6.8–31.0; P<0.0001). In additional, patient with *TERT* mutation and low TIL had significant better PFS compared to patients with *TERT* mutation and high TIL infiltration (HR = 4.80; 95 %, C.I = 2.30–7.890, P=0.002). *CHEK2* mutation status did not associated with PFS. However, patients with CHEK2 had increased TIL infiltration compared to *CHEK2* wild melanoma (P<0.0001). Patients with *NRAS* mutant melanoma had significant worse PFS compared to *NRAS* wild type melanoma (HR = 12.30; 95 %, C.I = 5.78–26.21, P < 0.0001). However, the association between NRAS mutant melanoma, TIL infiltration and PFS have not been observed.
Conclusion: *TERT* and *NRAS* mutant melanoma characterized by worse PFS compared to *TERT and* NRAS wild melanoma. Increased TIL infiltration contributed to the better PFS in *TERT* mutant melanoma. However, TIL infiltration did not associate with even better or worse PFS in *NRAS and CHEK2* mutant melanoma.

PS-06-012

Pathological and prognostic insights from SLN biopsy in melanoma: a single centre study of 1181 cases

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Background & Objectives: Melanoma prognosis is primarily determined by certain pathological features of the primary tumour and the status of regional lymph nodes. This study analyzes a cohort of melanoma patients with sentinel lymph node biopsy (SLNB) to identify prognostic and predictive markers, correlating tumour morphology with survival outcomes.
Methods: We analysed primary tumour pathology characteristics (Breslow thickness, ulceration, mitotic activity, Clark level, LVI, neurotropism) and SLNB results from January 2021 to December 2024 in the National Cancer Research Centre named after N.N.Petrov. Kaplan-Meier survival analysis was performed to estimate survival distributions and compare groups by log-rank tests. Cox proportional hazards regression was used for multivariate analysis of prognostic factors.
Results: A total of 1181 patients were analysed. Sentinel lymph node (SLN) biopsy was positive in 206 cases (17.4%) and negative in 975 cases (82.6%). Significant correlations were found between positive SLN status and major pathological prognostic factors: Breslow thickness (Chi-squared test, p < 0.001), ulceration (p < 0.001), mitotic rate (p < 0.001), and lymphovascular invasion (LVI) (p < 0.001). Positivity rates for SLN biopsies notably increased with greater Breslow thickness (>4 mm had the highest positivity), presence of ulceration, higher mitotic rates (≥5 mitoses/mm²), and presence of LVI. A total of 758 melanoma patients with available survival follow-up were included (median age ~55 years; 54% female). The median follow-up was 30 months. There were 19 melanoma-related deaths (2.5%) during the study period. Thickness >2 mm carried an HR ~10 (95%CI 1.4–79, p=0.03) for mortality compared to ≤2 mm.
Conclusion: Breslow thickness, ulceration, SLN status, mitotic rate, and LVI are confirmed as key prognostic indicators in melanoma. Thickness remains the dominant predictor of overall survival – thicker melanomas have drastically worse outcomes

PS-06-013

Divergent epigenetic landscapes and stem cell dynamics in psoriasis versus atopic dermatitis

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Background & Objectives: Atopic dermatitis (AD) and psoriasis (PS) are among the most common and clinically impactful chronic

inflammatory skin disorders worldwide, affecting hundreds of millions of individuals. They exhibit overlapping clinical features but distinct immune mechanisms. Both exhibit epidermal hyperplasia, but the mechanisms driving this hyperplasia are not fully understood, particularly the contributions of keratinocyte stem cells (KSCs) and epigenetic regulation. We aimed to delineate disease-specific epigenetic landscapes and KSC dynamics by analysing the distribution of 5-hydroxymethylcytosine (5-hmC), a key epigenetic mark, alongside markers for stem cells and transit-amplifying cells (TACs) in PS versus AD.
Methods: Human skin biopsies and mouse models of PS (imiquimod-induced) and AD (ovalbumin-induced) were evaluated. Immunofluorescence for 5-hmC, CK15 (KSCs), and FABP5 (TACs) was used to assess the epidermal stem cell and TCAs compartments. Additionally, NanoString GeoMx Digital Spatial Profiling (DSP) was performed on epidermal and dermal regions to measure expression of proteins related to stem cell regulation and immune signalling
Results: Psoriatic lesions confirmed prior observations of near-complete loss of 5-hmC in basal and suprabasal keratinocytes, accompanied by marked depletion of CK15+ KSCs and robust expansion of FABP5+ TCAs. DSP analysis established significantly elevated expression of keratinocyte activation and innate immune markers in PS (e.g., CD44, CD11b). In contrast, AD epidermis retained 5-hmC throughout the basal and suprabasal layers, with preserved CK15+ KSCs and minimal TCAs expansion. Proteomic profiling in AD highlighted a Th2-skewed immune response and barrier dysfunction, but not the pronounced epigenetic and stem cell alterations observed in PS.
Conclusion: These findings suggest that epidermal hyperplasia in psoriasis is driven by 5-hmC epigenetic dysregulation, KSC exhaustion, and excessive transit amplification cell accumulation, whereas AD maintains DNA hydroxymethylation and KSC homeostasis. This mechanistic divergence raises the prospect of distinct therapeutic approaches: epigenetic and stem cell restoration in PS versus abrogation of Th2 pathways and barrier repair in AD.

PS-06-014

Identification of BRAF/NRAS-mutated melanocytic lesions with spitzoid morphology versus true Spitz tumours using deep learning on histopathological whole slide images

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Background & Objectives: According to the World Health Organization's classification of skin tumours, it is recommended to distinguish BRAF-mutated melanocytic lesions with spitzoid morphology from true Spitz tumours, including both Spitz melanocytomas/atypical Spitz tumours and Spitz melanomas, which are characterized by wild-type BRAF and NRAS status. This study focuses on differentiating these entities by applying deep learning models to predict BRAF and NRAS mutational status directly from histopathological whole slide images (WSIs)
Methods: A total of 36 whole slide images (WSIs) were analysed, comprising 18 mutation-positive cases (harbouring BRAF or NRAS mutations) and 18 mutation-negative cases, all corresponding to atypical(melanocytomas) or malignant melanocytic spitzoid tumours. From these slides, a total of 286,391 image patches were extracted. Two convolutional neural network (CNN) architectures were evaluated: ResNet18 and InceptionV3. Each model was trained using 5-fold cross-validation, and performance was assessed using accuracy, sensitivity and specificity.
Results: Among the three evaluated models, ResNet18 achieved the best overall performance, with an accuracy of 0.9742 ± 0.0084, sensitivity of 0.9607 ± 0.0187, and specificity of 0.9497 ± 0.0244, indicating a balanced and robust ability to identify both mutated and non-mutated cases. In comparison, InceptionV3 showed good performance, with an accuracy of 0.9113 ± 0.0476, sensitivity of 0.9004 ± 0.0657, and specificity of 0.9360 ± 0.0280. These results confirm the superior ability of ResNet18 to distinguish between BAMS and true Spitz tumours using histopathological image data.
Conclusion: This study demonstrates the potential of deep learning models to detect BRAF and NRAS mutations in melanocytic tumours directly from histological images. ResNet18 outperformed other models in all evaluated metrics and may serve as a useful tool to support molecular diagnosis in melanocytic tumours.

Funding: This work was funded by grant PI23/01408, Instituto de Salud Carlos III and FEDER European Funds

PS-06-015

Merkel cell carcinoma (MCC) is a neuroendocrine skin cancer with high metastatic potential. Identifying prognostic biomarkers is crucial due to its aggressiveness. PRAME, studied in melanocytic tumours, is also expressed in various neoplasms. Prior studies reported PRAME expression in 30% of MCC cases, suggesting its role as a molecular driver. This study aims to confirm PRAME as a prognostic biomarker in our MCC cases

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Background & Objectives: Merkel cell carcinoma (MCC) is a neuroendocrine skin cancer with high metastatic potential. Identifying prognostic biomarkers is crucial due to its aggressiveness. PRAME, studied in melanocytic tumours, is also expressed in various neoplasms. Prior studies reported PRAME expression in 30% of MCC cases, suggesting its role as a molecular driver. This study aims to confirm PRAME as a prognostic biomarker in our MCC cases.
Methods: We analysed 34 MCC patients diagnosed between 2003 and 2025, with a median follow-up of 20.5 months. Tumour samples were reviewed by three pathologists. PRAME immunohistochemical expression was correlated with survival using Log Rank analysis. Metastatic lymph nodes were also assessed for PRAME expression.
Results: Of 34 cases, 16 (47%) exhibited PRAME positivity in primary tumours. Median disease-free survival was 14.5 months. PRAME-positive MCC patients had increased recurrence risk (HR: 6.7; p=0.005) and shorter disease-free survival (7 vs. 24 months). Median overall survival was 20.5 months; PRAME-positive cases showed reduced survival (15 vs. 24 months) and higher mortality risk, though not statistically significant (HR: 1.52; p=0.36). Metastatic lymph nodes (n=12, 35.3%) maintained PRAME staining patterns, except one case. This tumour was PRAME-negative, but 4/12 metastatic nodes exhibited focal PRAME positivity, showing a subclonal "island-like" pattern, also found in two primary tumours.
Conclusion: PRAME expression correlates with shorter disease-free survival in MCC, supporting its prognostic significance. PRAME may act as a molecular driver, suggesting potential for targeted anti-PRAME therapies in aggressive cases. Its subclonal expression pattern implies molecular heterogeneity, possibly as an acquired event in disease progression, similar to TP53 mutations in endometrial carcinoma. This finding could help refine risk stratification and guide therapeutic strategies in MCC. Further studies are necessary to confirm its role and explore therapeutic implications.

PS-06-016

Claudin-4 - an emerging biomarker for neoplastic lesions, serving as a specific diagnostic tool for skin melanoma

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Background & Objectives: Even though claudins, as a protein component of intercellular tight junctions, are native in human tissues, some studies hypothesize about claudin-4 being a marker for invasive skin melanoma phenotype. Objective of the study is to determine specific features of claudin-4 expression in skin melanoma.
Methods: An immunohistochemical reaction with monoclonal claudin 4 (CLDN4) antibody was performed for selected cases of compound nevi (n=15) and metastatic skin melanoma (n= 15), scanning these samples with „Pannoramic Viewer (3D Histech)". Each digitalized histological view was analysed in digital microimaging software „Slideviewer". 100 consecutive melanocytic neoplastic cells were ranked according to their membranous reaction intensity scale from 0 (no reaction) to 4 points (high intensity reaction) in one 20x microscopic magnification field (approx. 0.785 mm) for each sample (Cohen's kappa coefficient>0.9). Statistical analysis was applied ($p<0.05$).
Results: High intensity claudin-4 expression was greater in metastatic skin melanoma (median=26, interquartile range=34) compared to benign nevi, where no cases exhibited a high reaction ($p<0.001$). Similarly, moderate expression was observed exclusively in melanoma (median=37, interquartile range=40), while benign nevi demonstrated no moderate staining ($p<0.001$). Mild expression also followed this pattern, with corresponding melanoma cases (median=22, interquartile range=23) compared to the absence of mild staining in benign nevi ($p<0.00l$).
Conclusion: Study of claudin-4 immunohistochemical expression in melanocytic lesions suggest that benign nevi consistently lack any intensity of claudin-4 expression and may serve as an appropriate negative control group for evaluating benign and malignant melanocytic neoplastic lesions. Metastatic skin melanomas exhibit predominantly moderate to high intensity of claudin-4 expression, suggesting the potential diagnostic role of this immunohistochemical marker in clinic pathology practice testing for malignant melanocytic lesions.

PS-06-017

CD20 expression in tumour-stage mycosis fungoides: a retrospective analysis of 51 cases

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Background & Objectives: Mycosis fungoides(MF) is the most common primary cutaneous T-cell lymphoma,typically presenting as patches,plaques,or tumours.Although MF is T-cell lymphoma,B-cell marker expression has been observed in some cases.CD20 expression in MF is an understudied area in the literature,yet it is not particularly rare.This phenomenon can create diagnostic challenges in patients with tumour-stage mycosis fungoides (TMF).This study aimed to investigate the percentage and distribution of CD20-positive cells in TMF cases and to determine whether this cellular population represents reactive B-cell infiltration or aberrant expression by neoplastic T-cells.
Methods: We retrospectively analysed 51 TMF patients diagnosed between 2004-2024. All cases underwent immunohistochemical staining for B-cell markers CD20,CD79a,and PAX5, in addition to the previously performed pan T-cell markers.The percentage and distribution of CD20+ lymphocytes were evaluated by two pathologists.Double immunostaining for CD4-PAX5 and CD4-CD20 was performed in cases with >50% CD20 expression.
Results: Our cohort(mean age 56.5±16.0 years, 66.7% male) included various MF subtypes: follicular(58.8%), classical(27.5%), and rare variants(13.7%).Twenty-five patients had TMF at the time of diagnosis. Large cell transformation was observed in 35.3% of the patients. CD20 was negative in 8 patients(15.7%) and positive in 43 patients(84.3%). Among CD20 positive cases, 24 cases had less than 10% staining, with 6 of these showing scattered staining.13 cases had 10-50% ,and 6 cases(12%) showed greater than 50% staining. The expression patterns of CD79a and PAX5 were similar to that of CD20.Dual immunostaining showed that CD20 and PAX5 reactivity was confined to B cells, whereas CD4 marked T-cells.
Conclusion: This study demonstrates the substantial prevalence of CD20 expression in TMF.The co-expression patterns of CD20 with other B-cell markers(CD79a and PAX5) and the results of our dual immunostaining strongly indicate that this represents reactive B-cell infiltration rather than aberrant expression by neoplastic T-cells.These results contribute to our understanding of the immunophenotypic complexity of TMF and highlight the importance of comprehensive immunohistochemical evaluation.

PS-06-018

Clinico-pathological profile and MMR status of sebaceous carcinoma: a 22-year retrospective study

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Background & Objectives: Sebaceous carcinoma (SC) is a rare malignant adnexal tumour that occurs sporadically or as part of Muir-Torre syndrome (MTS), which is associated with germline mutations in mismatch repair (MMR) protein genes. Immunohistochemistry (IHC) is a key tool for MTS screening.
Methods: This cross-sectional study analysed the clinico-pathological profile and MMR status of 22 SC cases diagnosed at the pathology department of Farhat Hached Hospital over 22 years. IHC was performed on tissue microarray (TMA) blocks using MLH1, PMS2, MSH6, MSH2, p53, and RA antibodies.
Results: The cohort included 15 men (68.2%) and 7 women (31.8%) with a median age of 77.5 years. SC cases were classified as extraocular (68.1%) and ocular (31.8%), with most tumours located in the head and neck region (81.8%). The mean tumour size was 25 mm, and half of the cases were classified as grade III. Vascular emboli and perineural invasion were observed in 18.2% and 22.7% of cases, respectively, while pagetoid spread was noted in one ocular SC case. Immunohistochemical analysis revealed RA expression in 40.9%, p53 overexpression in 31.8%, and a dMMR phenotype in 36.4% of cases. No statistically significant differences were found between the dMMR and pMMR groups regarding epidemiological, clinical, or pathological features. Surgical resection was performed in most cases, with positive margins in 36.4% of cases. Recurrence occurred in 36.4% of cases, and the median overall survival was 13 months.
Conclusion: These findings highlight SC as an aggressive malignancy and underscore the importance of IHC as a screening tool for identifying dMMR cases and guiding genetic counselling for patients at risk of MTS.

PS-07 Poster Session Digestive Diseases Pathology - Liver/Pancreas

PS-07-001

Diagnosis and management of combined hepatocellular-cholangiocarcinomas

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Background & Objectives: Combined hepatocellular-cholangiocarcinoma (cHCC-CCA) is a rare primary liver carcinoma, which contains unequivocal elements of both hepatocarcinoma and cholangiocarcinoma. It is a tumour of complex morphology and immunohistochemical diversity, whose diagnosis and management are still under discussion.
Objective: Analyse the outcomes of patients with cHCC-CCA undergoing liver transplantation (LT), in comparison with partial resection, in order to investigate whether LT can be considered a therapeutic option.
Methods: A retrospective study was carried out in 15 patients diagnosed with cHCC-CCA after undergoing partial or total hepatectomy at our centre from January 2004 to August 2021. Sociodemographic, clinical, and histopathological variables were collected, and statistical analysis was performed.
Results: The median age was 57 years old (30-74) and 11 patients (73,3%) were men. 12 cases (80%) had underlying liver disease, being hepatitis C virus the most common aetiology. Six patients (40%) received a LT and nine patients (60%) underwent partial hepatectomy. The median cancer-specific survival in transplanted patients was 122 months and in non-transplanted patients, 27 months (p-value 0.081). Tumour recurrence was observed in five patients (33,3%), all of whom died as a result of cHCC-CCA. Among the five relapsed patients, four had undergone partial resection, while only one had received a transplant. The median cancer-specific survival for patients with tumours equal to or smaller than 5 cm was 107 months, and 14 months for tumours larger than 5 cm (p-value 0.017). The median cancer-specific survival in cases with vascular invasion was 52 months, and 109 months for tumours without invasion (p-value 0.182).
Conclusion: Since the survival of transplant patients was not worse than that of those who underwent partial resection, we believe that patients with cHCC-CCA should be considered as potential LT recipients, especially those within the Milan criteria. The most relevant prognostic factors were tumour size and vascular invasion.

PS-07-002

Compliance with reporting guidelines for intraductal papillary mucinous neoplasms of the pancreas: a retrospective audit

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Background & Objectives: The pathological features of intraductal papillary mucinous neoplasms (IPMN) are important predictors for the risk of recurrence post resection and malignant transformation to pancreatic adenocarcinoma. Comprehensive reporting of resected cases is essential for optimal patient management. The aim of our audit was to assess the completeness of reporting on pancreatic resections for IPMN over a 10-year period and to assess the impact of the introduction of a standardised template (ST).
Methods: Reports with a diagnosis of IPMN between January 2015 and December 2024 were extracted from the laboratory information system of a single tertiary hospital. Report completeness was assessed based on the criteria recommended by Del Chiaro & Verbeke (Histopathology, 2017). Key features included location, tumour size, duct type, epithelial type, grade of dysplasia, margin status, background pathology and lymph node status.
Results: 100 cases were identified, 46 cases prior to the introduction of the ST and 54 cases reported post-ST. Overall compliance to the standard was 87% with an improvement from 82.61% pre-ST to 90.74% post-ST. The most commonly omitted criterion was tumour size (38.46% of incomplete reports). Additionally, in 45.45% (5/11) of cases involving an invasive tumour, one or more key features of IPMN were missing. Of the 22 cases with high-grade dysplasia, 86.36% (19/22) were classified as mixed or main duct type, 1 as branch duct type, and 2 were unknown due to omissions. The most frequent type of differentiation was gastric (49% of cases).
Conclusion: The introduction of a standardised reporting template resulted in an improvement in report completeness for pancreatic resection specimens containing IPMNs. This audit also identifies areas for improvement, particularly the omission of key IPMN features in malignant cases.

PS-07-003

Morphomolecular characterization of hepatocellular adenomas: a single-centre experience

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Background & Objectives: Hepatocellular adenoma (HCA) is a benign liver neoplasia composed of hepatocellular-differentiated cells. However, certain cases present diagnostic challenges due to inconclusive morphological and immunohistochemical (IHC) findings. The most common differential diagnose in biopsy specimens being focular nodular hyperplasia (FNH). The aim of this study was to evaluate the utility of a next-generation sequencing (NGS) liver adenoma panel in diagnosing HCAs, particularly in cases with ambiguous histopathological and IHC results. We report our single-centre retrospective experience from 2022 to 2024.
Methods: A cohort of 18 patients with hepatic lesions underwent a comprehensive diagnostic evaluation, including haematoxylin and eosin (HE) staining, IHC markers (glutamine synthetase [GS], liver fatty acid-binding protein [LFABP], serum amyloid A [SAA], and β-catenin), and targeted NGS analysis using the liver adenoma panel. Cases were classified based on morphomolecular characteristics.
Results: After extensive workup, the 18 cases showed the following mutations: HNF1A (n = 1), IL6ST (gp130) (n = 5), FRK (n = 1), and CTNNB1 mutations (exon 3: n = 2, exon 7/8: n = 2). No mutations were detected in STAT3, GNAS, or JAK1 genes. These cases were classified as follows HNF1A-inactivated HCAs (H-HCAs): n = 1, Inflammatory adenomas (IHCAs): n = 6, β-catenin-activated HCAs (b-HCAs): n = 2, β-catenin-activated inflammatory IHCAs (b-IHCAs): n = 2, Unclassified: n = 5, Focal nodular hyperplasia (FNH): n = 2.
Conclusion: The implementation of the NGS liver adenoma panel proved beneficial, particularly in some mixed-phenotype cases such as β-catenin-activated inflammatory HCA, where conventional IHC and morphology alone were not sufficient for definitive classification. This molecular approach enhances diagnostic precision and aids in the appropriate classification of challenging HCA cases.

PS-07-004

A single-centre experience on histomorphological features of porto-sinusoidal vascular disease: is Glutamine Synthetase (GS) helpful in detecting the early subtle lesions of PSVH?

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Background & Objectives: Non-cirrhotic portal hypertension (NCPH) traditionally described portal hypertension without cirrhosis. Recently,

the term porto-sinusoidal vascular disorder (PSVD) has been introduced to describe vascular lesions of the portal venous system and sinusoids in non-cirrhotic livers, with or without portal hypertension. Histologically, PSVD includes specific and non-specific features. Early lesions may be subtle and under-recognized.
Glutamine synthetase (GS), normally expressed in perivenous hepatocytes, and has been suggested as a potential marker for lobular vascular flow changes and microvascular remodelling in PSVD.
This study aims to classify histopathological findings in PSVD-spectrum cases and assess GS zonal expression in relation to clinical and histological features, particularly in patients with subtle, non-specific changes—potentially identifying early PSVD.
Methods: Twenty-seven liver biopsies were retrospectively analysed: cases previously diagnosed within the NCPH spectrum: nodular regenerative hyperplasia (NRH, n=8), hepatoportal sclerosis (HPS, n=7), PSVD (n=5), obliterative portal venopathy (OPV, n=2), controls (n=5, congenital hepatic fibrosis and non-lesional liver tissue). GS immunostaining was evaluated for zonal distribution. Clinical and histological features were recorded.
Results: Sinusoidal dilatation was observed in 59% (16/27), portal vein abnormalities in 52% (14/27), and mild periportal or perisinusoidal fibrosis in 37% (10/27). These non-specific features were frequently found in PSVD-spectrum cases, including those without clinical signs of portal hypertension. In contrast, GS expansion into midzonal or periportal zones observed in 46% (6/13) of the PSVD-spectrum biopsies. These GS-positive cases often coincided with sinusoidal dilatation, portal vein abnormalities; and also observed in patients without clinical portal hypertension. Although the limited statistical analysis, these findings suggest a potential association between GS zonal distribution and early lobular microvascular changes.
Conclusion: Zonal GS expansion may reflect early lobular vascular remodelling in PSVD. GS zonal distribution is a potentially useful histologic marker in early/subtle NCPH. However, our investigation involves a small group of patients as a preliminary study; further studies are needed.

PS-07-005

The role of PCSK9 in tumour microenvironment and drug resistance in Hepatocellular carcinoma

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Background & Objectives: PCSK9, originally well-known for its critical role in cholesterol metabolism, has emerged as a tumour-promoting gene in various types of cancer, including Hepatocellular carcinoma (HCC). Noticeably, we demonstrate that proprotein convertase subtilisin/kexin type 9 (PCSK9) plays a crucial role in the oncogenic process of HCC. However, little is known about the molecular roles and clinical values of PCSK9 in governing the tumour microenvironment (TME) and drug resistance in HCC.
Methods: We use web-based bioinformatics tools to determine the clinical correlation and transcriptional factor binding sequence in the indicated promoter. Molecular mechanisms are primarily revealed by conducting immunoblotting, lentivirus-mediated shRNA knockdown or CRISPR/Cas9 sgRNA knockout, MILLIPLEX Multiplex Assays, and ELISA analysis.
Results: Herein, we find that sorafenib treatment dramatically downregulated PCSK9 protein expression in HepG2 cells. Conversely, PCSK9 expression is markedly upregulated in sorafenib-resistant HepG2 cells. Interestingly, SREBP2, a well-characterized transcriptional activator of PCSK9, is greatly increased in sorafenib-resistant HepG2 cells. Clinically, high-level SREBP2 and PCSK9 are significantly observed in HCC patients with sorafenib non-responder in comparison to sorafenib responders, as revealed by Gene Expression Omnibus (GEO) database. Notably, Kaplan-Meier analysis using web-based bioinformatics tools shows that elevated PCSK9 expression significantly correlates with poorer overall survival in sorafenib-treated HCC patients. In addition, co-culturing shPCSK9-expressing HepG2 cells with PMA-activated THP-1 cells results in lower IL-6 levels compared to shRNA control utilizing MILLIPLEX Multiplex Assays. Meanwhile, recombinant PCSK9 proteins markedly induce IL-6 expression in PMA-activated THP-1 cells. Importantly, the promoter of SREBP2 contained potential STAT3 binding sites, suggesting that the IL-6/STAT3 signalling pathway may regulate SREBP2 expression, thus facilitating PCSK9 expression.
Conclusion: In conclusion, this study aims to explore the molecular mechanisms and clinical significance underlying driving PCSK9 expression in resistance development and explore the interplay between the tumour microenvironment (TME) and HCC, ultimately leading to the development of more effective therapeutic strategies for HCC treatment.

PS-07-006

Prevalence of claudin 18.2 expression in patient subgroups and co-expression of claudin 18.2 with the KRAS G12D mutation in patients with locally advanced unresectable or metastatic pancreatic ductal adenocarcinoma in Germany

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Background & Objectives: The tight junction protein claudin 18.2 (CLDN18.2) is a potential predictive biomarker in pancreatic ductal adenocarcinoma (PDAC). We aimed to determine the prevalence of CLDN18.2 expression in locally advanced unresectable or metastatic PDAC (la/mPDAC) and examine co-expression with KRAS G12D, a common mutation.
Methods: Tumour Registry Pancreatic Cancer, an open, non-interventional, prospective, multicentre clinical research platform in Germany (NCT02089269), provided medical and biobank data. Participants initiated first-line treatment (2013–2022) for la/mPDAC at registry enrolment and donated tumour samples. For this study, in centralized testing in 2024, immunohistochemistry staining for CLDN18.2 expression was considered positive if ≥75% of tumour cells demonstrated moderate to strong membranous staining. KRAS G12D was detected by PCR. Descriptive statistics of CLDN18.2 expression included distribution by patient subgroups and co-expression with KRAS G12D.
Results: Among 245 enrolled patients, 66 (26.9%) had CLDN18.2-positive tumours and 179 (73.1%) had CLDN18.2-negative tumours. In patient subgroups, proportions of patients with CLDN18.2-positive tumours were as follows: age ≥70 years (27/109 [24.8%]) and <70 years (39/136 [28.7%]); male (32/131 [24.4%]) and female (34/114 [29.8%]); locally advanced unresectable disease (stage III; 5/13 [38.5%]) and metastatic disease (stage IV; 61/232 [26.3%]); sample site of primary tumour (22/88 [25.0%]), local recurrence (0/1 [0%]), distant metastases/lymph nodes (28/106 [26.4%]), and unknown (16/50 [32.0%]); and sample type of biopsy (24/117 [20.5%]), resection (20/62 [32.3%]), and unknown (22/66 [33.3%]). Eighty (32.7%) patients had KRAS G12D, and 148 (60.4%) patients did not; KRAS G12D status was missing in 17 (6.9%) patients. Nineteen of 66 (28.8%) patients with CLDN18.2-positive tumours and 61 of 179 (34.1%) patients with CLDN18.2-negative tumours had KRAS G12D.

Conclusion: Across most subgroups, 20.5%–38.5% of patients had CLDN18.2-positive tumours, and 28.8% of patients with CLDN18.2-positive tumours had KRAS G12D. Improved understanding of CLDN18.2 prevalence and co-expression with KRAS G12D may support development of targeted therapies for la/mPDAC.

Funding: This study was funded by Astellas Pharma, Inc. Medical writing/editorial support was provided by Karyn Liu, PhD, Pamela Barendt, PhD, and Cheryl Casterline, MA, from Peloton Advantage, LLC, an OPEN Health company, and funded by the study sponsor

PS-07-007

Frequency of IDH1 mutation in intrahepatic cholangiocarcinoma

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Background & Objectives: IDH1 mutation is one of the new targets for cholangiocarcinoma precise therapy. According to the literature IDH1 mutations are detected in 10-20% of intrahepatic cholangiocarcinoma cases and up to 5% of extrahepatic cholangiocarcinoma cases. The study aim was to evaluate frequency of IDH1 mutation in intrahepatic cholangiocarcinoma in Ukrainian patient cohort with the use of cheap NGS hotspot panel.
Methods: The study included 75 patients who underwent liver core biopsy or liver resection procedure for intrahepatic cholangiocarcinoma during the 2019-2023. Ethics approval and informed consent were obtained. DNA was extracted from the FFPE blocks. Genomic DNA was sequenced using IonAmpliSeq Cancer-Hotspot Panel and Ion S5 sequencer. Results were filtered using Franklin by Gennox. NGS was supported by NRFU [grant- 2021.01/0024]
Results: A total of 74 significant variants were found in 21 genes. The largest number of mutations was identified in genes: IDH1, TP53, RET, KRAS, PIK3CA, IDH2 (17, 8, 8, 5, 5, 2 respectively). Of the variants that have been identified 17 IDH1, 3 NRAS and 2 BRAF mutations are alterations for which a targeted therapy has been validated. IDH1 mutation was detected in 17% cases (22,6%). From those 17 IDH1-cases R132C was found in 6 samples (35,3%), R132L - in 5 samples (29,4%), R132G – 3 in samples (17,6%) and R132H in 1 sample (5,9%). 2 cases were non-R132X (11,8%). All IDH1-positive cases have small duct type morphology.
Conclusion: With the help of NGS hotspot panel IDH1 mutation was found in 22,6% of patients. This figure is slightly higher than in literature (10-20%). Considering the relative cheapness of such a test, it is recommended to test all intrahepatic cholangiocarcinoma samples. These data might help guide targeted therapies selection for patients treatment.

Funding: NGS was supported by NRFU [grant- 2021.01/0024

PS-07-008

Establishment of the Spanish childhood liver cancer biorepository: advancing clinical and pathological prognostic validation

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Background & Objectives: Childhood liver cancer is a rare disease. Limited biological samples have hindered understanding their molecular nature, affecting translational research. Our aims were (i) establish a Spanish biorepository of clinically-annotated biological samples from paediatric patients with liver cancer, (ii) set-up a national pathology review and (iii) identify prognostic clinical, and pathological parameters.
Methods: Establish a collaborative network with the main Spanish paediatric hospitals to collect samples (tissue, plasma) and clinical data,offer a national pathology review and fully annotate tumour samples (e.g. diagnosis type and subtype, histology, main epithelial component).
Results: From 2010-2024, 569 biological samples were collected from 128 patients: 119 HB (median age: 37.8 months, 55% male, 18% PRETEXT IV, 18% metastasis, 8% mortality) and 9 HCC (median age: 132 months, 45% male, 40% mortality). Pathology review confirmed HB in 95% of cases and reclassified 5% of them as HCN-NOS. HCC and HCN-NOS were associated with poor outcome. For HB patients, significant factors associated to survival included patient age $\geq$ 8 years, PRETEXT IV, multifocality, metastasis and high-risk CHIC-HS.
Conclusion: We established a unique biorepository of childhood liver cancer in Spain of clinically and pathologically annotated specimens and validated key prognostic clinical and pathological features.

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PS-08-001

Histopathological evaluation of high-grade and undifferentiated thyroid carcinomas: a retrospectives analysis

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Background & Objectives: Thyroid carcinomas encompass a spectrum of biological behaviour, ranging from indolent well-differentiated tumours to highly aggressive undifferentiated carcinomas. Poorly differentiated thyroid carcinoma (PDTC) and high-grade differentiated thyroid carcinoma (HG-DTC) represent intermediate forms, whereas anaplastic thyroid carcinoma (ATC) is characterized by rapid progression, resistance to therapy, and poor prognosis. Given their overlapping histological features but distinct clinical courses, accurate subclassification is crucial. This study evaluates the histopathological and clinical characteristics of patients diagnosed with PDTC, HG-DTC, and ATC.
Methods: A retrospective analysis was conducted on 33 patients(20 females,13 males).Parameters assessed included tumour localization, mitotic activity, necrosis, invasion patterns and proliferation markers. Both Ki-67 and Phh3 indices were utilized to evaluate proliferative activity. A maximum of 75 blocks were sampled in a single case, with an average of 29 blocks per tumour. Treatment modalities and follow-up data were also recorded. The number of sampled tissue blocks was also evaluated to reflect diagnostic sampling density.
Results: The mean age at diagnosis was 55 years. Among the six PDTC cases, mitotic counts ranged from 3–14 per 10 high-power fields (HPF), with necrosis present in four cases and Ki-67 indices ranging from 10% to 60%.Three PDTC patients had lung metastases at diagnosis, and two died from the disease. HG-DTC cases (n=22) exhibited mitotic activity between 5–10/10 HPF, necrosis in nine cases, and Ki-67 up to 30%.One HG-DTC patient had tracheal and oesophageal invasion with nodal metastasis. ATC cases (n=5) showed markedly aggressive behaviour with high mitotic and proliferative activity(Ki-67 up to 60%), frequent necrosis, vascular invasion, and widespread metastases in one patient. Consistent proliferative activity assessment was observed across mitotic count,necrosis,Ki-67 and Phh3.
Conclusion: In contrast to previous studies reporting more frequent lymph node involvement in HG-DTC, our cohort showed nodal metastases predominantly in PDTC cases (4/6),with three of these also presenting with pulmonary dissemination at diagnosis. The combined use

of Ki-67 and Phh3 provided a comprehensive evaluation of proliferative potential, aiding tumour stratification.

PS-08-002

Identification of mutations in follicular cell-derived non-anaplastic thyroid neoplasms: a clinical experience

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Background & Objectives: Follicular cell-derived thyroid carcinomas generally have an excellent prognosis. However, a small percentage of patients progress to advanced disease. In this setting, tumours harbouring translocations (most commonly RET, followed by NTRK) can be treated with personalized targeted therapies. Since there are multiple approaches to diagnosing these alterations, our centre opted to perform DNA- and RNA-based next-generation sequencing (NGS) in these tumours. Here, we present the results obtained over a five-year period.
Methods: We reviewed the NGS results of follicular cell-derived thyroid carcinomas analysed at our centre over the past five years. During this period, three different Oncomine Assay panels (ThermoFisher Scientific) were successively implemented, all capable of detecting RET, NTRK, and ALK translocations.
Results: Over the five-year period, 44 NGS analyses were performed, including 20 papillary thyroid carcinomas (PTCs), 15 high-grade carcinomas, 8 follicular carcinomas, and 1 oncocytic carcinoma. Molecular alterations were identified in 34 tumour samples (77.3%). Seven samples (15.9%) did not meet the RNA quality requirements, necessitating additional FISH studies to rule out translocations.
Three actionable mutations were detected: two ***CCDC6::RET*** fusions, identified in an infiltrative follicular variant of PTC and in a PTC with tall cell areas; and one ***NCOA4::RET*** fusion, found in a diffuse sclerosing PTC. Additionally, a ***NSD3::NUTM1*** translocation was observed in a poorly differentiated carcinoma. The most frequent molecular alterations were **14 *BRAF* mutations**, followed by **6 *NRAS* mutations** and **3 *HRAS* mutations**. High-grade carcinomas exhibited the lowest mutation detection rate (53.3%).
The number of NGS analyses performed on follicular cell-derived thyroid carcinomas steadily increased over the study period, from 4 in 2019 to 10 in 2024.
Conclusion: At our centre, our detection strategy has enabled the identification of actionable targets in 6.8% of follicular cell-derived thyroid carcinomas requiring systemic targeted treatment.

PS-08-003

Development and validation of an integrated model to predict BRAF V600E mutation in Papillary thyroid cancer from Cytological Slides and CT images

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Background & Objectives: The BRAF gene plays an essential role in papillary thyroid carcinoma (PTC). However the detection is time-consuming and expensive. We try to investigate the potential of an integrated model based on Cytological Slides and CT images in predicting BRAFV600E mutation in calcified PTC.
Methods: This study included 465 patients with pathology-confirmed PTC and proven BRAF V600E status by PCR. All patients underwent CT scan and fine needle aspiration cytology before surgery. They were randomly divided into the training/validation cohort (n = 295/100) and the testing cohort (n =70). The Integrated model was constructed by machine learning on the basis of two features: radiomics CT features and pathomics nucleus features. The accuracy for the prediction of BRAF V600E status was verified in retrospective internal validation cohort and further validated in a multicentre, prospective observational study. Model performances were evaluated using area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).
Results: Integrated model had favourable accuracy in the training cohort (AUC 0·864 [95% CI 0·826–0·901]), and in validation cohort (0·866 [0·819–0·913]). In the prospective validation study, Integrated model had an AUC of 0·812 (95% CI 0·716–0·903), sensitivity of 0·889 (0·729–0·998), specificity of 0·739 (0·590–0·876), NPV of 0·927 (0·861–0·994), and PPV of 0·513 (0·314–0·712). It also significantly outperformed single-modality prediction models (AUC 0·631 [0·509–0·755] for the radiomics CT model, and 0·739 [0·620–0·843] for the pathomics nucleus model; all $p<0·0001$).
Conclusion: Multimodal integration of pathomics and radiomics improved mutation risk score prediction relative to the single models.

PS-08-004

An integrated radiomic and pathomic approach for the detecting of BRAF V600E mutations in papillary thyroid cancer

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Background & Objectives: Papillary thyroid cancer (PTC) is the most prevalent form of malignancy among all thyroid cancers. It is characterized by BRAF mutations (mainly V600E) with more aggressive and iodine-resistant phenotypes. Because of the mutation detection is unaffordable and time-consuming for a considerable number of patients, predicting gene mutations based on routine clinical radiological scans or whole-slide images of tissue with AI-based methods has become a hot issue in actual clinical practice. In this study, we try to develop and validate an artificial intelligence integrated model using pretreatment CT and ThinPrep cytological slides as a highly potential decision-support tool to aid oncologists in future cancer treatment management.
Methods: This study included 465 patients with pathology-confirmed PTC and proven BRAF V600E status by PCR. All patients underwent CT scan and fine needle aspiration cytology before surgery. They were randomly divided into the training/validation cohort (n = 295/100) and the testing cohort (n =70). The Integrated model was constructed by machine learning on the basis of two features: radiomics CT features and pathomics nucleus features. The accuracy for the prediction of BRAF V600E status was verified in retrospective internal validation cohort and further validated in a multicentre, prospective observational study. Model performances were evaluated using area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).
Results: Integrated model had favourable accuracy for the prediction of BRAF V600E mutation in the training cohort and in validation cohort . It also significantly outperformed single-modality prediction models for the radiomics CT model, and for the pathomics nucleus model.
Conclusion: Multimodal integration of pathomics and radiomics improved mutation risk score prediction relative to the single models,which not only aid in accurate diagnosis but also provide useful information in guiding clinical decision-making in patients with thyroid cancer.

PS-08-005

Are micropapillary thyroid carcinomas indolent? Multiparameter description and comparison of a Colombian Cohort

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Background & Objectives: Papillary thyroid carcinoma (PTC) is the most common malignant thyroid neoplasm. Its rising incidence is attributed to the increased use of diagnostic imaging. Papillary thyroid microcarcinoma (PTMC), defined as a tumour ≤1 cm, is generally indolent; however, a subset may present aggressive behaviour. This study aims to describe and compare the clinical, histological, and molecular features of a Colombian PTMC cohort to conventional PTC cases (>1 cm).
Methods: A retrospective analysis was conducted on 229 patients diagnosed with PTC between 1993 and 2011 at Fundación Santa Fe de Bogotá, as part of the TIROSEC study. Clinical, epidemiological, and histopathological features were analysed. Molecular profiling was performed using next-generation sequencing (NGS) with the SOPHiA Solid Tumour Solution kit.
Results: Of the 229 PTC cases, 97 (42%) were classified as PTMC. Most PTMC patients were women under 55 years old (84.5%), and 78% were diagnosed incidentally. Compared to PTC, PTMC showed lower nodal involvement (71% vs. 80%), more frequent aggressive histologic variants (70% vs. 41%, p<0.001), and lower rates of positive surgical margins (31% vs. 47%, p=0.02), less lymphovascular invasion (11% vs. 30%, p<0.001), less perythyroideal soft tissue involvement (42% vs. 69%, p<0.001), no extrathyroidal extension (0% vs. 5%, p=0.04); absecence of mitosiss (0% vs. 5%, p=0.04), received less radioactive iodine therapy (65% vs. 85%, p=0.001), and had lower local recurrence (8% vs. 19%, p=0.03) and mortality at 15 years (2% vs. 5%, p=0.36). BRAF (69% vs. 72%) and RAS (7% vs. 6%) mutation frequencies were similar between groups.
Conclusion: Despite their size, PTMCs in this cohort showed a relatively high incidence, nodal involvement, and BRAF mutation rate. Prognostic factors include aggressive histological subtype, margin status, and molecular alterations. The application of risk stratification criteria, such as the Porto classification, may enhance management strategies. Further studies are required to evaluate environmental factors influencing these outcomes.

PS-08-006

Increasing utility of Ki67 and p53 immunohistochemistry in the diagnostic workup of pituitary neuroendocrine tumours

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Background & Objectives: Pituitary neuroendocrine tumours (PitNETs)/pituitary adenomas typically show indolent clinical course. However, up to 1% of PitNETs are designated aggressive pituitary tumours (APT) due to continuous growth and/or hormone hypersecretion despite adequate treatment. Rare patients (0,1-0,5%) develop metastasizing pituitary carcinoma (PC). Recent reports indicate a role of *TP53* mutations in PitNET aggressiveness.
Histological markers, including Ki67 index and p53 expression, are recommended for evaluation of PitNETs behaviour according to the European Society of Endocrinology guidelines. These markers are routinely assessed in PitNETs diagnostic workup and are integrated into proposed prognostic clinicopathologic classification systems.
In the first surgery specimens from 38 APT/PC and 12 benign PitNETs we recently showed significant heterogeneity in Ki67 and p53 immunolabeling in the APT/PC subgroup.
To facilitate the assessment of Ki67 and p53 immunohistochemistry (IHC) in the PitNETs diagnostic workup, we explored the performance of an AI tool as a quantification method.
Methods: Ki67 and p53 IHC expression, evaluated as a percentage of immunopositive cells in hot spots foci, was analysed in 26 APT/PC samples and 12 benign PitNETs. Two IHC-scoring methods were used and compared: manual microscopical evaluation (method 1) and automatized assessment using QuPath digital image analyser (method 2).
Results: We found a complete correlation between the manual and automatized Ki67 and p53 IHC-scoring methods when benign PitNETs samples were analysed, and relatively high concordance (>80%) in the APT/PC group.

Conclusion: Automatized AI-based methods may be useful and time-saving in the quantitative assessment of Ki67 index and p53 expression in PitNETs, especially in APT/PC where cell proliferation and p53 expression may largely vary. Studies on the larger cohorts of PitNETs of different behaviours and correlation with molecular genetic data are needed to optimise the utilisation of Ki67 and p53 IHC in routine diagnostic workup of PitNETs.

Funding: Grant from the Swedish state under the same agreement between the Swedish government and the county councils (ALF) and from the Region Uppsala research funds

PS-08-007

Molecular and immunohistochemical characterization of cribriform-morular thyroid carcinoma: insights into origin and therapeutic targets

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Background & Objectives: Cribriform-morular thyroid carcinoma (CMTC) is a rare malignant thyroid tumour with distinctive morphological features that can occur in association with familial adenomatous polyposis (FAP) or arise sporadically. While CMTC is known to involve activation of the WNT/β-catenin pathway, its cellular origin remains controversial, and comprehensive molecular and immunohistochemical analyses have been limited.
Methods: We retrospectively identified five CMTC cases diagnosed between January 2012 and December 2022 at Chonnam National University Hospital and Chonnam National University Hwasun Hospital. Next-generation sequencing (NGS) analysis and immunohistochemical analyses were performed to investigate potential therapeutic targets.
Results: All patients were female (age range: 19-47 years, mean: 28 years). Four cases presented as single nodules, while one exhibited multifocal and bilateral disease. Tumour size ranged from 7 to 28 mm (mean: 19.4 mm), with no lymph node metastasis observed in any case. All tumours displayed characteristic cribriform and solid/morular architecture, with nuclear β-catenin positivity present in four of five cases. Immunohistochemical analysis revealed low-level HER2 expression and CD56 positivity across all cases. No patients had APC germline mutations or associated clinical symptoms. Molecular profiling identified APC or CTNNB1 mutations in all cases, with one case harbouring an additional FBXW7 mutation. High tumour mutation burden (TMB) was detected in two cases.

Conclusion: Our study demonstrates that all CMTC cases exhibited APC/CTNNB1 mutations alongside CD56 positivity. This supports the hypothesis that CMTC originates from thyroid follicular epithelial cells and develops an endodermal (intestinal-like) phenotype following characteristic mutational events. The observation of HER2 positivity across all cases and high tumour mutation burden in two cases suggests additional therapeutic options may be available for aggressive presentations of this rare malignancy.

PS-08-008

When thyroid pathology becomes a clue to PTEN hamartoma tumour syndrome

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Background & Objectives: Phosphatase and tensin homolog (PTEN) hamartoma tumour syndrome (PHTS) is a rare autosomal dominant disorder caused by mutations in the PTEN tumour suppressor gene. It causes hamartomatous overgrowth in the thyroid, gastrointestinal tract, and skin. Patients with this disease are at increased risk of thyroid, breast, renal, endometrial, and possibly colorectal cancers. PHTS includes Cowden syndrome (CS), PTEN-related Proteus síndrome (PS), Bannayan-Riley-Ruvalcaba syndrome (BRRS), and Proteus-like syndrome. Harach et al. were the first to note the histologic findings of multiple adenomatous goiters and multiple follicular adenomas, including adenolipomas.
Methods: We present four PHTS, collected in three different hospitals.
Results: All patients were young and microscopically presented unusual thyroid histology with multiple follicular adenomas with monomorphic microfollicular growth patterns, numbering more than 4, and measuring up to 3,5 cm. They all were well-demarcated with most of them with fibrous capsule with medium to large vessels. Capsular or vascular invasion was not observed. A mixture of lipomatous metaplasia and follicles and chronic lymphocytic thyroiditis was characteristic. Based on these aspects PHTS was suspected. PTEN immunohistochemistry was performed. Proliferative thyroid lesions presented loss of expression for PTEN proteins, whereas the normal background thyroid tissue was positive, compatible with PTHS. Further examination of the patient's history in three cases revealed family history of multiple polyps in the gastrointestinal tract, and cutaneous haemangiomas. In one case, thyroid pathology was the first manifestation in a 13-year-old girl. According to the National Comprehensive Cancer Network guidelines for CS/PTHS, genetic testing was done and all of them had mutations in PTEN gen.
Conclusion: We aim to demonstrate the importance of recognizing the thyroid histology, and the clinical and immunophenotypical features that will aid pathologists and clinicians in properly diagnosing PHTS, which is critical for cancer screenings and genetic counselling.

PS-08-009

Clinicopathological features of high-grade differentiated thyroid carcinoma: five years' experience of a single hospital

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Background & Objectives: High-grade differentiated thyroid carcinoma (HGDTC) refers to any differentiated thyroid carcinoma, including papillary thyroid carcinoma (PTC), follicular carcinoma, or oncocytic carcinoma (OTC), that exhibits at least five mitoses per 2 mm² and/or tumour-type necrosis without an anaplastic component. HGDTC belongs to the group of follicular cell-derived malignancies with intermediate biological behaviour. We analysed the frequency and clinicopathological features of HGDTC over a five-year period.
Methods: The study included HGDTC diagnosed at our Institute from 2020 to 2025. Besides frequency of HGDTC, the following features were analysed for each case: age, gender, tumour type, tumour size, presence of lymph node metastasis (LNM), extrathyroidal extension (ETE), and vascular invasion.
Results: During the study, 544 thyroidectomies were analysed pathohistologically. Malignant cases totaled 243 (44.66%), with PTC being the most common (197; 81.06%), followed by OTC (14; 5.76%), follicular carcinoma (11; 4.52%), medullary thyroid carcinoma (10; 4.11%), and anaplastic carcinoma (1; 0.41%). HGDTCs accounted for 10 (4.11%) cases, including eight HGPTCs and two HGOTCs. Six patients were male and four female, with an average age of 57.8±17.02 years (range 31–80 years) and a mean tumour size of 43.4±31.17 mm. Two PTC cases were subcentimetric: one was a 2 mm incidental finding, and the other presented with multiple regional LNM. Gross ETE was observed in three cases. Pathological T3 and T4 stages were found in four and one case, respectively. Distant metastasis was noted in one case, with LNMs in two cases and vascular invasion in eight cases.
Conclusion: HGDTCs are rare yet not uncommon, with the majority of cases being diagnosed in male patients. A significant number of HGDTCs have a high pathological T stage and/or exhibit LNM. Distant metastasis at the time of HGDTC diagnosis occurs sporadically. Most HGDTCs belong to a PTC type, and high-grade features may also occur in subcentimetric PTCs.

PS-08-010

Clinicopathologic correlates of tumour size in paediatric, adolescent and young adult neuroendocrine tumours: a cohort from fundación Santa Fe de Bogotá (2004–2022)

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Background & Objectives: Neuroendocrine tumours (NETs) in children and adolescents are rare, with variable clinical behaviour and anatomical distribution. Diagnosis and management are challenging due to non-specific symptoms, clinical heterogeneity, and the lack of paediatric-specific guidelines. Some NETs are linked to genetic predisposition syndromes such as MEN and von Hippel-Lindau (VHL), requiring early and tailored surveillance.
Appendiceal NETs are the most frequent and typically indolent; pulmonary and pancreatic NETs are less common but may be more aggressive, particularly in hereditary contexts. Tumour size is a critical factor influencing surgical management and prognosis. This study aimed to characterize clinicopathologic correlations with tumour size in paediatric and young patients diagnosed with NETs over an 18-year period.
Methods: A retrospective cohort of 106 patients under 26 years of age diagnosed with NETs between 2004 and 2022 at Fundación Santa Fe de Bogotá was analysed. Variables included age, gender, tumour location, histologic grade, Ki-67 index, and tumour diameter. Descriptive

statistics were followed by ANOVA, Spearman correlation, and multivariable linear regression.
Results: The most frequent location was the cecal appendix, followed by bronchopulmonary tree, pancreas, and liver (metastases). Unusual anatomical sites were found like cervix, merkel cell carcinoma and biliar duct. Tumour diameter showed no correlation with age, gender, or Ki-67 index. However, it was significantly associated with both tumour location and histologic grade. Grade 2 tumours had significantly larger diameters than Grade 1 ($p < 0.05$), and tumours with hepatic metastases were significantly larger than those in other locations ($p < 0.05$). Multivariable analysis confirmed Grade 2 and liver metastases as independent predictors of larger tumour size.
Conclusion: Tumour grade and hepatic metastases are the main determinants of tumour size in this cohort. These findings highlight the prognostic relevance of tumour size and support the need for integrated clinicopathologic assessment and paediatric-specific management guidelines for NETs.

PS-08-011
High-grade papillary thyroid carcinoma: rarity, risks and outcomes
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Background & Objectives: Differentiated high-grade thyroid carcinoma is a newly defined diagnostic entity, first introduced in the 2022 WHO classification. These tumours are rare, typically diagnosed in the sixth to seventh decade, and uncommon in young adults. This study aims to compare clinicopathological characteristics and oncologic outcomes between high-grade papillary thyroid carcinoma (HGPTC) and low-grade papillary thyroid carcinoma (LGPTC) in a young adult population.
Methods: We collected cases of papillary thyroid carcinoma in patients from our institutional archives between 2020 and 2022. Histological diagnoses were reviewed, and the tumours were subsequently reclassified into HGPTC and LGPTC.
Results: The cohort included 145 patients, consisting of 135 females and 10 males, aged 9 to 72 years. The carcinomas were classified as HGPTC (n=44) and LGPTC (n=101). The latter was further subclassified into one case of the tall cell subtype, 91 cases of the classic subtype, and 54 cases of invasive EFVPTC. The mean tumour size was 30 mm for HGPTC and 15 mm for LGPTC ($p = 0.878$). Extrathyroidal extension was noted in 15 cases (10,3%) of HGPTC and 7 cases (4,8%) of LGPTC ($p = 0.193$).
Among HGPTC cases, 21 (14,4%) had lymph node metastases, while 7 (4,8%) of LGPTC cases had lymph node metastases ($p = 0,143$). Recurrence was noted in 8 HGPTC cases (5,5%) and 4 LGPTC cases (2,7%) ($p = 0,232$). Distant metastases were observed in 9 HGPTC patients (6,2%) and 4 LGPTC patients (2,7%) ($p = 0.094$). All patients were alive at the last follow-up.
Conclusion: Although HGPTC is rare, our findings suggest that its clinicopathological profile and oncologic outcomes do not significantly differ from those of LGPTC in this population. However, the higher frequency of lymph node and distant metastases in HGPTC, although not statistically significant, underscores the need for close monitoring and further studies to better characterize its prognosis.

PS-08-012
The unencapsulated follicular subtype of papillary thyroid carcinoma is associated with nodal metastasis, but not distant metastasis: a single-centre study
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Background & Objectives: The follicular subtype of papillary thyroid carcinoma (PTC) is common and exhibits various phenotypes. Encapsulated morphology often displays a favourable prognosis. This study aims to describe the clinicopathological features of follicular subtype of PTC and explore the association between unencapsulated phenotype and aggressive tumour outcomes.
Methods: We retrospectively collected all PTC cases diagnosed as follicular subtype at Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, from 2019 to 2022. The Chi-square test was performed to analyse the association between unencapsulated tumours with nodal and distant metastasis.
Results: There were 84 cases of follicular subtype of PTC. Most patients were female (79.8%) and under 55 years of age (77.4%), with a mean age of diagnosis at 43.7 years (SD=15.1 years). The tumour is frequently multifocal (64.3%) with a median tumour size of 2.9 cm (range = 0.3—12 cm). Most of the patients were classified according to the 8th American Joint Committee on Cancer as stage I (83.3%), followed by stage II (11.9%), and stage IV (4.8%). All cases exhibited PTC nuclei, with 64.3% of patients displaying a total nuclear score of 2. *RAS* mutation was identified in 32 patients and *BRAF*V6000E in 5 patients. We found 31 tumours were unencapsulated infiltrative and 53 were invasive encapsulated follicular subtype of PTC. Unencapsulated infiltrative follicular subtype of PTC was associated with nodal metastasis (p=0.04; OR [95% CI]= 3.2 [1-10.1]). We found no significant association between unencapsulated tumours with distant metastasis.
Conclusion: This study found a significant association between unencapsulated infiltrative follicular subtype of PTC with nodal metastasis, but not distant metastasis.

PS-09 Poster Session Haematopathology

PS-09-001
Assessment of CD19 expression in diffuse large B-cell lymphoma using QuPath: correlation with prognostic factors
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Background & Objectives: Despite significant advances in first-line treatments for diffuse large B-cell lymphoma (DLBCL), approximately one-third of patients still require subsequent therapy for relapsed or refractory disease. About 50% of refractory DLBCL patients achieve durable responses with CD19-targeted CAR-T therapy. This study aimed to assess CD19 expression in DLBCL patients and examine its relationship with prognostic factors.
Methods: Eight paraffin blocks were prepared using the tissue microarray technique, with each core having a diameter of 5 mm. Immunohistochemical staining for CD19 (clone BT5E) was performed, and slides were digitized for quantitative analysis using QuPath (version 2.1). The percentage of CD19 expression and H-scores were recorded.
Results: In the 78 evaluated DLBCL cases, CD19 expression percentages ranged from 0 to 97.68, and H-scores ranged from 0 to 264.91. No statistically significant correlation was observed between CD19 expression (percentage or H-score) and gender, nodal/extranodal disease, relapse status, Ann Arbor stage, IPI score, GCB/ABC subtype, or overall survival ($p > 0.05$).

Conclusion: Existing literature shows inconsistencies regarding the association of CD19 expression with survival, IPI score, and relapse status in DLBCL. These variations may result from small sample sizes and differences in assessment methods. In this study, objective analysis using QuPath found no significant association between CD19 expression and prognostic parameters.

PS-09-002

Clinicopathological characterization of primary large B-cell lymphomas of immune-privileged sites: a case series

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Background & Objectives: Primary large B-cell lymphomas (LBCLs) of immune-privileged sites (IP-LBCLs) are LBCLs that arise as primary neoplasms in the central nervous system (PCNS-LBCL), vitreoretina (PVR-LBCL) and testis (PT-LBCL) in immunocompetent patients. This case series aimed to study the clinicopathological features of IP-LBCLs diagnosed at a Portuguese tertiary centre since 2014.
Methods: We selected all IP-LBCLs (2014-2024) and reviewed their clinicopathological features.
Results: We identified 49 cases: 42 (85.7%) in the CNS and 7 (14.3%) in the testis. The median age at diagnosis was 69 years (range: 34-88). Regarding PCNS-LBCL, 16 (38.1%) patients were male. Median overall survival was 3 months (range: 0-127); 2 months (range: 0-127) in the PCNS-LBCL group and 8 months (range: 2-29) in the PT-LBCL group. Morphologically, 22 (44.9%) cases had a diffuse pattern, 3 (6.1%) a perivascular pattern, and 24 (49.0%) both. Six (12.2%) cases showed necrosis, and 11 (22.9%) had a starry-sky pattern. Among PCNS-LBCL cases, 21 (50.0%) exhibited reactive perivascular T-cell infiltrates. Regarding the immunoprofile, 4 (8.2%) cases were CD10-positive, and 39 (79.6%) were Bcl2-positive. The majority had a high Ki67 proliferation index (median 80%, interquartile range 80-90%). There was no significant difference in survival based on Bcl2 expression or necrosis status. The starry-sky pattern was associated with worse prognosis (median survival: 1 month vs. 5 months; P=0.006). In PCNS-LBCL, there was a trend toward higher survival in cases with reactive perivascular T-cell infiltrates (p=0.174).
Conclusion: Most IP-LBCLs arose in the CNS, had CD10-negative immunoprofile, and high Ki67 proliferation index, as expected. In this study, we demonstrated that there are potential factors that can carry prognostic value, namely the presence of reactive perivascular T-cell infiltrates and a starry-sky pattern.

PS-09-003

LMO2 as a promising immunohistochemical surrogate marker of MYC-rearrangement: our experience with high-grade lymphomas

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Background & Objectives: MYC is commonly rearranged in high-grade lymphomas (HGL) and other aggressive large B cell lymphomas (LBCL). Immunohistochemical (IHC) positivity for MYC does not accurately predict MYC rearrangements (MYC-R), and molecular studies such as FISH are required for confirmation. Previous studies have demonstrated that the RNA and protein expression of LMO2, a germinal centre (GC) marker, is down-regulated in LBCL carrying MYC-R, and suggested its possible role for screening these cases through IHC staining. Our objective is to establish the association between the IHC expression of LMO2 and other GC markers, and MYC-R in a series of HGL.
Methods: This is a retrospective series of HGL diagnosed over the last five years in our centre. Cases where MYC-R was studied by FISH at the time of sign-off were selected, and LMO2 IHC (SP51 clone) was performed. Clinical data, morphology, IHC staining and molecular alterations were analysed. No cut-off for LMO2 positivity was established.
Results: 12 cases of HGL were selected; the majority of them were women. Average age was 64 years, with one paediatric case. 90.0% showed IHC staining of MYC (EP121 clone) and 63.6% stained for LMO2. 81.8% were CD10-positive (56C6 clone). 50.0% were MYC-R; of those, 16.7% also carried a BCL2-R, and 50% were triple hits. 75% of cases showed an inverse association between LMO2 expression and MYC-R: 71% of LMO2-positive cases showed no MYC-R, and 80% of LMO2-negative cases carried the translocation.
Conclusion: These results support those from previous studies. LMO2 IHC positivity is inversely associated with MYC-R in 75% of cases, suggesting that it could be used as a surrogate marker to screen MYC-R, in combination with other IHC markers such as CD10 and MYC. The use of these three markers improves the sensibility of the screening over the use of MYC protein alone.

PS-09-004

Evaluation of automated special stainers in reticulin fiber staining of bone marrow: a retrospective, multicentre study

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Background & Objectives: Advancements in pathology laboratory instruments have played an increasingly important role in histochemistry, including in haematoxylin and eosin, immunohistochemical, and special staining techniques. However, a review of these instrument systems is critical to ensure proper staining. This study aimed to investigate the quality of automated platforms on special stains.
Methods: We retrospectively evaluated 1906 bone marrow biopsies from three different hospitals .All cases have been diagnosed correctly based on a manually modified Gordon and Sweets method. Fibrosis gradings were independently determined by two experienced hematopathologists using the European Consensus on grading of bone marrow fibrosis(MF-0: 830 cases, MF-1: 589 cases, MF-2: 401 cases and MF-3: 86cases). Reticulin fiber staining was performed again with a Ventana BenchMark Special Stains automated slide stainer.Fibrosis gradings were classified as the same.
Results: The automatic system, using a commercially available staining kit, demonstrated weak staining compared with manual procedures in MF-1 and MF-2.There was no statistically significant difference in MF-0 and MF-3.
Conclusion: Ventana BenchMark Special Stains platform may offer a new level of automation for special stains that improves turnaround times and optimizes workflow, further consideration for its use in reticulin fiber staining in bone marrow may be necessary.

PS-09-005

In Kikuchi-Fujimoto Disease (KFD), apoptosis and pyroptosis signalling are simultaneously induced to form lesions

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Background & Objectives: At the earlier meeting of this society, we reported that the endoplasmic reticulum stress (ER stress)-induced apoptosis is induced in Kikuchi-Fujimoto disease (KFD). In this study, we reported that pyroptosis was also induced in addition to apoptosis, and we will report this result together with our discussion.
Methods: Using electron microscopy, paraffin-embedded and frozen samples, we performed histopathological, immune-histochemical, and molecular biological studies.
Antibody used: PERK, ATF6, IRE1, CHOP, bcl-2, p53, GRP78(Bip), CD68, CD163, CD204, CD169, cCaspase 3, cGasdermin D.
Results: ①Apoptosis is induced by the extrinsic and intrinsic pathways and is processed by macrophages via efferocytosis.
② Pyroptosis form the holes in the cell membrane by activated GSDMD and takes part in secondary necrosis.
Conclusion: It was suggested that in this disease, apoptosis occurs in lymphocytes, while pyroptosis occurs in macrophages. These processes prevent infection and the spread of pathogens, activate the body's immune system, and help other immune cells defend against infection.

PS-09-006

Spanish idiopathic Multicentric Castleman Disease (iMCD) Registry. Epidemiology of iMCD in Spain (ARCANA) - prevalence cohort

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Background & Objectives: Multicentric Castleman Disease (MCD) is a rare lymphoproliferative disorder involving multiple lymph nodes, leading to systemic inflammation, cytopenias, and multiorgan dysfunction[1]. Approximately 33-50% of cases are human herpesvirus-8 (HHV-8) negative and classified as idiopathic (iMCD) after excluding infections, malignancies and autoimmune diseases[2] with CD-like features in lymph node biopsies. Diagnosis is challenging due to clinical and histopathological heterogeneity. Key features include a spectrum of regressed or hyperplastic germinal centres, follicular dendritic cells prominence, hypervascularization, and plasmacytosis[2]. Low incidence and clinical and histopathological overlap with mimicking conditions[2] often lead to misdiagnosis/unrecognized cases[3]. Given the limited prevalence data in Western countries[4-6], the Spanish iMCD Registry was proposed to provide real-world data on demographics, pathology, symptoms, treatments, and outcomes.
Methods: This observational, multicentre, prospective study aims to improve knowledge of iMCD epidemiology and treatment outcomes in Spain. It aims to enrol 60 patients from 20 centres, including a prevalence cohort (PC) (historical iMCD patients to describe clinical characteristics and treatment patterns), and an incidence cohort (IC) (newly diagnosed iMCD patients, followed prospectively).
Results: To date, 41 patients have been enrolled, 33 meeting diagnostic criteria (30PC / 3IC). Preliminary PC results: 30 patients from 15 sites. All underwent excisional lymph node biopsies, with histopathological features consistent with iMCD. Six cases (20%) had initial core biopsies before excision. Clinical subtypes were iMCD-NOS (76.6%) and TAFRO (23.3%). Histopathological patterns included plasmacytic (43.3%), mixed (33.3%), and hypervascular (13.3%), with 10% undetermined. Estimated iMCD prevalence was 0.51 cases per 100.000 (95% CI:0,32567-0,68863).
Conclusion: This is the first study assessing iMCD prevalence in Spain, with results consistent with previous reports. Excisional biopsies are crucial for accurately assessing histopathological features and differentiating iMCD from other lymphoproliferative disorders, supported by ancillary techniques (immunohistochemistry, flow cytometry, molecular methods) and clinicopathological correlation[7]. The study provides valuable epidemiological data that enhances global understanding of this rare disease.

PS-09-008

Histiocytic/dendritic cell neoplasms and stroma-derived neoplasms of lymphoid tissues: a retrospective analysis from a tertiary cancer centre of North India

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Background & Objectives: Histiocytic/dendritic cell neoplasms and stroma-derived neoplasms of lymphoid tissues (HDCN & SDNLT) are rare, accounting for <1% of all neoplasms occurring in lymph nodes and extramedullary locations. We aim to illustrate the clinicopathological characteristics of these rare disorders that pose significant clinical and diagnostic challenges.
Methods: A retrospective analysis was undertaken over a period of 4 years at a tertiary cancer centre after due approval from the institutional ethics committee.
Results: A total of 46 cases of HDCN & SDNLT were identified during this period, amongst which majority were paediatric males. Histiocytic sarcoma [HS] was the predominant neoplasm, followed by Langerhans cell histiocytosis [LCH], follicular dendritic cell sarcoma [FDCS], Langerhans cell sarcoma [LCS], Rosai-Dorfman disease, and Erdheim-Chester disease. Unisystem LCH predominantly involved the skeletal system whereas in multisystem LCH, lymph nodes and skeletal lesions were the commonest sites. The handy immunohistochemistry markers for diagnosing HDCN & SDNLT were CD68, CD163, CD4, CD1a, CD21 & CD23. Chemotherapy was the main modality of treatment (62.5%) due to multisystem involvement in the case of LCH or metastasis in other disease. Surgery was performed in 55% patients while radiotherapy was administered post-operatively in 15% patients. On a mean follow-up of 9.25 months, 13 patients were found to have no evidence of disease, 13 are alive with disease and 4 died of disease.
Conclusion: HDCN & SDNLT are extremely rare and intriguing diseases that ought to be ascertained using a combination of meticulous morphological examination and an array of immunohistochemistry markers to rule out mimics such as carcinoma, lymphoma, and neuroendocrine tumours and for precise subclassification of these lesions. Accurate subset diagnosis will contribute to enhanced data as well as treatment outcome analysis of these rare disorders in the future.

PS-09-009

Demystifying anaplastic large cell lymphoma: a clinicopathologic analysis from a tertiary cancer centre of North India

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Background & Objectives: Anaplastic large cell lymphomas (ALCLs) are high grade T cell lymphomas characterized by large pleomorphic cells, and expression of CD30, accounting for 2-8% of Non-Hodgkin lymphoma in adults and 10-15% in children. ALCL can be classified as ALK positive (ALK+) and ALK negative (ALK-) ALCL depending upon the expression of ALK protein by immunohistochemistry.
To comprehensively evaluate the entire spectrum of the clinical, histopathological, immunohistochemical and survival characteristics of ALCLs treated at our centre.
Methods: All cases diagnosed as ALCL on histomorphology and immunohistochemistry over a period of 6 years were explored.
Results: A total of 104 cases were identified, with an almost equal distribution of ALK+ (n=54) and ALK- (n=50) ALCL. Median age of presentation was 17years in ALK+ (2-64 years) while it was 46years (8-82 years) in ALK- group. While the most common presenting complaint was lymphadenopathy, 43% patients presented with B symptoms. Extranodal involvement was perceived in 75% cases, with the most common sites being soft tissue and bone, followed by skin, lung, stomach, intestine, etc. ALCL presented with diverse histomorphology, because of which immunohistochemistry was mandatory for accurate diagnosis. LCA was immunoreactive in 91% cases, while a potential pitfall was the negativity of CD3 in nearly 40%. On a median followup period of 9months, 31% patients experienced disease progression and 17% patients succumbed to disease, 38% ALK+ and 62% ALK-. The 3-year progression-free survival rate of the cohort was 50±7%, that of ALK+ 59.4±8.8% and ALK- 39.9±10.6%. The 3-year overall survival rate of the cohort was 72.6±6% (ALK+ 83.6±5.8%, ALK- 61.6±9.9%).
Conclusion: Meticulous histopathologic assessment is crucial in precise detection of ALCL, since it has a varied histomorphology with numerous close differentials including Hodgkin lymphoma, Diffuse Large B cell Lymphoma, Peripheral T cell lymphoma, as well as metastatic carcinomas, melanomas and sarcomas.

PS-09-010
Spatial transcriptional diversification of splenic extramedullary haematopoiesis in primary hematopoietic defect and cancer
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Background & Objectives: Extramedullary haematopoiesis (EMH) arises in response to hematopoietic stress due to bone marrow dysfunction, including primary hematopoietic stem cell defects and malignancies. The spleen is the principal EMH site, where the red pulp vascular niche supports expansion of immature progenitors. In cancer, EMH sustains myelopoiesis and reshapes immune architecture, yet its spatial transcriptional programs remain incompletely characterized. Here, we aimed at defining the splenic spatial organization and transcriptional regulation of EMH in mouse models of ineffective erythropoiesis due to haemoglobin beta mutation (Th3/+) and advanced breast cancer (MMTV-PYMT).
Methods: Spatial transcriptomics (Visum, 10x) was performed on spleens from tumour-free wild-type (WT) mice (n=3), tumour-free thalassemic (Th3) mice (n=3), and MMTV-PYMT tumour-bearing mice (n=2).
Results: Five spatial transcriptional clusters were expanded and three contracted in Th3 and PYMT spleens compared to WT controls. Three of the expanded clusters were transcriptionally associated with erythropoiesis. The first, dominant across red pulp areas, was enriched in early progenitors expressing *Mybl2*, *E2f2*, *Klf1*, and *Ccnd3*, alongside *Spic* and *Tcf21*, transcription factors implicated in red pulp macrophage/stroma specification and stromal remodelling. The second, particularly expanded in Th3, displayed a zonal distribution within the red pulp and expressed late-stage erythroid genes*(Hbb-bt, Fech, Alas2, Trim58, Epor).* The third, expanded in PYMT and confined to the red pulp–white pulp interface, showed co-expression of erythroid maturation genes (*Bpgm*, *Tfrc*) and macrophage-associated transcripts (*Marco*, *Stab2*), suggesting erythroid differentiation in proximity to white pulp myeloid elements. The remaining expanded clusters reflected granulocytic and megakaryocytic programs, while the contracted clusters were associated with T- and B-cell programs, indicating reduced adaptive immunity in EMH.
Conclusion: We described the emergence of transcriptionally and spatially divergent clusters that differentially characterize EMH in the context of a primary hematopoietic defect and in cancer.

Funding: The study has been supported by the Italian Cancer Research Foundation (AIRC)

PS-09-011
CD10 negative Burkitt lymphoma
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Background & Objectives: Burkitt lymphoma (BL) is an aggressive B-cell neoplasm characterized by *MYC* rearrangement (*MYC*-R) and a defined immunophenotype: CD10+, BCL-6+, BCL-2 negative (or dim small subset), and a Ki-67 proliferative rate of ~100%. In daily practice, there are some B-cell lymphomas with BL morphology, *MYC*-R, and an immunophenotype mostly compatible with BL except no CD10 expression (named CD10-negative BL-like lymphoma, or CD10-neg BLL, here). How to classify these lymphomas is challenge.
Methods: We identified 3 cases of CD10-neg BLL and compared them with 13 cases of typical BL and 16 cases of high-grade B cell lymphoma, not otherwise specified (HGBL-NOS) with *MYC*-R diagnosed at the same period. Immunophenotyping was performed by immunohistochemistry and/or flow cytometry immunophenotypic analysis. CD10, BCL6, BCL2 and MYC expression were designated as ≥30%, ≥30%, ≥50%, and ≥40%, respectively. *MYC, BCL2*, and *BCL6* status were assessed by fluorescence in situ hybridization analysis. The gene expression profile (GEP) of these neoplasms was assessed on a subset of cases using the HTG Whole transcriptome panel.
Results: The clinicopathologic features of these 3 cases of CD10-neg BLL were very similar to those of typical BL ($p>0.05$ for all) except CD10 expression ($p=0.002$). By gene expression profile (GEP) consisting of the top 40 differentially expressed genes between BL and HGBL-NOS with *MYC*-R, the 3 cases of CD10-neg BLL showed a GEP similar to BL and significantly different from HGBL (Figure). Two patients received R-EPOCH and one patient received R-HCVAD induction therapy. The median overall survival of these 3 patients with CD10-neg BLL was similar to that of the typical BL ($p=0.74$).
Conclusion: Our data shown that the clinicopathologic features as well as GEP of B-cell lymphoma with typical BL morphology and

immunophenotype but lacking CD10 expression is very similar to cases of typical BL. Therefore, such cases should be classified as BL.

PS-09-012

Intravascular lymphoma: a rare and challenging diagnosis – case report series from a single tertiary centre

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Background & Objectives: Intravascular lymphoma (IVL) is a rare but aggressive lymphoma primarily affecting blood vessels, leading to multisystem involvement, including the CNS, kidneys, and lungs.
Methods: Between 2005 and 2024, 5 cases of IVL cases have been reviewed based on their clinical and pathological data from Istanbul University-Cerrahpasa.
Results: The mean age was 67 (53–98), and all patients were female. Symptoms included B symptoms (2), pancytopenia (1), bicytopenia (1), and an abdominal mass (1). One patient had mild FDG PET uptake suggestive of vasculitis, another had ecchymosis-like lesions. Biopsies were taken from bone marrow (2), skin, abdominal mass, and lymph node.
The biopsies of the abdominal mass, lymph node, and skin revealed vascular proliferation and dilation, filled with thrombus formed by tumoral cells characterized by round/irregular nuclei, fine chromatin, 1–3 nucleoli, and wide cytoplasm. Bone marrow biopsies showed hypercellular marrow with CD20(+) large intravascular and intrasinusoidal cells. The biopsy taken from the abdominal mass is an incisional biopsy. No tumour was observed in the parenchyma, only an intravascular tumour component was present.
Immunohistochemically, four cases were CD20(+), while one biopsy from skin was CD20(-) but expressed CD3, CD4, CD56, TIA-1, Granzyme-B, and EBER. The Ki-67 proliferation index was very high (80-100%) in two cases. In one case, the Ki-67 result could not be concluded due to high activity in the bone marrow.
Molecular subtyping with FISH was performed on two patients; one showed 3q27 region rearrangement in 15% of interphase nuclei, while the other was negative (del5q33-34, del7q31, del20q12, del5q31, trisomy 8, t(3;3)(q26.2;q21.3)).
Four patients were diagnosed with large B-cell IVL, and one with NK/T-cell IVL.
Conclusion: IVL is difficult to diagnose due to its rapid progression and lack of detectable mass. Its insidious intravascular involvement complicates early diagnosis, often leading to fatal outcomes.

PS-09-013

Clinicopathological features of splenectomy cases: an 11-year experience with rare and common disorders

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Background & Objectives: The spleen plays a critical role in hematologic and immune functions. Splenectomy is performed for various indications, including hematologic disorders, oncologic conditions, trauma, and mass lesions. This study aims to categorize and analyse splenectomy cases over a 11-year period, evaluating their clinical presentations, underlying aetiologies, diagnosis and presenting interesting and rare pathological findings.
Methods: Retrospective review was conducted on 292 splenectomy cases received at our university hospital pathology department between 2014-2024. Cases were categorized based on their indications, including primary splenic lesions, hematologic disorders, oncologic conditions (during carcinoma surgery), trauma, infectious causes, inflammatory processes, and portal hypertension. Clinical and pathological data, including patient demographics, preoperative diagnoses, and histopathological findings, were analysed using descriptive statistics to evaluate their distribution and clinicopathological characteristics.
Results: The mean age was 54 years (range: 3-96 years), 11 cases were paediatric. The most common splenectomy indication was oncologic conditions (58.56%; n=171), with 6.97% (n=12) showing splenic parenchymal infiltration. Hematologic disorders accounted for 20.89% (n=61), including 18 cases with neoplastic involvement, primarily B-cell lymphomas (n=10), T-cell lymphomas (n=6), and myeloid neoplasms (n=2).
Primary splenic lesions represented 5.48% (n=16) and included cysts, lymphangiomas, haemangiomas, hamartomas, sclerosing angiomatoid nodular transformation, and angiosarcomas. Among 32 malignant cases, 6.25% were primary malignant neoplasms, 56.25% were hematologic malignancies, and 37.5% were metastases of oncologic tumours. Other splenectomy indications included portal hypertension (7.88%; n=23), trauma (2.74%; n=8), inflammatory processes (2.74%; n=8), and infectious causes (1.36%; n=4), which included parasitic (leishmaniasis), fungal (aspergillosis), and bacterial infections. Additionally, one case was operated on due to polycystic kidney disease.
Conclusion: Oncologic and hematologic conditions are the leading indications for splenectomy, with metastatic involvement more common than primary splenic malignancies. Understanding the clinicopathological characteristics of splenectomy cases provides valuable insights into disease patterns, enhances diagnostic accuracy and patient management.

PS-09-014

Proteasome localization as a predictive marker and therapeutic target in multiple myeloma

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Background & Objectives: We recently showed that cellular stress—such as amino acid deprivation—induces proteasome translocation from the nucleus to the cytosol, enhancing proteolysis to restore amino acid pools. This adaptive response is essential for cancer cell survival, and its inhibition triggers apoptosis. Interestingly, nuclear retention of the proteasome can be induced through a "false satiety" signal using tyrosine, tryptophan, and phenylalanine (YWF), which activate anabolic pathways without resolving the underlying stress. Here, we investigated whether proteasome localization correlates with therapeutic response in multiple myeloma (MM)—a malignancy treated with proteasome inhibitors—and whether YWF-driven nuclear sequestration can overcome drug resistance.
Methods: Proteasome localization was assessed in bone marrow biopsies from MM patients and in patient-derived cells, comparing treatment-sensitive and -resistant cases. Resistant cells were treated with either a proteasome inhibitor or the aromatic triad YWF, to test whether nuclear proteasome sequestration could overcome resistance to proteasome inhibitors.
Results: In resistant MM cells, the proteasome was predominantly cytosolic, even under nutrient-rich conditions, while in sensitive cells it remained nuclear. YWF treatment drove nuclear relocalization and induced marked cytotoxicity in resistant cells (93.2% efficacy, $p = 1.88 \times 10^{-7}$), representing a 14.7-fold increased efficacy relative to the effect of velcade, a clinically used proteasome inhibitor, on the same cells ($p = 1.26 \times 10^{-9}$). In diagnostic bone marrow samples, nuclear proteasome localization strongly correlated with favourable treatment response, while cytosolic localization predicted resistance (NPV = 0.89, $p = 0.001$). During relapse, a shift from nuclear to cytosolic proteasome localization was associated with treatment failure and a significantly shorter time to relapse (HR = 0.54, $p = 0.01$).
Conclusion: Proteasome subcellular localization is a potential predictive biomarker in MM, reflecting both treatment response and tumour

aggressiveness. Reinstating nuclear proteasome retention via YWF may represent a novel therapeutic strategy to overcome drug resistance in relapsed or refractory MM.

PS-09-015

Gastric diffuse large B-cell lymphoma: clinical, pathological and molecular characterization of 88 cases

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Background & Objectives: Gastric diffuse large B-cell lymphoma (DLBCL) is the most common extranodal lymphoma of the gastrointestinal tract. This study aims to characterize the clinicopathological and molecular features of primary gastric DLBCL, with emphasis on cell-of-origin classification, age-related patterns, and associations with infectious agents.
Methods: We retrospectively evaluated 88 cases of primary gastric DLBCL diagnosed between 2019 and 2024. Immunohistochemistry was performed to determine the COO subtype using the Hans algorithm (CD10, BCL6, MUM1). Additional markers, including BCL2 and c-MYC, were assessed. Epstein-Barr virus (EBV) infection was assessed by EBER in situ hybridization, and Helicobacter pylori status by histological examination. Statistical significance was defined as $p<0.05$.
Results: The median patient age was 60 years (range: 26-85), with a slight male predominance (54.2%). The non-GCB subtype predominated overall (66.3%), with significant age-related differences: GCB was more frequent in patients <50 years (61.9%) compared to ≥50 years (21.3%; p=0.002). H. pylori infection was detected in 20 cases (22.7%), suggesting a potential pathogenic role in a subset of gastric DLBCLs. EBER positivity was observed in 4 cases (4.8%), all in patients >60 years. One double-hit case (MYC/BCL2 co-expression) was identified in an older patient.
Conclusion: Gastric DLBCL exhibits distinct age-related molecular profiles, with younger patients displaying significantly higher rates of the prognostically favourable GCB subtype. The detection of H. pylori in 22.7% of cases highlights the heterogeneous aetiology of gastric DLBCL, potentially identifying a subset that might benefit from H. pylori eradication therapy as part of treatment. The predominance of non-GCB phenotype in older patients and occasional EBV association suggest multiple pathogenic pathways. These findings support age-stratified and aetiology-adapted therapeutic approaches in the management of gastric DLBCL.

PS-10 Poster Session Nephropathology

PS-10-001

VALIANT: Randomized, multicentre, double-blind, placebo-controlled, phase 3 trial of pegcetacoplan for patients with native or post-transplant recurrent C3G or primary (idiopathic) IC-MPGN

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Background & Objectives: C3 glomerulopathy (C3G) and primary Immune Complex-Membranoproliferative Glomerulonephritis (IC-MPGN) are complement-mediated diseases driven by C3 dysregulation with excessive accumulation of C3 breakdown products in the kidney. Pegcetacoplan (PEG), a C3/C3b inhibitor, targets the central components of the complement pathway, inhibiting C3 overactivation and preventing further deposition of C3 breakdown products in the glomeruli. VALIANT (NCT05067127) is the first Phase 3 trial investigating PEG in a broad cohort, including adolescents (≥12 yrs) and adults with native or post-transplant recurrent C3G or primary IC-MPGN.
Methods: VALIANT is a randomized, double-blind, placebo (PBO)-controlled trial evaluating PEG efficacy and safety. 124 patients (pts) were randomized to PEG (n=63) (twice weekly subcutaneous infusion) or PBO (n=61) for 26 weeks. The primary endpoint was log-transformed UPCR ratio at week 26 vs PBO. Key secondary endpoints at week 26 included the proportion of patients achieving ≥50% UPCR reduction, reduced C3c renal biopsy staining of ≥2 OOM, and eGFR change. Safety was assessed by treatment-emergent adverse events (TEAE) frequency and severity.
Results: The primary endpoint was met, with PEG demonstrating a 68.1% (95% CI: –76.2, –57.3) mean UPCR reduction vs PBO at week 26 ($p<0.0001$). Results were consistent across all subgroups (disease type, age, and transplant status). 60.3% of PEG-treated pts achieved ≥50% UPCR reduction vs 4.9% in PBO. Robust reductions in C3c staining (25 [71.4%] PEG patients achieved zero staining at Week 26) and clinically meaningful eGFR stabilization (adjusted LS mean difference +6.3 mL/min/1.73 m^2) were observed with PEG. Treatment-emergent AE frequency and severity were similar between arms. None of the 4 serious infections (3 PEG; 1 PBO) were attributed to encapsulated bacteria.
Conclusion: PEG achieved significant and clinically meaningful reductions in proteinuria (68.1% vs. PBO), C3c staining and eGFR stabilization in pts ≥12 yrs with C3G or primary IC-MPGN, was well tolerated with no new safety signals observed.

PS-10-002

Multimodal spatial profiling of the microvascular inflammation in kidney allografts

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Background & Objectives: Microvascular inflammation (MVI) in kidney allografts can occur in the absence of donor-specific antibodies (DSA) and C4d deposition. This MVI DSA- C4d- phenotype, newly recognized in the Banff 2022 classification, has an unclear pathogenesis. In this context, we aimed to decipher its immuno-molecular landscape.
Methods: MVI cases were identified in a multicentric cohort of kidney transplant patients and compared to MVI-negative controls (total n=309). Biopsies were graded according to Banff 2022 classification and sequenced using the Banff Human Organ Transplant panel. Whole-transcriptome spatial profiling and cell deconvolution were performed using the Nanostring® GeoMx platform. Microvascular infiltration

was characterized by multiplex immunofluorescence targeting CD34, CD68, CD3, NKp46, CD15, and CD20.
Results: Three MVI phenotypes were analysed: 1) MVI DSA- C4d- (n = 49, 15,9%), 2) MVI DSA+ C4d- (n = 45, 14,6%), 3) MVI DSA+ C4d+ (n = 46, 14.9%), along with non-MVI cases (n = 169, 54,6%). All MVI cases shared a common molecular signature, characterized by an upregulation of genes associated with antibody-mediated injury, interferon-gamma response, and activation of macrophages, NK cells, and T cells. This common signature was less intense in MVI DSA- C4d- cases, particularly for interferon-gamma response. Spatial profiling revealed that this molecular signal was more prominent in peritubular capillaries than in glomeruli. Cell deconvolution demonstrated that MVI DSA- C4d- cases were particularly associated with NK cells and conventional dendritic cells. Automated quantification of immunofluorescence staining revealed that microvascular infiltration was predominantly composed of CD68+ macrophages, CD3+ T cells, and NKp46+ NK cells.
Conclusion: We demonstrate that the immuno-molecular signature of kidney allograft MVI DSA- C4d- is moderate in intensity compared to DSA+ phenotypes and is predominantly associated with NK cells and conventional dendritic cells, as revealed by cell deconvolution analysis. These findings provide insights into the pathophysiology of MVI and support the development of mechanism-based therapeutic strategies.

PS-10-003
C4d in primary focal segmental glomerulosclerosis – not only passive entrapment?
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Background & Objectives: The role of the complement system (CS) in primary focal segmental glomerulosclerosis (pFSGS) is poorly understood. Here we tried to determine prognostic significance of C4d deposits in pFSGS.
Methods: Patients >18y with pFSGS, excluding those with kidney failure (KF) at the moment of kidney biopsy (KBx) and <1 non-globally sclerosed glomerulus (nGSG), were recruited from the Hospital registry of KBx from 2003-2021. Every KBx was analysed by light, immunofluorescent and electron microscopy and additional IHC for C4d was performed on paraffin-embedded tissue using monoclonal rabbit antibody (Ventana BenchMark Ultra). Every nGSG was classified as being C4d+ or C4d-. Based on ratio of C4d+ nGSG/total N of nGSG and C4d+ nonsclerotic glomeruli (NSG)/total N of NSG, patients were stratified into two groups: <50% and ≥50%. Primary outcome was defined as composite of KF and baseline eGFR decline >50%. Failure to meet criteria for remission at the last follow-up visit (KDIGO 2021 Guidelines) was defined as treatment failure (TF).
Results: A total of 58 patients were included (median age 50y, 58% males). During follow-up (median 90.7mo), 9 patients reached KF and 19 decline in eGFR. Patients with ≥50% of nGSG being C4d+ had higher proportion of TF (P=0.002) and worse renal survival (P=0.005). In multiple Cox regression model (age, eGFR, proteinuria, serum albumin, IFTA, % of C4d+ nGSG) only IFTA (HR=1.052, P=0.002) and ≥50% C4d+ nGSG (HR=4.077, P=0.035) remained independent predictors of outcome. Patients with ≥50% of C4d+ NSG had higher proportion of TF (P=0.030) and worse renal survival (P=0.037).
Conclusion: C4d deposition is an independent predictor of disease progression and TF in pFSGS. Components of CS were thought to be passively entrapped within sclerosis in pFSGS, but we showed that even C4d outside segmental sclerosis is associated with worse prognosis which may indicate active role of CS in pFSGS pathogenesis or even sclerosis development.

PS-11 Poster Session Neuropathology

PS-11-001
Case series of six patients with epithelioid malignant peripheral nerve sheath tumour: a rare subtype
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Background & Objectives: Epithelioid Malignant Peripheral Nerve Sheath Tumour (EMPNST) is a rare subtype of MPNST that differentiates from epitheloid schwannomas and it is commonly not associated with NF1 mutation. This study presents 6 different cases of this rare variant and displays its histopathological characteristics.
Methods: IHC and H&E slides were reviewed and additional stains were conducted.
Results: Mean age of the patients were 45.17 ranging from 20 to 71. Variable tumour localization was observed, with three cases involving the bones of the extremities, one in the trapezius muscle, one in the brachial plexus, and one unusually in the bladder.
Histologically, all tumours exhibited predominantly epithelioid morphology, characterized by eosinophilic to clear cytoplasm and prominent nucleoli, arranged in nests, clusters, or sheets within a multinodular growth pattern. High Ki-67 and mitotic count (≥5/10 HPF in all cases) indicated aggressive behaviour, with three cases demonstrating multiple metastases.
Immunohistochemically, diffuse and strong positivity for S-100 and SOX10 was consistent across all patients. All cases were negative for melanoma, neuroendocrine, and muscle markers. Except focal positivity in heterologous elements in 2 cases, epithelial markers were negative. H3K27me3 expression was retained, while SMARCB1 (INI-1) loss was identified in 3 cases, notably including both patients under 40 years of age (20 and 26 years). The final diagnosis of EMPNST was established after excluding other entities in the differential diagnosis.
Conclusion: The genetic background of EMPNST is still not fully understood. SMARCB1 loss is considered a key oncogenic event in the development of EMPNST. In this case series, SMARCB1 loss was observed in younger patients, while those over 40 were less likely to exhibit this alteration, suggesting the possible existence of an unknown sporadic mutation in older individuals.

PS-11-002
Comprehensive histopathological and molecular profiling of paediatric-type diffuse high-grade gliomas, H3-wildtype and IDH-wildtype: an Italian multicentre experience
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Background & Objectives: Paediatric-type diffuse high-grade gliomas, H3-wildtype and IDH-wildtype (pHGGs, H3-/IDH-WT) have recently been defined in the 2021 WHO CNS classification. Despite their clinical relevance, their histopathological and immunophenotypic profiles remain incompletely characterized. This multicentre Italian study aims to describe the clinical, histological, immunohistochemical, and molecular features of this novel tumour entity.
Methods: We retrospectively analysed 50 cases of pHGGs, H3-/IDH-WT. Data included clinical course, neuroimaging, surgical findings, histopathology, immunohistochemistry, molecular alterations, and DNA methylation profiling.
Results: Patients ranged from 1 to 26 years. Most tumours were located in the cerebral hemispheres (n=44); others involved the cerebellum (n=2), brainstem (n=1), thalamus (n=1), spinal cord, (n=1) and fourth ventricle (n=1). MRI consistently showed T1 hypo- to iso-intensity and T2 hyper-intensity, with 32 cases demonstrating inhomogeneous contrast enhancement. Histologically, tumours exhibited marked heterogeneity and diverse morphologies, including embryonal-like, pleomorphic xanthoastrocytoma-like, pseudosarcoma-like, pilocytic astrocytoma-like, and astroblastoma-like features. All tumours were GFAP-positive; Olig2 was partially expressed, and synaptophysin was variably positive, especially in embryonal-like areas. ATRX loss was observed in 6 cases. *CDKN2A/2B* homozygous deletions (n=3), *MYCN* amplification (n=4), and *MYC* gains (n=3) were also noted. DNA methylation profiling assigned all tumours to the diffuse paediatric-type high-grade glioma category, including RTK1 (n=21), RTK2 (n=12), and MYCN (n=9) subgroups.
Conclusion: This study underscores the significant histological and molecular diversity of pHGGs, H3-/IDH-WT. The combination of morphology, immunohistochemistry, and methylation profiling is essential to accurately diagnose these challenging tumours. Our findings enhance the current understanding of this emerging entity and support the integration of molecular diagnostics in routine practice.

PS-11-003
Spatial single-cell profiling reveals CD147 as a marker of tumour aggressiveness in paediatric posterior fossa ependymoma
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Background & Objectives: Ependymoma (EPN) is the third most common malignant central nervous system (CNS) tumour in the paediatric population. The spatial and temporal heterogeneity of neoplastic cell populations is believed to influence tumour adaptation within the tumour microenvironment (TME). This study aimed to characterize spatial immune dynamics and investigate the role of CD147 in posterior fossa type A ependymomas (PF-A EPN), classified as CNS WHO grades 2 and 3.
Methods: Bioinformatic analysis of public datasets revealed increased CD147 expression in gliomas, correlating with worse survival and elevated mutational burden. Spatial TME profiling was performed on PF-A EPN samples using multiplex immunofluorescence panels to evaluate immune, microglial, endothelial, and neoplastic components. In parallel, single-cell RNA-sequencing data from spinal ependymomas were analysed to identify tumour-associated macrophage (TAM) subsets.
Results: Grade 2 PF-A EPN exhibited higher infiltration of T lymphocytes, particularly cytotoxic CD8+ cells, compared to Grade 3 counterparts. Spatial analysis revealed reduced intercellular distance between CD4+ and CD8+ T cells in Grade 3 PF-A EPN, suggesting increased T cell–T cell interaction in higher-grade lesions. Two functionally distinct TAM subsets were identified (CD68+MCP1+ and CD68+CD44+), with a significant enrichment of CD68+CD44+ macrophages in Grade 3 tumours. CD147+ microglia were found in closer proximity to both CD8+ T cells and CD147+ proliferating tumour cells in Grade 2 tumours; in contrast, in Grade 3 tumours, CD4+ T cells were closer to CD147+ microglia and more distant from CD8+ lymphocytes and CD147+ tumour cells.
Conclusion: Our findings suggest that CD147+ microglia may contribute to immune evasion in PF-A EPN by promoting CD8+ T cell exclusion, particularly in higher-grade tumours. This study underscores the relevance of spatial TME remodelling in PF-A EPN and supports the potential role of CD147 as a modulator of tumour-immune interactions and disease progression.

PS-11-004
Using a non-human primate model to trace human BoDv-1 zoonosis: comparing intranasal and subcutaneous inoculation
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Background & Objectives: Borna disease virus 1 (BoDV-1) is a known cause of fatal encephalitis in humans and animals, though its

dissemination mechanisms within the brain are not fully understood. This study explores the histopathological effects of BoDV-1 in a non-human primate model. Twelve macaques were inoculated with BoDV-1, six intranasal to simulate the natural entry route and six subcutaneous to model peripheral infection. The primary aim of this investigation is to evaluate the viral distribution within the brain and compare the effects of these two infection routes.

Methods: Complete sagittal brain sections were immunohistochemically stained for BoDV-1 nucleoprotein, lymphocytic marker CD45, glial marker GFAP, microglial marker Iba1, and digitally reconstructed for detailed analysis. Quantitative assessment was performed using CellQuant with the NuclearQuant module and QuPath for quantitative analysis of cell distribution. Three macaques showed no detectable virus presence, correlating with their clinical presentation, as they were euthanized before symptom onset due to the expiration of the observation period. They were excluded for further analysis.

Results: Upon analysis, it became evident that several subcutaneously inoculated macaques exhibited substantial CNS involvement, indicating that the infection route does not determine the extent of CNS infection. Both intranasal and subcutaneous routes led to similar patterns of viral dissemination within the CNS, suggesting that factors beyond the entry site, such as specific cellular receptors or systemic mechanisms, may drive CNS infection. BoDV-1 may depend on particular receptor proteins on neural or glial cells to enter the CNS. Additionally, the virus's ability to bypass the blood-brain barrier or use neural pathways, including retrograde transport, could be critical in determining CNS involvement.

Conclusion: These findings provide insights into BoDV-1 pathogenesis, emphasizing the need to explore systemic factors influencing neurotropic virus dissemination, rather than focusing solely on the entry portal. Further research is needed to understand the mechanisms underlying BoDV-1 CNS involvement.

PS-11-005

Chemokine receptor expression profile in malignant melanoma and bain-specific metastases

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Background & Objectives: Cutaneous malignant melanoma is a common and potentially fatal malignancy in industrial countries, the development of metastases is associated with poor prognosis. One of many mechanisms involved in its developing process is the expression of chemokine receptors. Since expression patterns of different chemokine receptors in the development of brain metastases in primary malignant melanomas are still not known exactly, this thesis aimed on that issue. Furthermore, results in that field could be gate opening regarding the establishment of new therapeutical opportunities.

Methods: This thesis' target was to find out differences in expression patterns of chemokine receptors in primary malignant melanomas and their brain specific metastases. In total nine samples of primary melanomas and 25 samples of brain specific metastases as well as corresponding surrounding tissues were analysed regarding their chemokine expression patterns by using RT-qPCR.

Results: Five chemokine receptors (CCR4, CCR6, CCR9, CXCR4 and CXCR6) showed consistent expression patterns. All three CC chemokine receptors showed a decreased expression in melanomas in relation to control tissues as well as to metastases. Comparing CC chemokine receptor expression in melanomas and their surrounding skin tissue, significantly elevated levels of chemokine gene products were detected in melanoma's surrounding tissue ($p < 0.05$). Overall, CXCR4 was expressed in lower levels in all samples compared to control tissue. These results resembled to those of CXCR6

Conclusion: Chemokine expression patterns in melanomas are different to those in brain specific metastases. Furthermore, the chemokine profile is significantly different in primary melanomas compared to their surrounding skin tissue.

PS-11-006

CD80/CD163 macrophage signature identifies high-risk glioblastoma patients

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Background & Objectives: Glioblastoma (GBM) is the most common and aggressive glioma in adults, characterized by a highly immunosuppressive tumour immune-microenvironment (TIME). Tumour-associated macrophages (TAMs), which constitute nearly one-third of the TIME, are key regulators of tumour behaviour and treatment response. This study investigate the prognostic impact of macrophage polarization in a well-characterized cohort of primary and recurrent GBM patients.

Methods: Surgical specimens from 59 adult GBM patients were retrospectively collected, including recurrent tumour tissue when available. Formalin-fixed, paraffin-embedded samples were used to construct tissue microarrays in triplicate, including peritumoral/normal-like and tumour tissue. Clinical data on treatment, recurrence, and survival were gathered. Immunohistochemical expression of CD68, CD80, and CD163 was digitally quantified. Differences between tumour and peritumoral tissues were evaluated using non-parametric tests while survival analyses using Kaplan–Meier curves and log-rank tests.

Results: CD68, CD80, and CD163 were significantly upregulated in tumour tissues compared to peritumoral areas in primary GBM ($p<0.0002$, $p=0.0421$, and $p<0.0001$, respectively), whereas in recurrent GBM only CD163 remained significantly elevated ($p<0.0024$). When comparing primary *vs* recurrent GBM, a significant decrease in CD68 ($p=0.0023$) and an increase in CD80 ($p=0.0020$) were observed in tumour tissue, along with significantly higher CD163 expression in both tumour ($p<0.0001$) and peritumoral regions ($p=0.0078$). Patients classified in the CD163High/CD80High subgroup exhibited shorter overall survival (14.2 vs 23.4 months; HR=2.24; 95% CI: 1.2–4.4; $p=0.027$) and reduced progression-free survival (12.9 vs 15.1 months; HR=1.41; 95% CI: 0.8-2.5; $p=0.213$) compared to other subgroups.

Conclusion: This study highlights the complexity and dynamic architecture of the GBM TIME, driven by multifaceted interactions and cellular plasticity. It challenges the traditional M1/M2 polarization model by revealing synergistic behaviour among TAMs subpopulations. In particular, the CD80High/CD163High phenotype emerged as a distinct subset associated with poor prognosis. These findings highlight the prognostic relevance of TAMs polarization and support their potential use as therapeutic targets.

PS-11-007

Automated mitosis detection in meningioma pathology: a comparative analysis of AI vs. pathologist-based Grading

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Background & Objectives: Mitotic count is a key factor in meningioma grading, directly impacting prognosis and treatment decisions. However, manual mitotic figure identification is time-consuming and subject to intra- and inter-observer variability. This study evaluates an artificial intelligence (AI)-based algorithm designed to automatically detect mitotic figures and hot spots in whole-slide images of meningiomas, comparing its performance to pathologist-based grading and assessing its potential impact on tumour classification.
Methods: Fifty-two meningioma cases (632 slides) were analysed using an AI algorithm to detect mitotic figures within predefined high-power fields (2 mm^2 and 1.6 mm^2). Initial AI-generated mitotic counts were compared to manual pathologist assessments. To improve accuracy, pathologists performed a secondary review of AI-identified mitotic figures, confirming or rejecting them as true mitoses. Statistical analyses included mean mitotic count differences, intra-case variability, and t-tests to evaluate the impact of AI refinement on grading outcomes.
Results: The AI identified 26,163 mitotic figures across the dataset. Variability between slides of the same case was observed in 51 cases. Compared to pathologists, AI alone overestimated mitotic counts, with an average difference of 3.43 ± 4.83 ($p = 0.0018$). After expert review, the difference decreased to 0.88 ± 1.91 ($p = 0.0014$). AI-based grading resulted in an upgrade in 12.7% of cases (from WHO grade 1 to 2) and 1.8% of cases (from grade 2 to 3).
Conclusion: Automated mitosis detection offers a promising tool for enhancing accuracy and efficiency in meningioma grading. By reducing variability and mitigating the risk of missing mitotic hot spots, AI-assisted pathology could improve diagnostic precision and clinical decision-making. Further validation is required before clinical implementation.

PS-12 Poster Session Paediatric and Perinatal Pathology

PS-12-001

Shallow placental implantation in placental abruption: a significant link with foetal vascular malperfusion

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Background & Objectives: Placental abruption (PA) is the premature separation of the placenta, classified as early (<34 weeks) or late (≥34 weeks) due to differing pathophysiological mechanisms. This study aimed to assess shallow placental implantation in these subgroups within a tertiary centre cohort.
Methods: A total of 135 placentas from pregnancies between 19 and 40 weeks were analysed retrospectively. Examined variables included maternal age, gestational age, maternal vascular malperfusion (MVM), foetal vascular malperfusion (FVM), villitis, intervillitis, ascending infection, and shallow placental implantation (chorionic pseudo cysts, maternal floor multinucleated trophoblasts, and excessive extravillous trophoblasts). Statistical analyses included chi-square tests for categorical variables and t-tests for continuous variables ($p<0.05$).
Results: Among 135 cases, 83 were classified as early PA and 52 as late PA. Maternal age was similar (32 ± 6 years, p=1.00). Chorionic pseudo cysts were present in 18% of early and 23% of late PA cases (p=1.00). Excess extravillous trophoblasts were found in 55% of early and 65% of late PA cases (p=0.33). Maternal floor multinucleated trophoblasts were observed in 39% of early and 26% of late PA cases (p=0.18). MVM was more frequent in early PA (60% vs. 44%, p=0.10). FVM was significantly associated with shallow implantation (p=0.03), while no significant links were found with MVM (p=0.89), ascending infection (p=0.37), or villitis (p=0.97).
Conclusion: Shallow placental implantation did not differ significantly between early and late PA. However, its association with FVM suggests a potential link between foetal vascular malperfusion and shallow implantation in placental abruption.

PS-12-002

Paediatric liver disease in transfusion-dependent thalassemia major

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Background & Objectives: Thalassemia is an inherited hematologic disorder characterized by the production of abnormal haemoglobin. Patients with thalassemia major present with severe anaemia and related clinical symptoms. It is a prevalent condition in Türkiye and other Mediterranean countries. This study aims to investigate the histopathological features of the liver in patients with transfusion-dependent thalassemia major.
Methods: Liver biopsies were performed on 42 patients prior to allogeneic bone marrow transplantation between 2011 and 2025. Iron deposition was graded using the Scheuer method (grades 0–4), and fibrosis was assessed using the Ishak scoring system. Histological evidence of hepatitis was also evaluated. Statistical analysis included Pearson correlation to assess relationships between variables, with significance set at $p < 0.05$. Descriptive statistics were used to summarize the distribution of scores.
Results: The distribution of Scheuer scores and fibrosis levels demonstrated that 69.05% of patients had grade 4 (heavy) iron deposition, and 26.19% exhibited minimal fibrosis (grade 1). Correlation analysis revealed significant relationships between certain histopathological features. The most notable associations were observed between portal inflammation and interface hepatitis ($r = 0.66$, $p < 0.01$) and between fibrosis and portal inflammation ($r = 0.45$, $p < 0.05$). These findings highlight the impact of increased liver iron content on the progression of hepatic inflammation and fibrosis in transfusion-dependent thalassemia major patients.
Conclusion: Our findings indicate that severe haemosiderosis and hepatic fibrosis are common histopathological features in transfusion-dependent thalassemia major patients. The significant correlations between liver iron deposition, inflammation, and fibrosis emphasize the importance of early monitoring and management to mitigate hepatic complications in these patients.

PS-12-003

Placenta, the black box of stillbirth: a single-centre retrospective observational study

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Background & Objectives: Occurring worldwide at every 16 seconds, stillbirth is defined as the birth of a baby after 28 weeks of pregnancy who dies before or during labour. Maternal conditions, foetal growth restriction and placental abnormalities represent the most significant causes. The aim of this study was to examine the demographic data and placental findings from a series of autopsies following stillbirth.
Methods: We conducted a retrospective observational study including all singleton stillbirths autopsy reports from the Emergency Clinical

County Hospital of Targu-Mures between January 2020-December 2024. The autopsy reports of stillbirth from twin pregnancies were excluded. Histopathological findings of the placenta and maternal clinical records of the autopsy reports were examined.
Results: Of a total of 57 registry-identified stillbirth autopsies during the study period, 42 cases (73.68%) met the inclusion criteria. Our data indicated the following maternal portrait: multiparous (61.90%) without any remarkable medical records (76.19%) of average age 27±7.3. 59.52% of stillborns were of female sex. 45.23% of all foetal demise occurred at late foetal stage (37-39 weeks). Microscopically immature foetal pulmonary parenchyma represented the main diagnosis in 85.71% cases. Placental abruption was present in 33.3% cases. Nuchal umbilical cord was reported in 14.28% of cases. Histopathological findings of the placenta described foetal vascular malperfusion lesions in 47.6% cases and maternal vascular malperfusion lesions in 42.85% cases.
Conclusion: Our study highlights the importance of placental examination and the inclusion of histopathological findings in the final reporting of stillbirth cases. Frequently the evaluation of the foetus does not provide sufficient insight into the possible causes of the foetal demise, however placental findings may do. The identification of placental pathologies represent an essential assessment in cases of unexplained stillbirth. It is therefore mandatory for residents who perform stillbirth autopsies to have a basic understanding of placental pathology.

PS-12-004
Clinico-pathological and imaging correlation of non-Wilm's renal tumours of childhood
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Background & Objectives: The diagnosis of paediatric renal tumours comprising of Wilm's tumours (WT) and Non-Wilm's tumours (NWT) relies on radiological imaging since preoperative biopsy is not recommended in routine WT cases. Thus, some NWT are misdiagnosed as WT on prior imaging.
International Society of Paediatric Oncology (SIOP) recommends neo-adjuvant chemotherapy followed by nephrectomy for treating WT. Thus, sometimes benign NWT cases misdiagnosed as WT on antecedent imaging may inadvertently receive chemotherapy and get exposed to its hazards.
Determining clinical, imaging and histopathological features of NWT and correlating the final histopathological diagnosis with prior imaging.
Methods: Retrospective data collection of paediatric NWT (<18 years of age, from 2014-2024). 98 cases were included in the study. History of NACT and preoperative diagnosis of WT on imaging were recorded. Clinico-pathological correlation was established for NWT cases categorized as WT on prior imaging studies.
Results: Radiological inference was divided principally into 3 subgroups: WT, NWT and indeterminate. The pathological and imaging discordance was 43.86% (42 cases of NWT were incorrectly diagnosed as WT on prior imaging). Amongst NWT, clear cell sarcoma was the most frequently diagnosed tumour (n=39), showing sheeted architecture, thin arborizing vasculature and positivity for CyclinD1 and BCOR on immunohistochemistry(IHC). Malignant rhabdoid tumour of the kidney was the second most frequent tumour (n=19) exhibiting abundant eosinophilic cytoplasm, eccentric vesicular nucleus, prominent nucleolus and loss of INI-1 staining on IHC. Translocation-associated renal cell carcinoma (n=10) showed nuclear TFE3 positivity in 8 cases.
Conclusion: No pathognomonic imaging characteristics exist to distinguish WT from NWT. A differential of NWT should be considered in a child more than 5 years/ less than 1 year of age with large lymphadenopathies, pulmonary metastasis and imaging characteristics of hyper-enhancing lesions, multiple calcifications with extrarenal extension and infiltrating margins. In these situations, a preoperative biopsy is advised before administering cytotoxic therapy.

PS-12-005
Paediatric-type follicular lymphoma in WHO-HAEM5 vs ICC 2022: diagnostic criteria and classification differences
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Background & Objectives: Paediatric-type follicular lymphoma (PTFL) is a distinct entity recognized in both the World Health Organization's 5th Edition Classification of Haematolymphoid Tumours (WHO-HAEM5) and the International Consensus Classification (ICC) 2022. PTFL primarily affects children and adolescents, with unique clinical and pathological features distinct from adult follicular lymphoma. Accurate diagnosis and management require understanding these differences. We compare diagnostic criteria and definitions of PTFL from WHO-HAEM5 (2022) and ICC (2022), highlighting key similarities and differences.
Methods: A thorough review of WHO-HAEM5 and ICC 2022 publications was conducted, focusing on sections pertaining to PTFL. Key aspects such as clinical presentation, histopathological features, immunophenotypic profiles, genetic characteristics, and recommended diagnostic approaches were extracted and compared.
Results: • Definition and Clinical Features: Both recognize PTFL as a localized nodal B-cell lymphoma occurring primarily in paediatric and adolescent patients. The typical presentation includes painless lymph node enlargement, often in the head and neck region, without systemic B-symptoms.
• Histopathological Characteristics: Both describe PTFL as exhibiting a purely follicular growth pattern with enlarged, irregularly shaped germinal centres. The neoplastic follicles are composed of intermediate-sized blastoid or large cells, often retaining a "starry sky" pattern due to tangible body macrophages.
• Immunophenotype: PTFL cells express germinal centre markers such as CD10, BCL6, and HGAL. Notably, both classifications highlight the absence or weak expression of BCL2 protein, distinguishing PTFL from typical adult follicular lymphoma.
• Genetic Features: Both WHO-HAEM5 and ICC note that PTFL lacks BCL2, BCL6, and IRF4 gene rearrangements. However, mutations in MAP2K1 and TNFRSF14 genes have been identified in some cases, suggesting alternative oncogenic pathways.
Conclusion: WHO-HAEM5 (2022) and ICC (2022) provide consistent criteria for diagnosing PTFL, emphasizing its distinct clinical and pathological features. Both classifications underscore the importance of recognizing PTFL as a separate entity from adult follicular lymphoma, ensuring appropriate clinical management and prognosis.

PS-12-006
Molecular and epigenetic characterization of Rhabdomyosarcomas within the first two years of life
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Background & Objectives: Rhabdomyosarcomas (RMS) are the most common paediatric soft tissue sarcomas, and are stratified in *PAX3/7::FOXO1* (F+) and fusion-negative (F-). This study aims to characterize the molecular and epigenetic features of RMS diagnosed in the first two years of life.
Methods: 26 RMS in patients <24 months, diagnosed between 2017 and 2024, were re-evaluated. Histology was integrated with whole RNA sequencing and methylation analysis.
Results: Age range was 19-726 days (less than 6 months in 11 patients). At histology there were: 7 alveolar RMS (ARMS), 8 embryonal RMS (ERMS), 1 ectomesenchymoma, 7 spindle cell RMS (ScRMS) and 3 RMS not otherwise specified (nos). At molecular characterization, among ARMS four were F+ and 2/3 F- showed *PAX3::NCOA1* and *MYB::NBAS* fusions, respectively. Among ERMS, two cases showed *FUS::ACVR1B* and a *PAX3::NCOA1* fusions, respectively, and one case a *PTCH* duplication. Among ScRMS, 2 were *VGLL2* rearranged (infantile fibrosarcoma-like histology), 2 *SFR::NCOA2* (myoid-like, MyoD1+/myogenin+), 1 *PAX3::NCOA2* (mixed blue round and spindle cells), 1 *PTCH* duplication, and one had no fusions. Among RMS nos, a case with *NSD3:NCOA2* (predominantly epithelioid morphology) was reclassified as ScRMS; two showed a *SMARCA4* mutation with an additional *BRCA1* mutation in one. At methylation (20/26 cases analysed), 4 F+ and 2 F- (*PAX3::NCOA1; MYB::NBAS* fusion) classified as ARMS; the classifier was unreliable for ERMS and ScRMS, except for the two *PAX3::NCOA1/2* (an ERMS and an ScRMS, respectively), which clustered as ARMS. An internally developed bioinformatics pipeline showed similar results.
Conclusion: Three novel fusions were identified in an ARMS (*MYB::NBAS*), in an ERMS (*FUS::ACVR1B*), and in a ScRMS (*NSD3::NCOA2*). The morphology of two *SMARCA4* RMSs was unique. All *PAX3::NCOA1/2* clustered as ARMS independently from morphology, suggesting that methylation may contribute to redefining this group as F+.

PS-12-007

The spectrum of placental findings of first trimester cytomegalovirus infection related to the presence of symptoms in the newborns and stillbirths

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Background & Objectives: Cytomegalovirus (CMV) is one of the most common congenital infections worldwide and one of the main causes of prenatal neurological disorders, sensorineural deafness and stillbirths. Placental factors involved in the CMV transmission from the mother to the foetus are not yet well known. Our aim is to evaluate the histopathological placental findings of first trimester CMV infection related to stillbirth and the presence of symptoms in the newborns.
Methods: This is a retrospective case-control study that analysed those pregnancies with first trimester CMV infection followed up on two tertiary referral hospitals between 2012 and 2024. The symptomatic newborns with the asymptomatic ones and the symptomatic newborns with the stillbirths were compared. A univariate statistical study was performed.
Results: A total of 40 placentas were studied, 23 of the asymptomatic newborns, 11 of the symptomatic newborns and 6 of the stillbirth cases. Smaller placentas with higher chronic plasma cell deciduitis, chronic villitis (without avascular villi, breakdown villi, necrosis or hemosiderin deposits), more CMV inclusions in fibroblasts and positive CMV immunostaining were observed in the symptomatic newborns' placentas when compared with the asymptomatic ones. Higher rates of chronic villitis (with avascular villi, breakdown villi, necrosis or hemosiderin deposits), intervillous fibrin deposits, CMV inclusions in endothelial cells and trophoblasts, maternal and foetal malperfusion pattern were present in the stillbirth's placentas when compared with the symptomatic newborns' placentas.
Conclusion: The greater villous and vascular barriers involvement, both directly and indirectly, appears to be related to a greater foetal involvement probably allowing greater transmission of the virus to the foetus. Complementary treatments that could attenuate the villi and vascular damage may be useful in reduction newborns symptoms and stillbirths due to first trimester CMV infection.

PS-12-008

Triplet pregnancies conceived through oocyte donation: placental pathological findings and clinical outcomes in 77 triplets

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Background & Objectives: Triplet pregnancies have increased over the past few decades due to an increase in assisted reproductive technology (ART), especially in the oocyte donation cases. Oocyte donation pregnancies develop high complications rate but their placentalpathological findings are not well known. Our aim is to study if triplet placentas conceived by oocyte donation present more placental abnormalities and pregnancy complications than those conceived by non-oocyte donation-ART.
Methods: This was a retrospective case-control study. It includes all triplet pregnancies followed up in a tertiary referral hospital between 2000 and 2024 and whose placentas were analysed in a Pathology Department. The control group included non-oocyte donation ART triplet pregnancies, and the case group included oocyte donation-conceived triplet pregnancies. Univariate and multivariate statistical analyses were performed.
Results: A total of 77 triplet pregnancies were analysed: 29 triplet pregnancies in the oocyte donation conception group and 48 triplet pregnancies in the non-oocyte donation group. Multivariate analysis revealed that pregnancy-induced hypertension (p=0.03) and preeclampsia (p=0.03) were significantly more frequent in the oocyte donation group. The foetal growth restriction (p=0.04) and foetal death (p=0.01) rates were higher in the oocyte donation group. Gross intraparenchymatous infarcts were observed in more oocyte donation placentas (P =0.04). Chronic inflammatory findings (chronic villitis, p=0.02; chronic deciduitis, p=0.03), foetal vascular malperfusion data (avascular villi, p=0.02; stromal-vascular karyorrhexis, p=0.01), and intervillous fibrin deposits (p=0.02) were present in more oocyte donation placentas.
Conclusion: The higher rates of placental abnormalities in oocyte-donation triplet pregnancies may justify the higher rates of maternal and foetal complications in these cases. Placental evaluation should be performed in these cases because it is key to understanding pregnancy outcomes. Further studies analysing the possible immunological and vascular mechanisms underlying these findings are needed.

PS-12-009

The ıncıdence and prognostıc value of ALK and Pan-TRK proteın expressıons ın neuroblastoma, ganglıoneuroblastoma and ganglıoneuroma patıents

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Background & Objectives: Targeted therapies for mutations in *NTRK* and *ALK* genes have recently emerged, though they are not yet widely adopted. Immunohistochemical staining using pan-TRK and ALK antibodies is effective in identifying mutations involved in tumour pathogenesis and is recommended for diagnostic and predictive screening purposes. This study aims to evaluate the impact of ALK and pan-TRK expression on tumour biology and prognosis in patients diagnosed with neuroblastoma (NB), ganglioneuroblastoma (GNB), and ganglioneuroma (GN).
Methods: A total of 39 cases (24 NB, 6 GNB, and 9 GN) diagnosed between 2016 and 2024 at Ümraniye Training and Research Hospital Pathology Department were retrospectively reviewed. ALK and pan-TRK expression was assessed via immunohistochemistry and correlated with clinical parameters such as age, tumour type, stage, and treatment outcomes. Statistical analyses included Pearson correlation, Mann-Whitney U, Kruskal-Wallis H, and Kaplan-Meier survival tests.
Results: ALK positivity was significantly more frequent in NB cases ($p=0.004$), with higher staining intensity observed in poorly differentiated subtypes ($p<0.001$). ALK expression increased with higher risk categories ($p=0.019$, $p=0.007$) and decreased with age ($p=0.034$, $p=0.050$). Among patients with 11q23 mutations, 80% showed strong and diffuse ALK positivity. Pan-TRK expression decreased significantly post-treatment ($p=0.048$) and was more prominent in favourable histology ($p=0.01$, $p=0.042$). Surviving patients exhibited higher pan-TRK levels ($p=0.028$, $p=0.006$), and expression correlated positively with survival duration ($p=0.027$, $p=0.015$). Pan-TRK intensity decreased with advancing stage and risk level ($p=0.045$, $p=0.025$). In 75% of MYCN-positive and 80% of 11q23-positive cases, pan-TRK expression exceeded 50% with moderate to strong intensity.
Conclusion: ALK expression is associated with poor prognosis in neuroblastic tumours and appears unaffected by chemotherapy, supporting the potential benefit of ALK inhibitors in NB treatment. In contrast, pan-TRK expression correlates with better outcomes and may be enhanced by chemotherapy, suggesting a synergistic role for NTRK-targeted therapies. These findings may guide personalized therapeutic strategies in neuroblastic tumours.

PS-12-010

Clinicopathological correlations in placentas of pregnancy after Assisted Reproductive Technology

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Background & Objectives: The American Centre for Disease Control defines Assisted Reproductive Technologies (ART) as any fertility-related treatments in which eggs or embryos are manipulated. These techniques play an important role in the treatment of infertile couples. Infertility is outlined by the World Health Organization as a disease of the male or female reproductive system characterized by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse.
Methods: We analysed the clinical data and data referable to placental histopathology of 34 patients treated with ART in comparison with a cohort of 18 patients with a spontaneous pregnancy. The case group was further divided into two group depending on the type of ART: homologous (14) or heterologous (20).
Results: In relation to SGA babies, a different incidence was observed, as this occurrence was more frequent in the group of ART pregnancy (+6%).
The mean age showed a statistically significant difference in the group of patients treated with heterologous ART compared to patients treated with homologous PMA (p-value=0.007).
As well, the gestational age at birth was lower in patients treated with heterologous techniques compared to patients treated with homologous techniques (p-value= 0.006).
Finally, the incidence of placental hypoplasia presented a statistically significant difference, being higher in the group of heterologous ART pregnancies compared to the group of homologous ART pregnancies (p-value = 0.03).
Conclusion: In this retrospective study, our results are consistent with the literature: the gestational age at delivery is lower in ART pregnancies than in spontaneous. This data was also associated with a higher rate of admission to neonatal intensive care unit due to preterm birth. Histologically, in placentas derived from ART pregnancies we observed a higher incidence of lesions attributable to maternal vascular malperfusion, inflammation, anomalous villous development and fibrinoid material deposits.

PS-12-011

Silent witness: placental abnormalities in SARS-CoV-2 infection and autoimmune disease contributing to adverse pregnancy outcome

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Background & Objectives: Pregnancies of patients with autoimmune diseases and SARS-CoV-2 infections are frequently subjected to complications that negatively impact maternal and foetal outcome. Current evidence shows that immunological processes affecting placental development and function might contribute to pathologies in both maternal autoimmune disorders and SARS-CoV-2 infection. Our study investigated placental histological abnormalities in patients with autoimmune disorders and SARS-CoV2 infection.
Methods: 142 patients treated at the Department of Obstetrics and Gynaecology of the Medical University of Vienna were included in our study. Our cohort comprised 55 patients with autoimmune disease and 24 patients with SARS-CoV-2 infection during pregnancy. 63 patients were included as healthy controls. Placentas of all patients were examined histologically according to the Amsterdam classification of placental pathologies. Statistical association between underlying disease and histological anomalies was investigated using univariable multinomial logistic regression, separately for each fixed factor.
Results: Placentas of patients with autoimmune disease and SARS-CoV2 infection both showed increased intervillous fibrin depositions and signs of maternal and foetal vascular malperfusion. However, incidence of these changes did not show significant association with autoimmune diseases. In contrast, signs of maternal (33.3% vs. 3.3%, $p<0.0001$) as wells as foetal (95.8% vs. 58.1%, $p<0.0001$) vascular malperfusion were significantly more often identified in SARS-CoV-2 infection compared to controls. In particular, presence of segmental avascular villi demonstrated a significantly increased incidence (83.3% vs 53.2%; $p=0.014$). SARS-CoV2 infection was also associated with

a significant increase in chorangiosis (33.3% vs. 14.3%; p=0.033) and intervillous fibrin depositions (45.8% vs 9.7%; p=0.001).
Conclusion: Our study points to the involvement of common biological pathways in maternal autoimmune disease and SARS-CoV-2 infection that contribute to placental pathologies. The incidence of changes appear higher in SARS-CoV2 infection when compared to autoimmune disease. Further studies that identify these pathways to develop effective preventive strategies for maternal and foetal morbidities are warranted.

PS-12-012
Pathological changes in the heart in toxic damage in foetuses of 18-22 weeks of gestation according to autopsy data
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Background & Objectives: Pathomorphological changes in the neuronal structures of the heart in foetal alcohol syndrome (FAS) are extremely poorly described in the scientific literature. We analysed the dynamics of macro- and pathomorphological indices in the heart in toxic damage in foetuses of 18-22 weeks of gestation, born to mothers who abused alcohol during pregnancy.
Methods: Retrospective analysis of 10 FAS cases and 10 controls included cardiac macrometry (weight, chamber dimensions, ventricular index), histochemical staining (haematoxylin-eosin, van Gieson, Bielschowsky-Gross, Lee), and immunohistochemistry (NSE, S-100, synaptophysin). Statistical/correlation analyses assessed gestational age-dependent trends.
Results: The main lethal factors in the study group compared to the examined group were malformations, intrauterine infection and foetal hypoxia. Intrauterine growth retardation of the foetus was observed in 60% of cases. Cardiac macrometry was hemodynamically significant and directly depended on the gestational age of the foetus and the underlying cause of death. In all cases, an increase in the weight of the heart was noted, mainly due to the right chambers of the heart, myogenic dilation of its cavities. FAS was accompanied by signs of endocardial fibrosis, perivascular sclerosis, focal necrosis in contractile and vacuolar degeneration in conductive cardiomyocytes, fuchsinophilic degeneration in the muscle bundles of the interventricular septum; in the epicardium, rhythmogenic zones and myocardium along the vessels, extremely scanty positive staining of S-100 and NSE of neuroblasts and neurocytes in the nerve ganglia of the study group (80%) was noted; weakly expressed synaptophysin expression correlated with signs of sclerosis and hypoganglionosis in the intracardiac nerve ganglia.
Conclusion: The dynamics of macrometric indices and pathomorphological changes in the autonomic ganglia, contractile and conductive cardiomyocytes in miscarriages with FAS have a direct dependence on the gestational age ($r > 0.65$). The noted macrometric indices force us to reconsider the existing standards for examining the heart in foetuses born to mothers who abuse alcohol.

PS-12-013
Bone marrow evaluation in neuroblastomas: bone marrow aspirates have little additional value over trephine biopsies
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Background & Objectives: Bone marrow involvement is essential for staging, evaluating treatment response, and detecting progression or relapse in neuroblastoma patients. Currently, bilateral trephine biopsies (TBs) and bilateral bone marrow aspirates (BMAs) are used for this evaluation. Recent addition of immunohistochemical stains has improved the diagnostic accuracy of TBs. Furthermore, no study has investigated clinical implications of relying solely on TBs for morphological examination of bone marrow. Therefore we aim to evaluate the diagnostic accuracy of TBs and the additional value of BMAs cytomorphology.
Methods: Data were collected from all patients diagnosed at our centre over a period of 7 years. Complete bone marrow evaluation (combined bilateral TBs and BMAs) was performed at diagnosis and at predefined time points according to the treatment protocol. Cohen's kappa was used to compare test results. Representativeness was assessed for each TB and BMA and presence or absence of tumour infiltration was reported.
Results: A total of 197 neuroblastoma patients underwent bone marrow evaluation, which yielded 1,880 biopsies (947 procedures) and 1,856 aspirates (934 procedures). Bilateral TBs were technically adequate for histological evaluation in 94.9%, bilateral BMAs in 76.8% and complete bone marrow evaluation was achieved in 98.4%. Bone marrow infiltration was reported in 40.1% of all patients. TBs reported infiltration in 35.5% and BMAs in 19.7%. There was an almost perfect agreement when comparing TBs with complete evaluation ($\kappa = 0.901$, $p<0.001$).
Conclusion: TBs showed higher sensitivity and are more frequently representative than cytomorphology of BMAs. In 4.6% of procedures, the biopsy was negative while the aspirate was positive. In none of these patients the treatment strategy was altered based on positive aspirate only. These findings suggest that bilateral TBs alone may be sufficient to detect bone marrow involvement.

PS-12-014
Automated segmentation of placental structures using AI: a quantitative morphological analysis
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Background & Objectives: The placenta is essential for foetal development, facilitating nutrient exchange, oxygen supply, and immune protection. Traditional pathological assessments are manual, time-consuming, and subjective. This study developed an AI-based segmentation system for automated identification of placental structures (villi, blood vessels, nuclei, and stromal cells) to improve diagnostic accuracy and enable quantitative, reproducible assessments.
Methods: Histological samples from FFPE placental blocks were scanned, and a CNN model was trained using manually segmented structures and IHC staining to mark trophoblasts. Model performance was evaluated using intersection over union (IoU), and overlap ratios. The model was then evaluated in a number of clinical scenarios including detection of avascular villi, chorangiomatosis and Delayed Villous Maturation (DVM).
Results: The segmentation accuracy was evaluated using a classification system where **1:1** represents a perfect overlap between the AI-predicted and manually annotated regions, **1:2** or **2:1** indicates partial agreement with under-segmentation or over-segmentation, and **1:0** denotes false positives. Villi segmentation achieved an IoU of 0.88 ± 0.12 (IoU), with 60.18% perfect overlap (1:1) and 22.55% partial agreement (1:2, 2:1). Vessel segmentation accuracy had IoU of 0.30 ± 0.05 (IoU), with 58.11% perfect overlap (1:1) and 38.13% false positives (1:0). The algorithm was able to identify avascular villi and patches with villi showing chorangiomatosis. Analysis of placentas with DVM

showed reduced vascular area at the periphery of the villi (0.045 ± 0.021) compared to normal controls (0.061 ± 0.026, p<0.001).
Conclusion: The AI-based segmentation model showed high accuracy in placental morphology analysis, demonstrating its potential as a tool for quantitative placental evaluation. Future research will refine segmentation boundaries to enhance accuracy.

PS-12-015
TRIM28 immunohistochemistry in an Indian institutional cohort of Wilms tumours
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Background & Objectives: *TRIM28* gene on 19q13.4 is a transcriptional co-repressor that plays a role in nephrogenesis. *TRIM28* germline loss-of-function mutations predispose to familial and non-familial Wilms tumour (WT). These *TRIM28*-mutated WTs are typically described in infantile, stage I, low-risk, favourable histology WTs with excellent outcomes. Loss of immunoexpression of TRIM28/KAP1 protein is a reliable method for identifying *TRIM28*-mutant WT, with complete concordance with molecular analysis.
Methods: WT cases of all histological subtypes diagnosed between 2019 and 2024 were retrieved. HE-stained slides were reviewed. TRIM28 immunohistochemistry was performed on whole tissue sections.
Results: Ten of 92 WTs (11%) showed TRIM28 loss. Age range was 0.5 to 11 years; sex ratio was 1.5. Six cases (60%) showed epithelial predominance, with epithelial component in more than 80%. Two cases (20%) showed diffuse anaplasia; one had predominance of epithelium (70%) and the other had 28% epithelial component. The remaining two cases were regressive and blastemal types, with epithelial component in 35% and 15%, respectively. One of the epithelial predominant tumours showed multiple variably sized cysts lined by flat epithelial cells and had been reported as "Wilms tumour with lymphangioma-like areas". Similar cysts and tubules lined by flattened cells were seen focally in six other cases. TRIM28 loss WTs spanned stages I to III.
Conclusion: Unlike most previous reports that have focussed on epithelial WT, we have assessed the entire histological spectrum of WT to identify *TRIM28*-deficient tumours. *TRIM28* loss is seen in 11% of WT in Indian patients, and occurs across stage I to III. While epithelial WT seems to be the predominant subtype among *TRIM28*-mutated tumours, blastemal WT or anaplasia does not exclude the possibility of *TRIM28* mutation. Lastly, *TRIM28*-mutant tumours dominated by thin-walled cysts lined by flattened cells are likely to be misdiagnosed as other less malevolent neoplasms, which may lead to undertreatment.

Funding: AIIMS intramural grant

PS-13 Poster Session Pathology in Favour of Developing Countries

PS-13-001
Prognostic significance of Ki-67 in diffuse large B-cell lymphoma: a retrospective analysis in a developing country
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Background & Objectives: Diffuse Large B-Cell Lymphoma (DLBCL) is the most common subtype of non-Hodgkin's lymphoma (NHL), accounting for approximately 30% of cases worldwide. Research has shown that Ki-67, a proliferation marker, plays a crucial role in prognosis, with high Ki-67 expression associated with poorer outcomes and lower levels linked to better therapeutic responses. This study aims to evaluate Ki-67 as a prognostic indicator and analyse survival outcomes in NHL, with a specific focus on DLBCL patients in Albania, representing the first study of its kind in this population.
Methods: This retrospective study analysed malignant lymphomas, particularly DLBCL, from 2010 to 2017 at two major diagnostic and treatment centres. A total of 88 DLBCL cases, diagnosed through H&E morphology and IHC per WHO classification. Patient data included age, sex, region, and Ki-67 index, categorized as low (<65%) or high (>65%). Standard follow-up lasted approximately five years. Overall survival (OS) was measured from diagnosis to death or last follow-up.
Results: This study analysed 88 DLBCL cases.
Key Findings:• Ki-67 & Survival: High Ki-67 (>65%) was found in 67% of cases and was significantly correlated with older age and male sex ($P < 0.005$).
• OS & Follow-up: High Ki-67 cases had poor survival (3–4 years), while low Ki-67 cases had better outcomes (5–10 years+). Long-term OS analysis was challenging due to early deaths, treatment migration, and non-lymphoma-related mortality.
Conclusion: In the study 67 % of the patients that demonstrated a high value of Ki-67 presented a worse prognosis and survival than those with a low value.
Some of the correlations in a study were significant between Ki-67 and age and gender showing that age is an important predictive factor and the male were most affected from DLBCL.These findings highlight Ki-67 as a crucial prognostic marker in DLBCL, warranting further study with extended follow-up.

PS-13-002
Enhancing diagnostic capacity in Jordan through AI and telepathology: insights from EU collaborations and the Hakeem initiative
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Background & Objectives: Pathology services in developing countries face challenges such as limited subspecialty expertise, high workloads, and disparities in access to diagnostic services. In Jordan, these obstacles are compounded by geographic and resource constraints. However, the national Hakeem Program, Jordan's first electronic health record (EHR) initiative, provides a robust digital infrastructure that can support the integration of artificial intelligence (AI) and telepathology services. Recent EU-Jordan collaborations, including the REAYAH Project and the Strategic and Comprehensive Partnership (2025), have further enhanced digital health capacity and provide a framework for implementing innovative pathology solutions. This project explores how existing EU-funded programs and the Hakeem digital health system can be leveraged to integrate AI-powered diagnostics, telepathology, and capacity building for pathology services in Jordan.
Methods: We reviewed the Hakeem Program's nationwide EHR network and its potential to support telepathology workflows and AI-based diagnostic tools. Additionally, we analysed recent EU-Jordan healthcare collaborations, focusing on infrastructure improvements (REAYAH Project) and capacity-building initiatives (Erasmus+ medical training programs.
Results: The Hakeem Program's digital infrastructure, combined with EU-supported health facility upgrades and staff training, creates an opportunity to expand telepathology services and introduce AI algorithms for diagnostic support. Integrating these technologies could enhance diagnostic accuracy, reduce turnaround times, and improve access to expert pathology consultation, particularly in underserved areas. Capacity-building programs further ensure sustainable adoption through workforce development.

Conclusion: By leveraging the Hakeem Program and EU-Jordan collaborations, Jordan has a unique opportunity to advance digital pathology. Implementing AI and telepathology solutions can address diagnostic gaps, improve patient outcomes, and position Jordan as a leader in digital healthcare transformation within the region.

PS-13-003

Histopathological characteristics and prognostic outcomes of paediatric Hodgkin lymphoma in Albania: a 5-year cohort study

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Background & Objectives: Hodgkin lymphoma (HL) accounts for less than 1% of all cancers but 5–6% of childhood malignancies. This study evaluates the impact of early diagnosis, HL subtypes, and prognostic factors (age, BMI, disease stage, OS) in Albanian paediatric patients (2012–2017). It also highlights the role of an inter professional team in optimizing follow-up and treatment outcomes.
Methods: This retrospective cohort study analysed 37 paediatric Hodgkin lymphoma (HL) cases in Albania (2012–2017). IHC on lymph node biopsies (CD15, CD30, CD3, CD20, CD45, CD79a, PAX5, EBV LMP-1) confirmed diagnoses, classified per WHO criteria. Clinical data (symptoms, age, BMI, stage) were reviewed. OS was assessed over 5 years using Kaplan–Meier survival analysis and chi-square tests, alongside a literature review on paediatric HL.
Results: We identified 36 cases of primary dcHL and one case of NLPHL. Cervical lymph nodes were most frequently involved (11 cases), followed by axillary and supraclavicular nodes. To assess the BMI-HL association, BMI was calculated (weight/height²) using primary care records when available. Among confirmed HL cases, only 9 children had a normal BMI, while the majority were obese. Statistical analysis showed a significant correlation ($P < 0.05$) between higher BMI and HL, consistent with findings from meta-analyses and prospective studies.
Conclusion: The retrospective ,cohort study conducted by an oncology centre in a developing country , even though with a small number confirmed cases (n=37) , tried to provide a little help not only in diagnosis but also in careful follow-up in dynamic.
HL as a systemic disorder is best managed by an multidisciplinary team for best outcomes. Regular follow-up visits are necessary to detect relapses and long-term sequelae as early as possible.

PS-13-004

Enhancing gastric lesion diagnosis: a retrospective analysis with an AI-enabled approach in Boyacá, Colombia

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Background & Objectives: In Boyacá, the diagnosis of gastric lesions heavily relies on the endoscopy and quality of biopsy preparations and adherence to standardized protocols like the Sydney protocol. Aims to understand histopathological characteristics and the prevalence of precursor lesions in midle-risk populations on historical slide archives of Tunja´s University hospital before 2000, while exploring the potential of artificial intelligence (AI) to enhance risk stratification based on image analysis platforms like QuPath and CAMYLEON.
Methods: A total of 200 gastric biopsy from 1989 and 1994 preparations were analysed. The study assessed compliance with the Sydney protocol and comparison around 1991; the prevalence of diagnoses according to OLGA (Operative Link on Gastritis Assessment) and OLGIM (metaplasia) categories, and only histopathological findings. Additionally, specific types of gastric cancer were identified, emphasizing their diversity. The study also evaluated the educational impact on medical students engaging with gastric pathology.
Results: Eighty percent of the biopsy preparations did not meet the criteria of the Sydney protocol, highlighting significant diagnostic gaps. OLGA IV and III were the most common categories, with prevalences of 33.6% and 32.7%, respectively, indicating relevant presence of advanced lesions and frequently anecdotal cases. Histopathological findings included chronic atrophic gastritis with lymphoid follicles (59.3%) and in them, colonic metaplasia (66.4%). Gastric cancer types identified were intestinal adenocarcinoma (8.8%), adenosquamous carcinoma (0.9%), and signet-ring cell carcinoma (3.5%).
Conclusion: The results emphasize the need to improve compliance with diagnostic protocols and encourage interdisciplinary research, including AI, to optimize early detection and management of precancerous lesions. Moreover, this investigation inspires medical students to deepen their understanding of gastric pathology, strengthening their educational foundation and commitment to public health. Training on diagnostic protocols and modernizing by merging evidence-based practices with AI-driven innovations creates curricula for medical students and early pathologists, enhancing detection and management of gastric lesions to advance community public health.

Funding: Universidad Pedagógica y Tecnológica de Colombia

PS-14 Poster Session Thymic and Mediastinal Pathology

PS-14-001

Thymoma in children, a rare mediastinal tumour: pathological study of 6 cases and review of the literature

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Background & Objectives: Mediastinal tumours in children are rare. Around 25% of them can be malignant. The thymoma is an uncommon neoplasm, and during adulthood it corresponds to 30% of anterior mediastinum tumours. The peak incidence is between 55-65 years.
The aim of this study was to describe clinocopathological characteristics of this entity with literature review.
Methods: Between 2004 and 2024, 6 children with thymomas were diagnosed at our department of pathology. Hospital files were reviewed for presenting complaints, clinical, radiologic, and pathological characteristics.
Results: There were 2 male and 4 female patients, aged between 12 and 19 years, with a mean of 15,5. Most common initial complaints were dyspnea, cough, chest pain, and fever. Chest x-rays and/or thoracic computed tomographies displayed masses in anterior mediastinum accompanied by pulmonary metastases ($n = 1$), and cervical lymph node metastasis ($n = 1$). Five cases underwent initial tumour resection; one case experienced trucut biopsies. On gross examination, tumours size ranged between 7 and 15 cm with mean of 9,87 cm. Histological examination identified type B1 thymomas in 4 cases, type B2 in one case and type AB thymoma in one case. Immunohistochemically, epithelial cells expressed EMA and cytokeratin, while immature T lymphocytes expressed CD1a, TdT, and CD99 markers. The outcome was satisfactory in all cases.
Conclusion: Thymoma in children are rare tumours but should be considered in the differential diagnoses for mediastinal anterior lesion. It poses a significant challenge due to its unclear histogenesis and its atypical clinical presentation. Early diagnosis and complete resection are the basis for management and prognosis.

PS-14-002

Cystic lesions of the mediastinum: the clinical spectrum and histopathological analysis

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Background & Objectives: The mediastinal cysts are rare lesions, comprising 12% to 18% of all mediastinal tumours. They form a group of heterogeneous lesions of congenital or inflammatory conditions. These cysts may cause diagnostic challenges : they can simulate both benign and malignant lesions.
The aim of our study was to assess the major characteristics of these entity.
Methods: We performed a retrospective study of mediastinal cystic lesions diagnosed at our department of pathology, from 2010 to 2024. Cystic teratomas, cystic thymomas, cystic thymic carcinomas and cystic lymphomas weren't included.
Results: This study included 107 cases. There were 66 females and 41 males. The mean age of the patients was 47.84 years, average from 3 to 84 years. The most frequent reason for consultation was respiratory symptoms including chest pain, thoracic pain, haemoptysis or dyspnea. The lesions were located in the anterior mediastinum in 20 cases, the middle mediastinum in 49 cases and the posterior mediastinum in 38 cases. All patients underwent a surgical resection. On gross examination, mean size of the masse accounted for 4.85 cm, average (1-17cm). Histologically, the pleuropericardial cysts were the most frequent and represented 41.12% of all lesions (n=44) followed by bronchogenic cysts in 33.65% (n=36), thymic cysts in 15.89% (n=17) and lymphangiomas in 3.74% (n=4). Oesophageal and hydatid cysts are rare in our series, represented respectively 1.87% and 0.93% of the cases. The final diagnosis was based on the microscopic exam. No recurrence was observed after a follow-up period of 12 months.
Conclusion: The clinicopathological features of the mediastinal cysts in our study are similar to those reported in the literature. These cysts may be located in any part of the mediastinum and may be difficult to diagnose. The treatment is based on surgical excision and the diagnosis is based on the microscopic analysis of the cystic wall.

PS-14-003

Clinicopathological analysis of cystic masses in the anterior mediastinum: A mixed bag of non-neoplastic and neoplastic aetiologies

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Background & Objectives: Cystic anterior mediastinal masses include a variety of entities with overlapping radiologic manifestations. The pure cystic masses are generally benign cysts, and many changes may occur by the degenerations. Many anterior mediastinal tumours can undergo a cystic degeneration and demonstrate a cystic mass with solid portion at computed tomography.
The aim of our study was to assess the clinical presentation and histologic subtypes of cysts in the anterior mediastinum.
Methods: All patients who underwent surgical resection of anterior mediastinal cyst mass from January 2004 to December 2024 were included in the study. Patients' personal characteristics and histopathological data were analysed.
Results: Of the 156 cases included in our study, 88 were females and 68 were males. The mean age of the patients was 43.26 years, average from 3 to 84 years. The majority of the patients were symptomatic (96.8%). The most common pathology was benign lesion, represented by pleuropericardial cysts in 32% of cases (n=50), followed by bronchogenic cysts in 25% of cases (n=39), 25 cases of thymic cysts (16%), 3 cases of hydatid cysts (7.92%) and 2 cases of oesophageal cysts (1.28%) which are rare. In contrast, malignant cystic masses often display aggressive histopathology. The most common pathology was cystic thymomas in 9.61% (n=15) followed by cystic teratomas in 8.97% of cases (n=14) contain ectodermal, mesodermal and endodermal derivatives, with malignant transformations seen in immature variants and lymphomas in 0.64% of cases (n=1).
Conclusion: Cyst mediastinal masses create significant diagnostic dilemma for the clinicians, radiologists and histopathologists. While imaging studies help in narrowing the differential diagnosis, accurate histopathological assessment is essential for prognosis and management.

PS-14-004

Next generation sequencing analysis of enteric-type adenocarcinoma of the thymus

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Background & Objectives: Enteric-type thymic adenocarcinoma (ETA) is an exceptionally rare and poorly characterized subtype of thymic carcinoma, defined by its morphological enteric differentiation and distinctive immunohistochemical features. This study presents a comprehensive clinicopathological and molecular analysis of ETA cases and incorporates a systematic review of previously published cases to expand the understanding of this rare tumour and explore potential therapeutic targets.
Methods: We comprehensively reviewed 41 previously reported ETA cases regarding their clinicopathological features, immunostaining results and genetic alteration. We performed immunostaining and targeted next generation sequencing analysis in our 2 cases.
Results: In a total of 43 patients, the mean age of ETA patients is 48.3 years, with a slight male predominance. Chest pain or discomfort was the most common presenting symptom. Elevated carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 levels were reported in more than half of the tested cases. Immunohistochemically, ETA demonstrated positivity for at least one of CK20, CDX2, or MUC2, which are characteristic of enteric differentiation. Treatment strategies varied across cases and included surgery, chemotherapy, and radiotherapy in different combinations. In 9 cases of NGS analysis (8/9) and KRAS mutational analysis (1/9), molecular profiling revealed a heterogeneous genomic landscape with recurrent mutations in TP53 (5/8), KRAS (2/9), CDKN2A (2/8), and EGFR (2/8).
Conclusion: Our findings provide insights into the clinicopathological and molecular features of ETA, understanding of this rare entity. These results highlight the need for further molecular studies to elucidate the pathogenic mechanisms of ETA and to identify opportunities for personalized therapeutic strategies.

PS-15 Poster Session Autopsy Pathology

PS-15-001

Histopathological patterns of myocarditis in Sudden Death: insights from 23 years of forensic autopsies

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Background & Objectives: Cardiac disease accounts for 80 % of sudden deaths (SD). Although myocarditis is a rare cause, it remains significant, especially among young individuals. Its diagnosis relies on histopathological examination. The aetiology of myocarditis varies, with infectious agents, particularly viruses, being the most common. Furthermore, the histological pattern often correlates with the underlying cause, which underscores the importance of comprehensive histopathological analysis in SD cases.
Methods: Forensic autopsies performed in the province of Bizkaia (Spain) between 2002 and 2024 were analysed. The study followed the European guidelines of the AECVP, including a standardized cardiac examination, histopathological analysis, and toxicological tests. Histological patterns were evaluated, and microbiological and immunohistochemical studies were carried out in selected cases.
Results: Thirty-eight cases of SD due to myocarditis were identified (18 females), with a mean age of 40 ± 20 years (range: 2 to 85 years). Among these cases, 20 were diagnosed as bearing lymphocytic myocarditis, 13 as neutrophilic myocarditis, and 4 with eosinophilic myocarditis. The aetiologies included infections, sarcoidosis, autoimmune diseases, toxins, and hypersensitivity reactions. Eosinophilic myocarditis was observed only in adults.
Conclusion: Myocarditis is an uncommon cause of SD that requires histopathological evaluation for diagnosis. It seems hence crucial to identify its specific histological pattern in order to steer the investigation toward the likely provocative agent. Therefore, forensic pathology services should include a pathologist with expertise in SD.

PS-15-002
CAR-T therapy and bispecific antibodies, ICANS and its post-mortem neuropathological correlation: a review of 7 cases
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Background & Objectives: CAR-T cell therapy has transformed the treatment of hematologic malignancies. By modifying autologous T lymphocytes to express a chimeric antigen receptor (CAR), these cells can specifically target tumour antigens like CD19 or BCMA, leading to effective tumour cell destruction. While highly effective in leukemias and lymphomas, CAR-T therapy is associated with complications such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Despite extensive clinical documentation of ICANS, few studies explore its correlation with cerebral histopathological changes.
Methods: We analysed the brains of 7 patients treated with cellular therapies. This series included 5 patients who died during treatment, 1 who died from disease progression post-treatment, and 1 with multiple myeloma treated with bispecific BCMA antibodies suspected of having ICANS. Collected between 2019 and 2025, these cases underwent detailed neuropathological examination to identify treatment-related alterations or structural changes.
Results: The patients' average age was 45 years (range: 22-63), with a male predominance (57%). Six received CAR-T targeting CD19, and one received therapy targeting BCMA. The most common diagnosis before therapy was diffuse large B-cell lymphoma (DLBCL) (5/7). All patients who received CAR-T developed ICANS, with five cases classified as grade 4 severity. All patients experienced CRS, with grade 2 being the highest severity recorded. Among the 5 patients who died during treatment, the median survival was 41 days (range: 18-80). The most common histopathological findings included cerebral oedema and gliosis. Notably, four of the five patients who died during CAR-T treatment showed interstitial, perivascular, and meningeal CD3/CD8+ lymphocyte infiltration.
Conclusion: Studies on neuropathological findings in CAR-T patients are limited. Our post-mortem analysis explored the link between ICANS and brain histopathological changes. While cerebral oedema and gliosis were common but nonspecific, notable CD8+ lymphocyte infiltration was observed. Further research is needed to understand the mechanisms of CAR-T-related neurotoxicity and improve patient management.

PS-15-003
Accuracy of a novel simplified protocol for minimally invasive tissue sampling in stillbirths
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Background & Objectives: Stillbirth rates remain unacceptably high in low- and middle-income countries (LMICs). Understanding the causes of death (CoD) is mandatory to develop effective strategies to reduce this high mortality. Minimally invasive tissue sampling (MITS) is a promising alternative to conventional autopsy (CA) but its validation in stillbirths remains limited. Existing evidence indicates that most samples of conventional MITS (c-MITS) lack diagnostic relevance in stillbirths. This study aimed to validate c-MITS against CA in stillbirths and design and assess a cost-efficient, simplified MITS (s-MITS) protocol.
Methods: The study comprised two subsets of stillbirths occurring at the Maputo Central Hospital, Mozambique. The first cohort (n=90; 2017-2018), in which both c-MITS and CA were performed, was used to validate c-MITS and to determine the diagnostic value of each sample and design a s-MITS. The second cohort (n=98; 2021-2022), which included only s-MITS, was used to evaluate CoD in the same population but during a different time period.
Results: Almost perfect overall agreement (Kappa=0.82) was observed between the c-MITS and CA-attributed CoD. Lung and placenta samples were identified as the most informative in cMITS. When using only lung and placenta results to model an s-MITS, substantial agreement (Kappa=0.79) was found between the s-MITS-derived CoD and those attributed by CA. Similar CoD distributions were observed when applying the s-MITS to a MIBio cohort, while the costs reduced by 55.7%. The leading CoDs were primarily related to maternal conditions and pregnancy complications (70.0–72.4%) and infectious diseases (25.6–27.6%.
Conclusion: c-MITS is a simpler and cost-effective alternative to CA for determining CoD in stillbirths. s-MITS has a similar diagnostic accuracy to c-MITS, while significantly reducing costs, making it adequate for implementation in routine clinical practice in LMICs.

PS-15-004
Resuscitation-associated thoracic injuries observed in autopsies: analysis from a large Irish autopsy centre
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Background & Objectives: Cardiopulmonary resuscitation (CPR) is a life-saving intervention that can lead to observable thoracic injuries at autopsy. Understanding the patterns and extent of thoracic injuries caused by CPR is crucial in distinguishing them from ante-mortem trauma. The reporting of rib fractures varies between practitioners as no guidelines exist in this area. University Hospital Waterford (UHW) is a large centre providing autopsy services to the south-east region of Ireland. In 2024, UHW completed over 500 autopsy investigations.
Methods: A retrospective analysis of 148 autopsy reports from 2024 specifically stating the use of CPR in the clinical details was conducted. Data was categorised based on laterality, number of rib

fractures on either or both sides and whether an automatic CPR device was utilised. Additional factors such as the type of automatic CPR device used and whether the sternum was fractured were considered.
Results: Rib fractures were reported bilaterally in 40% cases, a further 28% were reported as "anterior rib fractures'" with no laterality. No rib fractures were observed in 25% cases. Only 2% cases reported unilateral rib fractures. The most commonly observed pattern of rib fractures were the 3^{rd}-6^{th} ribs on the right side and the 2^{nd}-6^{th} on the left side. An automatic CPR device was utilised in 36% cases and of those cases, 46% involved the use of a LUCAS machine. Sternal fractures were observed in 25% cases. Of the cases where sternal fracture was recorded, 39% involved the use of a LUCAS machine. Three cases recorded a sternal fracture only. A LUCAS machine was used in all three of those cases.
Conclusion: Understanding and accurately reporting injury patterns in autopsies is crucial to gold standard death investigation. This is particularly important where autopsy training is being undertaken. This study details the variation in rib fracture reporting practices in a large autopsy centre.

PS-15-005
Clinical and morphological analysis of the interrelationships of acute pancreatitis and acute myocardial infarction in patients in the postoperative period
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Background & Objectives: The study highlights the need to integrate surgical and cardiological approaches to reduce mortality in postoperative patients. The logistic model of moderate accuracy allows patients to be singled out for aggressive cardioprotection.
Methods: A retrospective analysis of patients (192 patients, 108 men, 84 women) with acute pancreatitis (ICD-10:K85) who underwent abdominal surgery was performed. The main focus is on adverse outcomes (61 deaths), including acute myocardial infarction (11 patients). Clinical, autopsy, and histological data were evaluated.
Results: Acute myocardial infarction in patients occurred on average 3.2 ± 2.1 days after surgery. The key predictors of acute myocardial infarction after laparotomy in acute pancreatitis are: age over 47 years, presence of cardiovascular diseases and type 2 diabetes mellitus, increased white blood cell count ($>14.5\times109$/l), hypocalcemia, dynamic decrease in APTT, increased fibrinogen (up to 4 g/l) and increased amylase (>115 Units/l). The temporary marker of the onset of acute myocardial infarction is the level of troponin I and ECG changes, which is confirmed histologically. Women have a slightly higher risk of death from acute myocardial infarction, while overall postoperative mortality is higher in men, especially in the older age group. The logistic model (AUC=0.75, F1=0.75) confirmed the predictive value of these parameters.
Conclusion: The study highlights the need to integrate surgical and cardiological approaches to reduce mortality in postoperative patients. The logistic model of moderate accuracy allows patients to be singled out for aggressive cardioprotection.

PS-15-006
A compilation of 101 medical autopsy cases – a way to learn pathology and medicine
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Background & Objectives: Medical Autopsy is the strongest teaching tool in medicine and has no substitute. It is the most scientific method to learn pathology and medicine, by correlating the clinical details and pathology of a patient via the 'Clinico- Pathologic Conferences'. Unfortunately, the practice of medical autopsy has declined worldwide. Dept of Histopathology, PGIMER, still performs 500 – 600 medical autopsies per year which include adults, children, infants, neonates, still births and previable foetuses. Three clinicopathological conferences are held every week in PGIMER, attended by the entire medical fraternity. These conferences are also relayed 'LIVE' by our 'Telemedicine Department' world wide and are a **'Pride of PGIMER'**. Apart from this, neonatal and still birth mortality rounds are conducted where the obstetricians, neonatologists and the pathologists meet once a month and discuss all the autopsied cases.
Methods: All medical autopsy cases (adult and paediatric) over the last 30 years on whom clinicopathological conferences were conducted or were discussed in the paediatric rounds, formed a part of this compilation.
Results: Each autopsy case was a complete journey of the deceased and has been concisely discussed under the following headings – title, highlights of the case, clinical details, investigations, clinical diagnosis, complete histopathological/ autopsy findings with a gallery of gross and microscopic photographs, final autopsy diagnosis, review of literature and take home message. The cases have been grouped in the following order- Hematologic disorders, malignancies, infections, hepatobiliary/pancreatic disorders, cardiovascular disorders, systemic vasculitides, primary renal mucormycosis, histiocytosis, primary immunodeficiencies, infantile Nephrotic Syndromes, congenital heart disease, storage disorder, paediatric renal cystic disease etc .
Conclusion: Each compiled case is an infinite 'Wealth of Knowledge' proving the point that 'Medical autopsy is the strongest teaching tool in medicine'. This is the first such compilation of 767 pages of medical autopsy cases in the world.

PS-16 Poster Session Cardiovascular Pathology

PS-16-001
Benign cardiac neoplasia: study of local trends in rare cardiovascular pathology
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Background & Objectives: Benign cardiac neoplasm (BCN) is a relatively uncommon cardiac pathology with a significant impact on cardiac mechano-electrophysiological activity and a highly invasive therapeutic approach. Its benign biological nature is confirmed by specific histomorphological features. Study objective is to identify specific local morphological trends of BCNs.
Methods: Histological type, size, anatomical localization of BCN, patient's age, and sex in 43 selected BCNs cases of surgical material processed and analysed by light microscopy in local pathology laboratory from 2001 through 2021. Descriptive statistics (frequency, mean (standard deviation)), $\chi 2$, and Kruskal-Wallis tests were applied ($p<0.05$). Local bioethical committee approval no. BEC-MF-164.
Results: 53% (n=43) males and 47% (n=20) females (p=0.418) were confirmed with BCNs (mean age - 56.8 (18.51) years old). Myxoma was confirmed in 65.1% (n=28), with less common cases of papillary fibroelastoma (23.3%, n=10). The least common cases of BCN were diagnosed as fibroma (4.7%, n=2), haemangioma, rhabdomyoma, and teratoma (2.3%, n=1 per each type of neoplasm). No significant sex predominance was detected among different BCN histological

types (p=0.221). Myxoma was predominantly located in left cardiac atrium (48.8%, n=21), while papillary fibroelastoma was mostly detected in aortic / mitral cardiac valve (13.9%, n=6; p=0.01). The largest neoplasms identified were teratoma, rhabdomyoma (4 cm), and myxoma (3.62 cm, p=0.07).
Conclusion: Considering rarity of this cardiovascular pathology, accurate characterization of BCNs in local population is presented in the context of histological type, size, anatomical localization. Predominating trends of BCNs histological type, anatomical site, size, and patient's sociodemographic features that align with global epidemiological data are detected. This may contribute to optimization of local population-focused diagnostic criteria and local population-targeted treatment strategies.

PS-16-002
Early remodelling of cardiomyocytes: searching for morphological and immunohistochemical markers of pre-symptomic ischemic heart failure
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Background & Objectives: Early protein expression and corresponding shape changes within cardiomyocytes exposed to ischemia can eventually exhaust their potential during remodelling, leading to HF. Study objective is to determine morphometric and immunohistochemical criteria for early cardiomyocyte remodelling and pre-symptomatic ischemic HF.
Methods: 84 male patients of study were classified as risk HF (n=25), pre-HF (n=23), and symptomatic/advanced HF (n=34) groups according to ACC / AHA classification. Men who died suddenly with no prior cardiovascular diseases were a control group (n=25). Left cardiac ventricular myocardium of selected cases stained by Heidenhain's azan trichrome were analysed by light microscopy, calculating cardiomyocytes' volume. Immunohistochemical reactions with antibodies against desmin, osteopontin, gremlin 1, and iRNA heterogenous nucleic ribonucleoprotein C were performed and evaluated in cardiomyocytes. Statistical analysis was applied (p<0.05). Local bioethical committee approval no. BE-2-77.
Results: Volume of cardiomyocytes was already increasing in a risk HF group compared to the control group (p<0.001). This parameter continued to increase in pre-HF group, comparing to the risk HF (p<0.001) and control groups. Volume of cardiomyocytes was the greatest in the symptomatic / advanced HF group, compared to the pre-HF (p<0.001), risk HF (p<0.001), and the control groups (p<0.001). Strong correlation was detected between the volume of cardiomyocyte and intensity of immunohistochemical reaction against desmin (r_S=0.681; p<0.001), osteopontin (r_P=0.524; p<0.001), and gremlin 1 (r_P=0.701; p<0.001). Correlation between cardiomyocytes' volume and iRNA heterogenous nucleic ribonucleoprotein C was weak (r_S=0.248; p<0.05).
Conclusion: Volume of cardiomyocytes already increases in the early remodelling during at risk HF of ischemic origin and continues to increase significantly in pre-HF of ischemic origin compared to control group. Changes of cardiomyocytic geometry correlate significantly with protein expression changes within cardiomyocytes. Therefore, morphometric and immunohistochemical data reflecting the earliest cardiomyocytic geometry and protein expression shifts during remodelling can contribute to ancillary diagnostics detecting early pathological remodelling before symptomatic ischemic HF.

PS-16-003
Morphometric assessment of myocardial vascular network depending on age
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Background & Objectives: Aging is one of the influential factors of cardiac wall remodelling both regarding their structural and functional components. The authors compared the variations of myocardial interstitial capillary network density-VD between the different cardiac wall regions during patients´ ageing.
Methods: Five epicardium-to-endocardium cross sections (left ventricle walls-LVWs: anterior-LV_AW, lateral-LV_LW and posterior-LV_PW, interventricular septum-IVS and right ventricle wall-RVW) were taken during autopsy from 95 patients with different ages (0-24 years-AP_01, 25-44 years-AP_02, 45-64 years-AP_03 and >64 years-AP_04) died and autopsied in the hospital. Tissue samples were processed and immunomarked with CD34 antibody. Slides were digitized. The VD was measured with an "in-house" designed software. Average values-AV were compared using Pearson's test.
Results: The VD increases slowly since youth to elderly in LV_Ws and decreases with age in the IVS and RVW. It has the lowest values in LV_Ws till AP_03 and in RVW in elderly. The highest values are in RVW till 44 years and then in IVS.
VD has higher values in women than in men along the cardiac wall`s regions and a divergent behaviour in the two sexes with age. Thus, in men, VD has an increasing trend with age from LV_AW to RVW (Correlation Matrix-CM positive, "p"value>0.05) whereas in women, the trend is decreasing with age from LV_AW to RVW (CM negative, "p"value>0.05), excepting IVS where it increases (CM positive).
Conclusion: Myocardial interstitial capillary network density is generally higher in women than in men and is remodelling with aging in different ways both along the cardiac wall`s regions and in the two sexes.

PS-16-004
Expression of desmin in myocardium of rats with low and high stress resistance in post-traumatic period of experimental blunt cardiac injury
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Background & Objectives: High- and low-stress-resistant individuals may have different changes in the expression of the cytoskeletal protein desmin in the posttraumatic period of cardiac contusion after blunt cardiac trauma modeling.To evaluate the expression of desmin structural protein in myocardium of rats with high and low stress resistance in the dynamics of posttraumatic period of cardiac contusion.

Methods: The study was carried out on 106 white rats. The control group included subgroups with high and low stress resistance, the experimental group included subgroups with high and low stress resistance and experiment duration of 6, 12, 24 hours. The experimental group simulated cardiac injuries, extracted hearts, made histological slices, conducted immunohistochemical research with monoclonal mouse anti-Desmin antibodies (clone GM007, RTU, PrimeBioMed).
Results: Immunohistochemical study revealed a statistically significant decrease in the expression of desmin and the number of insertion discs in the myocardial damage zones of the experimental group compared with the control group, regardless of the stress resistance status. However, subgroups of low-stress-resistant animals showed lower values compared to highly resistant animals. After 6 hours posttraumatic period, the expression level of desmin in the myocardium of highly stress-resistant rats was higher than that of low stress-resistant individuals. Quantification of insertion discs in the myocardium of highly stress-resistant rats also revealed higher values compared with low-resistant individuals. Similar differences in desmin expression and number of insertion discs between high- and low-stress-resistant animals were observed 12 h and 24 h after injury.
Conclusion: In the posttraumatic period there is a gradual decrease in the expression of cytoskeletal protein desmin in the areas of myocardial damage. Expression status is differ in animals with high and low stress resistance. The level of reduction in low-stress-resistant animals is more pronounced compared with highly resistant ones and reflects more significant structural damage of cardiomyocytes in the posttraumatic period of cardiac contusion.

PS-16-005
METTL3/METTL14 RNA methyltransferase complex drives NLRP3 inflammasome priming in atherosclerotic apolipoprotein E knockout mice
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Background & Objectives: Dysregulated epitranscriptomic mechanisms have emerged as important triggers of key pathological processes associated with different forms of cancer. Hitherto, the potential implication of epitranscriptomic-related pathways in atherosclerosis remains incompletely understood. METTL3/METTL14 RNA methyltransferase complex controls RNA metabolism and function by regulating the status of m6A RNA methylation. NLRP3 inflammasome priming and activation leading to enhanced production of IL1β and IL18 cytokines are important pro-inflammatory processes underlying atherosclerotic plaque development. We aimed to determine whether a functional connection exists among dysregulated METTL3/METTL14 and NLRP3 inflammasome priming in atherosclerosis.
Methods: Human carotid artery-derived non-atherosclerotic and atherosclerotic tissue specimens, apolipoprotein E-deficient (ApoE-/-) mice, and human macrophages (Mac) were examined by real-time PCR, western blot, and immunofluorescence microscopy. The METTL3 catalytic inhibitor STM2457 (5 mg/kg), or its vehicle, were administered to ApoE-/- mice fed a normal or a high-fat, cholesterol-rich diet, for 4 weeks. Mac were subjected to in vitro polarization and activation procedures toward a pro-inflammatory (M1) or an anti-inflammatory (M2) phenotype, and further exposed to STM2457/vehicle for 24 hours.
Results: We determined significant increases in METTL3 and METTL14 gene and protein expression levels in human atherosclerotic tissue specimens, aorta of atherosclerotic mice, and pro-inflammatory Mac. Long-term treatment of atherosclerotic ApoE-/- mice with the STM2457 pharmacological inhibitor significantly decreased the aortic mRNA and protein levels of NLRP3, caspase-1, IL1β, and IL18. Blockade of METTL3 catalytic activity prevented the up-regulation of NLRP3, caspase-1, IL1β, and IL18 transcript levels in cultured M1-Mac.
Conclusion: We present evidence supporting the functional implication of METTL3/METTL14 RNA methyltransferase complex in mediating NLRP3 inflammasome priming in experimental atherosclerosis. METTL3/MTTL14-oriented pharmacological interventions may be considered as potential supportive therapeutic modality to mitigate inflammation in atherosclerosis-associated cardiovascular disorders.

Funding: Work supported by Romanian Ministry of Research, Innovation and Digitization, UEFISCDI (PN-III-P4-ID-PCE-2020-1898) and Romania's National Recovery and Resilience Plan, PNRR-III-C9-2022-I8, CF148/15.11.2022, 760061/23.05.2023

PS-16-006
MLL1 histone methyltransferase mediates the up-regulation of NADPH oxidase expression in atherosclerotic mice
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Background & Objectives: Changes in specific epigenetic mechanisms have a significant impact on atherosclerotic disease development and clinical outcome. Mixed lineage leukaemia 1 (MLL1) histone methyltransferase is an important epigenetic regulator of gene transcription. MLL1 is functionally related to active gene expression via increased abundance of H3K4me3 across regulatory regions of the target genes. Excess formation of reactive oxygen species (ROS), potentially generated by up-regulated NADPH oxidases (Nox) is a hallmark of atherosclerosis. We hypothesized that MLL1 may contribute of Nox up-regulation in atherosclerosis.
Methods: Carotid endarterectomy-derived non-atherosclerotic and atherosclerotic human tissue samples, apolipoprotein E knockout (ApoE-/-) mice, and cultured human macrophages (Mac) were investigated using real-time PCR, western blot and immunofluorescence microscopy techniques. Male ApoE-/- mice fed a standard rodent chow or an atherogenic diet were randomized to receive 5 mg/kg MI-503, a specific MLL1 pharmacological inhibitor, or vehicle, for 4 weeks. In vitro, resting and activated pro-inflammatory (M1)/anti-inflammatory (M2) Mac were subjected to MI-503 intervention.
Results: MLL1 gene expression and H3K4me3 were found significantly elevated in human atherosclerotic specimens, atherosclerotic aorta of ApoE-/- mice, and in M1-Mac. MLL1 protein was detected in endothelial cells, vascular smooth muscle cells, and infiltrated immune cell within human atherosclerotic lesions. Pharmacological inhibition of MLL1 mitigated the gene and protein expression of Nox1, Nox2, and Nox4 subtypes, and attenuated the formation of 4-hydroxynonenal-protein adducts in the atherosclerotic aorta of mice. MI-503-induced inhibition of MLL1 function reduced Nox1, Nox2, Nox4, Nox5 and p22phox transcript levels in cultured M1-Mac.
Conclusion: Here, we report that MLL1 plays a role in mediating the up-regulation of Nox expression, an important mechanism leading to ROS overproduction in experimental atherosclerosis. Pharmacological inhibition of MLL1 could become an additional therapeutic target to attenuate oxidant stress in atherosclerotic cardiovascular disorders.

Funding: Work supported by Romanian Ministry of Research, Innovation and Digitization, UEFISCDI (PN-III-P4-ID-PCE-2020-1898) and Romania's National Recovery and Resilience Plan, PNRR-III-C9-2022-I8, CF148/15.11.2022, 760061/23.05.2023

PS-16-007

Insights into amyloid burden and fibrosis in myocardial interstitial expansion: a study on transplanted hearts

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Background & Objectives: Cardiac amyloidosis represents an interstitial disease caused by the accumulation of transthyretin (TTR) or immunoglobulin light chain (AL) proteins in the myocardial interstitial space. The aim of this study is to quantify the extent and distribution of cardiac fibrosis and amyloid burden in explanted hearts of patients with terminal cardiac amyloidosis undergoing transplantation.
Methods: We used trichrome staining and AI-assisted Upath analysis to examine 6 whole explanted hearts (3 TTR, 3 AL) discriminating myocytes from fibrosis and amyloidosis. Virtual sampling of common biopsy site was performed in various areas of the heart, including the right and left ventricle and bilateral interventricular septum, to compare the results with cardiac MRI.
Results: The results demonstrate that amyloidosis is the major factor in myocardial extracellular space expansion (52,76%) with minimal contribution from interstitial fibrosis (3,77%). Although the presence of fibrosis was observed in all examined hearts, its quantification by endomyocardial biopsy specimens proved to be highly variable and not reflective of the total amyloid burden, therefore biopsy cannot be used as a surrogate for the quantification of amyloid in the heart. Also, inflammation is not an accompanying feature of end-stage cardiac amyloidosis and, therefore, does not contribute to expansion of the myocardial interstitium.
Conclusion: This study highlights the predominance of amyloidosis over fibrosis in contributing to interstitial space expansion in hearts with end stage disease. The potential reversibility of cardiac amyloidosis, suggested by the reduction of amyloid burden following specific treatments, offers new perspectives for the treatment, underscoring the importance of proper quantification of amyloid burden.

PS-16-008

A human stem cell–derived model of cardiac transthyretin amyloidosis reveals structural and functional pathomechanisms

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Background & Objectives: Cardiac transthyretin (TTR) amyloidosis is an underdiagnosed cause of heart failure and arrhythmias. The lack of relevant human cardiac tissue models has hindered mechanistic understanding of the disease and stalled therapeutic development due to the absence of effective preclinical screening tools. We aimed to establish a human in vitro model of cardiac amyloidosis using induced pluripotent stem cell–derived cardiomyocytes (hiPSC-CMs) and aggregated TTR, and to investigate the structural and functional changes associated with amyloid deposition.
Methods: Wild-type and mutant TTR proteins were aggregated and applied to cultured hiPSC-CMs in single-cell, two-dimensional, and physiologically relevant three-dimensional configurations. Amyloid deposition was confirmed using histological stains and immunohistochemistry. Cellular phenotypes were assessed via oxidative stress assays, cell viability tests, transmission electron microscopy (TEM), calcium and voltage imaging, and proteomic analysis by mass spectrometry.
Results: TTR aggregates deposited robustly within hiPSC-CM tissue models. Exposed cells exhibited elevated reactive oxygen species production and pronounced structural abnormalities. TEM revealed sarcomeric disarray and mitochondrial pathology—including swollen cristae and disrupted membranes—particularly in response to mutant TTR. Morphological alterations extended to both cell and population levels, including cell shrinkage and tissue scarring, resulting in impaired conduction and arrhythmogenic activity. Viability of cardiomyocytes was reduced, and functional assays demonstrated aberrant calcium handling, characterized by oscillatory and double-peaked transients. Proteomic profiling revealed consistent alterations in pathways related to stress response, metabolism, proteostasis, and immune signalling.
Conclusion: This human stem cell–derived model recapitulates key features of cardiac TTR amyloidosis, including oxidative stress, ultrastructural damage, conduction abnormalities, and calcium dysregulation. Proteomic analysis identifies potential disease mechanisms and therapeutic targets. Ongoing perturbation studies are investigating the roles of candidate proteins, paving the way for translational applications and preclinical drug screening.

PS-16-009

Unveiling the pathogenesis of hypertrophic cardiomyopathy: a 3D approach to explore vascular alterations in the natural feline model

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Background & Objectives: Hypertrophic cardiomyopathy (HCM) is a relevant cardiac disorder in humans, characterized by unexplained left ventricular hypertrophy with myocyte disarray, interstitial fibrosis and microvascular alterations, leading to impaired cardiac function. Feline hypertrophic cardiomyopathy (fHCM), with a prevalence of 15% the most common cardiomyopathy in cats, shares many pathological features with its human counterpart, offering itself as a valuable natural animal model to study the disease pathogenesis. Here, we present a novel three-dimensional (3D) approach to investigate myocardial microvascular alterations.
Methods: Forty consecutive sections (5 µm) were prepared from formalin-fixed, paraffin embedded left ventricular free wall samples collected from cats with fHCM and without cardiac disease. Sections were immunohistochemically stained for the endothelial cell marker CD31 and digitalized. Using the HeteroGenius Medical Image Manager (MIM) software, a convolutional neural network (CNN) classified structures such as vessels, cell cytoplasm, and nuclei. The data was processed using Visiopharm, QuPath and 3D Slicer softwares to quantify the classified components in two and three dimensions.
Results: In the fHCM myocardium, we observed a decrease in the number of blood vessels (mainly capillaries), yet these vessels exhibited increased volume and surface area and were more widely spaced. Myocardial nuclei were fewer, smaller in size, and had a significantly lower volume. The overall cell volume was markedly reduced, while the interstitial space was notably enlarged compared to the controls.
Conclusion: This 3D approach corroborates earlier 2D findings of reduced overall cellularity and vascular density in the fHCM myocardium. The increased vessel volume and surface area suggest compensatory mechanisms as an attempt to offset the loss of functional myocardial tissue, a feature that could also play a role in human HCM.

PS-17 Poster Session Gynaecological Pathology

PS-17-001

Prostatic metaplasia of the uterine cervix: histopathologic and immunohistochemical findings in patients with gender-affirming hysterectomies

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Background & Objectives: Prostatic metaplasia in the female genital tract is a rare phenomenon, often attributed to various aetiologies including exogenous androgen exposure. This study aimed to investigate the presence of prostatic metaplasia in uterine cervical specimens from patients undergoing hysterectomy for gender-affirming.
Methods: This retrospective study included two groups. The case group consisted of 24 patients who underwent hysterectomy for gender-affirming between 2010 and 2024. The control group comprised 17 patients who underwent hysterectomy for benign gynaecological indications between 2018 and 2020. Cervical tissue samples from both groups were evaluated morphologically, and immunohistochemically using prostatic acid phosphatase (PAP) and prostate-specific antigen (PSA) antibodies.
Results: The mean age was 32.8 years (range: 22–56) in the case group (n=24) and 35.35 years (range: 27–39) in the control group (n=17). The cervical tissue from the gender-affirming therapy group showed superficial clusters of small basophilic cells, and surface prostatic metaplasia. Combined evaluation of PAP and PSA immunostaining revealed positive expression in 8 patients (33.3%) in the case group, whereas no immunoreactivity was observed in the control group samples.
Conclusion: Immunohistochemical expression of PAP and PSA in cervical tissue was observed in a subset of patients with gender-affirming who had undergone hysterectomy, with no expression detected in the control group. These findings suggest a potential androgen-induced epithelial differentiation or metaplastic transformation within mullerian-derived tissues under long-term exogenous hormonal influence. The absence of staining in the control group supports a correlation with androgen exposure rather than incidental ectopic prostatic rests. Further investigations are warranted to determine the prevalence, pathogenesis, and diagnostic relevance of this finding.

PS-17-002

Intraoperative Pap smear, HPV testing, endocervical curettage and histological evaluation of the cone margins as predictors of persistent/recurrent disease after conization

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Background & Objectives: To evaluate the diagnostic performance of intraoperative diagnostic tests in predicting residual or recurrent disease after conization for high-grade squamous intraepithelial lesions (HSIL/CIN2–3) of the uterine cervix.
Methods: A total of 666 women (mean age 39 ± 10 years; range 22–74) with histologically confirmed HSIL treated by conization were included. Immediately after the surgical procedure, an endocervical sample was collected intraoperatively using a cytobrush and preserved in PreservCyt medium (Hologic) for cytology and HR-HPV testing (Cobas HPV, Roche). All patients also underwent endocervical curettage (ECC), and cone margins were histologically evaluated. Patients were followed for at least 12 months. The diagnostic accuracy of intraoperative tests—including cone margin status, ECC, cytology, and HPV testing—was assessed for predicting residual or recurrent disease.
Results: Residual/recurrent disease was confirmed in 60 of 666 patients (9%). Intraoperative HPV testing showed the highest sensitivity (85%) with acceptable specificity (65%), with recurrence rates of 19% and 2% among HPV-positive and HPV-negative patients, respectively ($p < 0.0001$). The sensitivity and specificity of the other tests were 60% and 90% for cytology, 55% and 72% for margin evaluation, and 37% and 95% for ECC. Adding other tests to HPV testing had minimal benefit, with the best-performing combinations being HPV plus cytology and HPV plus margin evaluation. These two combinations slightly increased sensitivity, but reduced specificity (sensitivity 88%, specificity 61% for HPV + cytology; sensitivity 88%, specificity 51% for HPV + cone margin evaluation).
Conclusion: Intraoperative HPV testing using endocervical samples collected immediately after conization shows high diagnostic accuracy for identifying patients at risk of residual or recurrent disease. The addition of other tests offers minimal additional benefit. Incorporating this approach into routine clinical practice could reduce unnecessary diagnostic procedures and follow-up visits, optimizing post-treatment surveillance.

PS-17-003

Genomic features associated with survival status in endometrial endometrioid carcinoma of no specific molecular profile

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Background & Objectives: Endometrioid endometrial cancer (EEC) is classified in The Cancer Genome Atlas (TCGA) as p53 mutant, POLE mutant, MSI-H and no specific molecular profile (NSMP). However, the latter group still represents a heterogeneous group of cases and poses a challenge in terms of treatment planning and prognosis. In our study, we aimed to further characterize the molecular features of this group by dividing them into two groups according to survival status using TCGA data.
Methods: Cases (n=200) with a diagnosis of endometrioid carcinoma and mutation profile information in the Uterine Corpus Endometrial Carcinoma (TCGA, Firehose Legacy) dataset were used. Cases with p53, POLE, MLH-1, MLH-2, MSH-2, MSH-6, PMS-2 mutations and high tumour mutation burden (>10 mutations/per megabase) were excluded. Included cases were grouped according to survival status and compared for DNA mutations, copy number variations (CNV), mRNA and protein expression, and DNA methylation. P and $q < 0.05$ were considered significant.
Results: Among the 124 patients included in the study, 111 were alive (89.5%) while 13 were deceased (10.5%). The analysis identified 361 differentially expressed genes were detected (p and $q<0.05$). In terms of protein expression, CCNB1 exhibited expression in the ex group (p=1.196e-5, q=2.571e-3). In the comparison for DNA methylation, one gene (*OASL*, p=4.039e-5, q=0.0235) was more highly methylated in the surviving group while two genes (*GPR21*, p=5.32e-7, q=9.303e-4; *ALPK3*, p=9.434e-6, q=8.245e-3) were more highly methylated in the ex group. However, no significant difference was found in terms of mutation frequency and CNV ($p>0.05$).
Conclusion: We identified various molecular alterations in EECs that had a substantial impact on the prognosis in a molecularly heterogeneous group of NSMP patients. Consequently, experimental studies on these alterations hold great promise in terms of developing predictive markers that will affect the treatment plan of patients.

PS-17-004

Molecular determinants of invasion at the tumour-microenvironment interface of low-grade serous ovarian neoplasia

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Background & Objectives: Low-grade serous ovarian carcinomas (LGSCs) account for 5% of ovarian cancers and typically present with advanced stage disease that is resistant to therapy. LGSCs are thought to develop from serous borderline tumours, which are associated with much better outcomes. The molecular differences between LGSCs and serous borderline tumours that drive treatment resistance are poorly understood. We sought to understand the tumour and microenvironmental differences between LGSC and serous borderline tumour through single cell-resolution spatial transcriptomics.
Methods: We assembled a cohort of 20 LGSCs and 20 serous borderline tumours. Tissue microarrays were constructed from areas of invasive and borderline disease. Spatial transcriptomes for over 750,000 cells were performed using the 10X Genomics Xenium platform.
Results: LGSCs and serous borderline tumours show significant differences in cell type composition, tumour cell and stromal cell phenotypes. Compared to serous borderline tumours, LGSCs showed upregulation of c-MET and TGF-beta signalling and downregulation of hormone receptor pathways. Several invasion-associated genes showed spatially variable expression patterns with upregulation at the tumour-stromal interface in LGSCs but not in serous borderline tumours.
Conclusion: Low-grade serous carcinomas show spatially distinct patterns of tumour and stromal cell gene expression from serous borderline tumours. These differences may be exploitable through molecularly targeted therapies.

Funding: Carraresi Foundation Gynaecologic Cancer Initiative Grant

PS-17-005

Expression of PAX2, Beta-catenin and PTEN in 63 cases of atypical polypoid adenomyoma: association with recurrence and development of adenocarcinoma

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Background & Objectives: Atypical polypoid adenomyoma (APA) is a rare lesion involved in the differential diagnosis of endometrioid intraepithelial neoplasia (EIN) and endometrioid adenocarcinoma. This study aims to determine whether Beta-catenin nuclear positivity and PAX2/PTEN expression loss, which aid in EIN diagnosis, predict recurrence or adenocarcinoma development in APA and to assess MMR protein status.
Methods: A total of 63 biopsies from 41 patients meeting the WHO criteria for APA were included. These biopsies were classified as preserved or lost for PAX2, PTEN, MSH6, and PMS2, and as nuclear or membranous for beta-catenin. Immunohistochemistry results were statistically analysed for correlations with recurrence and development of adenocarcinoma.
Results: The median age was 36.4 years (range: 25–63). Recurrence occurred in 14 (34.1%) of 41 patients. The mean age of recurrent cases (33±5.35) was lower than non-recurrent cases (38.39±8.71) (p=0.035). Nuclear beta-catenin positivity, PAX2, and PTEN loss were more frequent in recurrent cases (80%, 53%, 60%) but not statistically significant (p=0.112, p>0.05, p>0.05). Similarly, nuclear beta-catenin positivity, PAX2, and PTEN loss were more common in adenocarcinoma cases (55.6%, 55.6%, 66.7%) but remained insignificant (p=0.62, p>0.35, p>0.82). Only one patient had MSH6 and MSH2 loss but did not develop adenocarcinoma or recurrence.
Conclusion: Loss of PAX2 and PTEN expression in APAs does not predict recurrence and adenocarcinoma development. Moreover, PAX2 and PTEN expression was preserved in nearly half of the cases, their diagnostic utility in APA is limited compared to EIN. They should also not be used to distinguish from EIN. Additionally, it was found that, although rare, MMR loss can occur in APA. Younger age at diagnosis was significantly associated with recurrence.

PS-17-006

Unraveling the impact of BRCA1/2 mutations and DNA Mismatch Repair protein expression on clinicopathological features in ovarian carcinomas

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Background & Objectives: Ovarian cancer remains the most lethal gynaecological malignancy. This study aims to investigate the prevalence of BRCA1/2 mutations and deficient DNA mismatch repair (dMMR) status in ovarian carcinoma and to evaluate their correlation with clinicopathological parameters.
Methods: This retrospective study included 132 patients diagnosed with ovarian carcinoma at our centre who were tested for BRCA1/2 mutations using Next-Generation Sequencing and for DNA MMR protein (MLH1, MSH2, MSH6, and PMS2) expression via immunohistochemistry. Clinicopathological and histopathological parameters (including solid, pseudoendometrioid, and transitional cell carcinoma-like(SET) pattern), poly(adenosinediphosphate–ribose) polymerase(PARP) inhibitors (PARP-i) therapy, progression-free survival (PFS), event-free survival (EFS), and overall survival (OS) analysis were assessed. Somatic and germline mutation detection were compared, and the associations of BRCA1/2 mutations and dMMR status with clinical outcomes were analysed.
Results: Somatic BRCA1/2 mutations were detected in 25.7% of cases, germline mutations in 20.9%, and overall (somatic or germline) mutations in 28%. Somatic mutations were detected in 8 cases without corresponding germline mutations, whereas 3 of the 5 cases deemed non-effective by somatic testing carried germline mutations. The concordance rate between somatic and germline testing was 87.6%. BRCA1/2 mutations were associated with significantly longer OS. Among patients treated with PARP-i, 71% had no recurrence, and the mean PFS was 21 months. OS was significantly longer in the PARP-i group*(p=0.005),* whereas the difference in EFS was not statistically significant*(p=0.473)*. The SET pattern was observed in 17.4% of cases, with a statistically significant association to BRCA1/2 mutations*(p=0.010)*. dMMR was observed in 7.6% of cases, without any statistically significant impact on clinical outcomes.
Conclusion: BRCA1/2 and dMMR status are critical for treatment strategies in ovarian cancer. Somatic or germline BRCA1/2 mutations, particularly when treated with PARP-i, lead to improved survival outcomes. Additionally, recognizing the presence of the SET pattern morphologically may provide insight into BRCA1/2 mutation status, potentially guiding prognosis and treatment decisions.

PS-17-007

Sex Cord Stromal Tumours of the ovary, a 24 years clinicopathological study in Farhat Hached University Hospital of Sousse. About 50 cases

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Background & Objectives: Malignant SEX CORD STROMAL TUMORS OF THE OVARY (SCSTs) are a group of rare neoplasms. The importance of investigating these neoplasms stems from their rarity and heterogeneity and their limited data and treatment recommendations.
Purpose of the study: Characterize these rare tumours by analysing epidemiological features, clinical and paraclinical features, histological characteristics, treatment modalities, and survival rates. Identify the factors associated with the prognosis of these tumours and propose a management diagram tailored to the Tunisian context.
Methods: This was a descriptive and analytical monocentric observational study concerning female patients who were treated for SCSTs of the ovary, in the Department of Gynaecology-Obstetrics, at the Farhat Hached University Hospital from January 1999 to December 2023. The clinical, radiological and histological data were collected via patients' files and from the Centre cancer registry.
Results: A total of 50 patients were eligible for this study. The incidence of SCSTs was 0.1 per 100 000 per year. The mean age at diagnosis was 48,46 ± 19.92 years with extremes ranging from 6 to 86 years. The distribution differed by histological type. SLCTs occurring more frequently in the third decade of life while adult GCTs occurred mostly in the 6^{th} and 5^{th} decades of life. Ultrasound revealed a tumour in 97.90% of cases. Histologically, the mean tumour size was 13.20 cm. The most common histological subtype was Granulosa Cell tumours (GCTs) which account for 74% of cases and are divided into Adult Granulosa Cell tumours (AGCTs) (68%) and Juvenile Granulosa Cell tumours (JGCTs) (6%), the second ranked subtype was the Sertoli-Leydig cell tumour (SLCT) accounting for 26% of patients.
Conclusion: Malignant SCSTs, are rare tumours comprising different entities, the most common being GCTs and SLCTs. additional research is needed to establish a clear protocol for treatment especially in case of recurrence.

PS-17-008

Clinicopathological and molecular features of mesonephric-like adenocarcinoma of the ovary: a small series

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Background & Objectives: Mesonephric-like adenocarcinoma (MLA) is a rare ovarian tumour, and the correct diagnosis requires an extended immunohistochemical and molecular characterization. We evaluated the clinicopathological and molecular parameters of a small series of MLAs.
Methods: Four MLA cases were retrieved from our archives. Clinicopathological data was reviewed. H&E slides, immunohistochemistry (ER, PR, p53, PAX8, GATA3, TTF1, WT1) and Idylla TM Mutation Assay evaluation for KRAS/NRAS/BRAF were evaluated.
Results: Patients' median age was 67.5 years (53-94). Three patients had total hysterectomy with bilateral adnexectomy and omentectomy (3 pts), and unilateral adnexectomy (1 pts). All had complete cytoreduction. One patient had adjuvant chemotherapy. FIGO stage distribution was IA, IC1, IC2 and IIIB. Morphologically several patterns were identified: glandular (n=4), solid (n=2), cystic (n=2), papillary (n=1) and cords (n=1), and cells were predominantly atypical with elevated mitotic activity and pale chromatin. In three cases we detected admixture of different areas (mixed tumours), namely benign/borderline mucinous component, endometrioid carcinoma with focal transformation into carcinosarcoma and carcinosarcoma with chondroid differentiation associated with MLA. Additionally, adnexal endometriosis was found in two cases, and no mesonephric remnants were identified. The immunohistochemistry profile was: ER and PR - (n=4); p53+ve, wild-type (n=4); PAX-8+ve (n=4). GATA3+ve (n=3); TTF1+ve (n=4); WT1-ve (n=4). The molecular evaluation detected KRAS mutation[35G>A p.(Gly12Asp)] (n=3) and NRAS mutation [182A>G p.(Gln61Arg)] (n=1). The median follow up was 11 months (3,9 – 34,8). All patients are alive, two of them with clinical evidence of early disease relapse after primary treatment (stage IC1 and IIIB).
Conclusion: Our series confirms, despite the limited follow-up data, that MLAs are aggressive tumours, even in early stages of disease. The immunohistochemical profile and presence of other mullerian-derived components, in this series, support a mullerian origin of these tumours, with frequent KRAS mutations.

PS-17-009

HER2 assessment in endometrial serous carcinoma: comparative evaluation of scoring systems and diagnostic concordance in a multicentre Italian cohort

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Background & Objectives: Endometrial serous carcinoma (ESC) is a highly aggressive subtype of endometrial cancer, often diagnosed at advanced stages and associated with poor prognosis. A subset of ESCs (~15%) shows HER2 overexpression and/or *ERBB2*amplification, which may benefit from targeted anti-HER2 therapy. However, HER2 testing remains non-standardized in ESC. This study aimed to compare ASCO/CAP 2007, ASCO/CAP 2018, and an ESC-specific scoring system in terms of diagnostic concordance and clinical utility.
Methods: We retrospectively analysed 113 hysterectomy specimens diagnosed as ESC, mixed carcinoma with serous component, or carcinosarcoma, collected from two Italian institutions. HER2 immunohistochemistry (clone 4B5) was performed and scored according to all three systems. Equivocal and discordant cases underwent dual-colour dual-hapten brightfield in situ hybridization (DDISH) for *ERBB2*. Statistical analyses included kappa concordance and association with clinicopathological variables.
Results: HER2 positivity (IHC 3+ and/or *ERBB2* amplification) was detected in 17/113 cases (15%). ASCO/CAP 2018 identified the highest number of HER2-positive cases (13 scored as 3+), demonstrating greater sensitivity compared to ASCO/CAP 2007 and the ESC-specific system, which each identified 10 cases as 3+. Four cases showed scoring discordance, with ASCO/CAP 2018 correctly classifying them as HER2-positive based on ISH results. Overall concordance was excellent between ASCO/CAP 2007 and the ESC system ($\kappa = 0.98$), and moderate between ASCO/CAP 2018 and the other two ($\kappa \approx 0.71$). HER2 positivity correlated significantly with age >70 years ($p = 0.016$). HER2 intratumoral heterogeneity was present in 12% of cases.
Conclusion: ASCO/CAP 2018 guidelines demonstrated superior sensitivity in identifying HER2-positive ESCs, potentially expanding

therapeutic eligibility. However, the ESC-specific and ASCO/CAP 2007 systems remain more conservative and closely aligned with prior clinical trial data. A harmonized, ESC-adapted scoring strategy is essential to optimize HER2 testing and ensure accurate patient selection for targeted therapy.

PS-17-010

Endometriosis-associated ovarian carcinomas: histotypes and molecular profiling

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Background & Objectives: The Cancer Genome Atlas (TCGA) classifies endometrial carcinoma into four molecular subgroups: POLE (ultramutated), mismatch repair-deficient (MMRd, hypermutated), TP53-mutated (copy-number-high), and no specific molecular profile (NSMP, copy-number-low). While some studies have analysed the distribution of molecular subtypes in specific ovarian carcinoma histotypes, data on endometriosis-associated ovarian carcinomas (EAOCs) remain limited.
Methods: We examined a series of 39 consecutive ovarian carcinomas (OCs) arising in the context of endometriosis. Two pathologists independently reviewed all cases based on morphology and an immunohistochemical panel. IHC and next-generation sequencing (NGS) were used to assign surrogate molecular subtypes: POLE-mutated (POLE), mismatch repair-deficient (MMRd), TP53-mutated (p53abn), and NSMP. Clinical data, including age at diagnosis, FIGO stage, and follow-up, were collected.
Results: Our cohort included 20 (51.3%) low-grade endometrioid adenocarcinomas, 7 (18%) high-grade endometrioid adenocarcinomas, 8 (20.5%) clear cell carcinomas, and 4 (10.2%) mesonephric-like adenocarcinomas. Molecular classification identified 3 (7,7%) POLE OCs, 5 (12,8%) p53 abn, 2 (5,1%) MMRd, and 29 (74,4%) NSMP. The mean age at diagnosis was 56 years (range: 31–79). FIGO stage ranged from IA to IIIC, with the majority of cases classified as stage I (19 cases), stage II (13 cases), and stage III (7 cases). During a follow-up period ranging from 6 to 120 months, recurrence was observed in 8 cases, with 2 disease-related deaths. All recurrent cases belonged to the NSMP molecular subgroup, except for one case in the p53-mutated subgroup. Histologically, recurrent cases included 3 clear cell carcinomas, 2 mesonephric-like adenocarcinomas, 1 high-grade endometrioid adenocarcinoma, and 2 low-grade endometrioid adenocarcinomas with advanced-stage disease at diagnosis.
Conclusion: Endometriosis-associated OCs exhibit a higher prevalence of the NSMP molecular subtype compared to their endometrial counterparts, with low-grade endometrioid adenocarcinoma being the most represented histotype. Among NSMP tumours, FIGO stage at diagnosis and histotype remain the most reliable parameters for prognostic stratification.

PS-17-011

PD-L1 expression in high-grade serous ovarian carcinoma is associated to specific types of lymphocytic infiltrate and tumour segments

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Background & Objectives: Research on ovarian cancer predominantly focuses on high-grade serous ovarian cancer (HGSOC). Patients with this aggressive form of ovarian cancer often exhibit resistance to therapy and have a generally poor prognosis. HGSOC suppresses the host's immune response by activating checkpoint mechanisms, such as programmed death protein 1 (PD-1) and its ligand, programmed death-ligand 1 (PD-L1). This interaction renders tumour cells resistant to effector lymphocytes. The infiltration of lymphocytes plays a crucial role in regulating PD-L1 expression.
Methods: This study involved 91 patients with HGSOC. Immunohistochemical analysis was conducted using the tissue microarray (TMA) technique, with correlations made between carcinoma segments and the localization of lymphocytic infiltrates. PD-L1 expression was scored as follows: negative (0), with no positive cells or only a single positive cell (<1%); low (1+), with fewer than 10% positive cells; moderate (2+), with 10-50% positive cells; and strong (3+), with more than 50% positive cells. The lymphocytic infiltrate was assessed on whole slides prior to TMA construction, comparing central and peripheral tumour regions, and its localization was correlated with PD-L1 expression on tumour cells.
Results: High levels of PD-L1 expression were more commonly found in the invasive regions of the tumour compared to the central parts ($p<0.001$). No significant correlation was observed between the peritumoral lymphocytic infiltrate and PD-L1 expression, regardless of the tumour segment. In contrast, intratumoral lymphocytic infiltration was more frequent (84.3%) in the central tumour regions and was associated with higher PD-L1 expression ($p=0.003$).
Conclusion: The most prominent PD-L1 expression was observed in the invasive regions of HGSOC. Only the central tumour regions showed significant PD-L1 expression associated with notable intratumoral lymphocytic infiltration. Our findings support the hypothesis that PD-L1 inhibitors could offer an effective therapeutic strategy for aggressive ovarian cancers like HGSOC, particularly in cases with prominent intratumoral lymphocytic infiltration.

PS-17-012

Utility of HOXB13 in differential diagnosis of female genital tract lesions with putative prostatic differentiation

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Background & Objectives: Female genital tract lesions with putative prostatic differentiation include tubulosquamous polyps (TSP), ectopic prostatic tissue (EPT), and adenoid basal cell carcinoma (ABC). HOXB13 is a transcription factor highly specific for the prostate, however its diagnostic utility in gynaecologic pathology has not been studied.

Methods: The cohort of 13 TSPs, 6 EPTs, 13 ABCs, and 8 adenoid basal hyperplasias (ABHs) was analysed for expression of prostatic markers HOXB13 and NKX3.1. Additional 18 HSILs, 10 squamous cell carcinomas (SCCs), 11 endocervical adenocarcinomas (EACs), and 5 poorly differentiated endometrial endometrioid carcinomas (ECs) were studied with HOXB13 and p16. The results were recorded as immunoreactive score (IRS).
Results: In benign lesions (TSPs, EPTs), HOXB13 and NKX3.1 was positive in 100% and 89.4%, respectively. No expression of HOXB13, NKX3.1, and p16 was observed in ABHs. In contrast, all ABCs showed diffuse p16 positivity. NKX3.1 was positive in 76.9% of ABCs (median IRS 2), while HOXB13 was positive in 100% ABCs (median IRS 8) and the extent of positivity differed significantly (p=0.0004). NKX3.1 stained preferentially glandular structures but not basaloid cells in majority of the cases. HOXB13 was regularly observed in basal zone of normal ectocervical epithelium and in a subset of HSILs (44.4% of all HSILs and in 87.5% of HSILs associated with ABC). HOXB13 was positive in 2 EACs and in 2 G3 EC (IRS≤2 in all 4 cases). Thus, any HOXB13 positivity in invasive carcinoma was 100% sensitive and 84.6% specific for the diagnosis of ABC. In contrast, NKX3.1 was only 76.9% sensitive for the diagnosis of ABC.
Conclusion: HOXB13 is a more robust and sensitive marker of ABC. All studied ABHs lacked p16 immunoreactivity as well as prostatic markers and this further support its unrelatedness to ABC.

PS-17-013
MTAP deficiency: a novel potential predictive marker in high-grade and undifferentiated uterine sarcomas
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Background & Objectives: Uterine sarcomas, including high-grade endometrial stromal sarcoma (HG-ESS) and undifferentiated uterine sarcoma (UUS), are aggressive tumours with limited treatment options. Methylthioadenosine phosphorylase (MTAP) deficiency, frequently associated with 9p21 deletions (CDKN2A/B), may serve as a predictive marker for targeted therapy or antifolate therapy in various cancers. In this study, we analysed MTAP at the DNA and protein levels in HG-ESS and UUS to identify potential therapeutic targets.
Methods: A cohort comprising 57 HG-ESS, 3 low-grade ESS with HG transformation, and 41 UUS underwent next-generation sequencing (NGS) using a DNA-targeted panel, which included *MTAP*, *CDKN2A/B*. Copy number variation (CNV) analysis focused on the *MTAP*, *CDKN2A/B* genes. Immunohistochemistry (IHC) was performed using the MTAP antibody clone RBT-MTAP (Bio SB).
Results: Homozygous deletion of the *MTAP* gene was observed in 2/41 (5%) UUS, 1/3 low-grade ESS with HG transformation, and 8/57 (14%) HG-ESS. Co-deletions of *CDKN2A* and *CDKN2B* were found in 9 of 11 MTAP-deleted tumours. The remaining two MTAP-deleted tumours exhibited either deletion of *CDKN2A* exon 1 or complete deletion of *CDKN2A* with intact *CDKN2B*. CNV analysis strongly correlated with IHC results. All MTAP-deleted samples had H-scores of 0 (except one), indicating no MTAP protein expression. *MTAP* non-deleted samples had a median IHC H-score of 160 (range 30–300, IQR=100–200).
Conclusion: We observed that 11% of HG-ESS/UUS tumours harbour MTAP deletion, providing the first comprehensive characterization of its frequency and occurrence in these rare, aggressive gynaecological tumour types. Our study suggests potential treatment strategies for MTAP-deficient tumours, including PRMT5 and MAT2A inhibition, as well as antifolate therapy. We demonstrated high concordance between MTAP IHC and CNV analysis. Further clinical validation is necessary to assess the therapeutic relevance of these approaches.

Supported by the Ministry of Health, Czech Republic (MH CZ DRO-VFN 64165), the European Regional Development Fund (BBMRI_CZ LM2023033), and Charles University (Project UNCE 24/MED/018).

PS-17-014
Should HER2 in uterine serous carcinomas be evaluated in biopsy or hysterectomy material?
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Background & Objectives: HER2 is an important prognostic and therapeutic target in uterine serous carcinoma. Our aim was to determine our HER2 rate in endometrial biopsy and hysterectomy materials in patients with uterine serous carcinoma and to determine the effect of sample differences on the results.
Methods: Endometrial biopsy and hysterectomy materials of 35 patients diagnosed with uterine serous carcinoma between 2021 and 2024 were included in the study. HER2 positivity by IHC and CISH was determined according to ASCO/CAP version 1.2.0.0 HER2 guidelines.
Results: In our biopsy materials, 5 of our 35 patients showed +3 reaction with immunohistochemical HER2. In 3 patients, +2 reaction with HER2 was observed and 2 of these patients were HER2 positive and 1 was negative by CISH method. HER2 positivity was seen in 7 of 35 patients in total. In hysterectomy material, 7 of 35 patients had +3 reaction with immunohistochemical HER2. In 4 patients, +2 reaction with HER2 was observed and 2 of these patients were HER2 positive and 2 of them were negative by CISH method. HER2 positivity was seen in 8 of 35 patients in total. When compared to both groups, 2 patients who were negative in biopsy material were HER2 positive in resection material.
Conclusion: There are no standardised protocols for the selection of the optimum sample type or algorithm for HER2 testing in endometrial serous carcinomas. We compared HER2 immunohistochemical scores, heterogeneity of HER2 expression, CISH results, and overall HER2 status between the 2 sample types. As a result, we actually found high concordance between biopsy materials and histrectomy materials.

PS-17-015
Riluzole inhibits ovarian cancer cell migration by altering extracellular matrix structure
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Background & Objectives: The glutamate release inhibitor riluzole has been shown to slow the progression of amyotrophic lateral sclerosis, a rapidly progressive neurodegenerative condition. However, recent studies suggested that riluzole may also possess antitumor properties, but its effects on ovarian cancer remain unexplored.
Methods: The ovarian cancer cell lines OVCAR5 and OVCAR8 were treated with different concentrations of riluzole (10-1000 μM) for 48 hours. MTT and wound healing assays were performed to assess the effects of riluzole on cell viability and migration, respectively. Additionally, bulk RNA-Sequencing was performed in order to analyse the impact of riluzole on ovarian cancer cells transcriptome.
Results: Riluzole treatment (10–1000 μM) for 48 hours had no significant effect on cell viability in either OVCAR5 or OVCAR8 cells. Conversely, wound healing assays demonstrated a significant reduction in cell migration following riluzole treatment at 10 and 50 μM ($p < 0.05$). Migration rates of both cell lines decreased by more than 30% when compared to the untreated control groups. Transcriptomic

analysis revealed that riluzole significantly altered the expression of genes involved in extracellular matrix organization and structural integrity, suggesting a potential mechanism underlying its antimigratory effects.
Conclusion: Our preliminary findings indicated that riluzole has no effect on cell viability but can significantly slow migration capacity in both cell lines, probably through the modulation of extracellular matrix. These results suggest that riluzole may interfere with key pathways involved in tumour cell motility, offering new perspectives on its potential as an antimetastatic drug. However, a more extended research is required to further investigate the molecular targets of riluzole and its underlying antitumor mechanisms in ovarian cancer.

PS-17-016
Survival comparison analysis between Endocervical adenocarcinoma and Squamous cell carcinoma cervix with a special focus on HPV status
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Background & Objectives: Squamous cell carcinoma (SCC) accounts for 75% of all cervical cancers (CC), while endocervical adenocarcinoma (EAC) represents about 25%. Based on Human papillomavirus (HPV) status, WHO 2020 has classified both tumour types into HPV-associated (HPVA) and HPV-independent (HPVI). Our study examines the impact of HPV status and patient-specific characteristics on overall survival (OS) and recurrence-free survival (RFS) for SCC and EAC.
Methods: This multi-continental retrospective study analysed clinicopathologic data of 634 patients with microscopically confirmed CC (only SCC and EAC histology) across Asia, Europe, and North America. HPV status was determined using PCR or ISH for HR- and LR-HPV, using same platform. Descriptive analysis and Cox regression models produced.
Results: 533 (84.1%) patients were HPVA and 101 (15.9%) HPVI. 412 had SCC morphology (88.1%: HPVA; 11.9%: HPVI) and 222 had EAC differentiation (76.6%: HPVA; 23.4%: HPVI). Compared to EAC, patients with SCC were older (median age: 51 vs. 45 years; $P < 0.001$), had higher HPV ISH+ status (88.1% vs. 76.6%; $P < 0.001$), and higher rates of lymph-vascular invasion (LVI; 64.8% vs. 56.8%; $P = 0.004$). However, patients with EAC had higher metastasis rates in pelvic organs (13.5% vs. 2.4%; $P < 0.001$). In univariable analysis, patients with HPVI status; SCC; higher stage; older age; LVI+; regional/remote lymph node metastasis (RLNM); adjuvant treatment (AT) had worse OS or RFS than those with HPVA status; EAC; lower stage; young age; without LVI, RLNM, and AT (all $P \leq 0.007$). European patients had worse OS than North American patients; those with higher grade had worse RFS than lower grade (all $p<0.05$). In multivariable analysis, age, stage, LVI, and tumour type remained significant for OS, while tumour grade, LVI, and HPV status remained significant for RFS.
Conclusion: Study highlights significance of tumour type and HPV status in determining CC survival, underscoring need for personalized treatment strategies.

PS-17-017
Mismatch Repair Protein Status in Tubo-Ovarian High Grade Serous Carcinoma
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Background & Objectives: Testing of tumour biomarkers is rapidly evolving with expanding therapeutic indications. In ovarian carcinoma, Mismatch Repair Protein (MMR) immunohistochemistry (IHC) has mainly been performed to screen for Lynch Syndrome (LS) in non-high-grade serous carcinoma (HGSC) and, more recently, to select patients with advanced/metastatic disease for immunotherapy. This study assessed the prevalence of MMR deficiency (MMRd) in Tubo-ovarian HGSC (T-O HGSC) by IHC.
Methods: MMR status was assessed in full sections from sequential routine 33 T-O HGSCs from 2024 and a tissue microarray (TMA) of 416 T-O HGSCs (2000–2013) that had at least a cystectomy. Gynaecologic pathologists determined histologic typing and MMR IHC status. Cases with non-HGSC histology or prior/synchronous endometrial carcinoma were excluded. Cases with MMRd or equivocal TMA results were retested on full section. Stromal cell immunoreactivity was confirmed for adequacy. P53 was defined as abnormal (overexpressed (OE), null or cytoplasmic) or normal. ER and PR were considered positive if moderate to strong nuclear staining was present in ≥1% of tumour cells.
Results: Among 449 T-O HGSC patients, all 4 MMR proteins were intact in 32/33 routine cases and 412/413 TMA cases, totalling 444/446 (99.5%). PMS2 loss with intact MLH1/MSH2/MSH6 was detected in two cases. In these MMRd patients, hysterectomy and bilateral salpingo-oophorectomy revealed benign endometrium and no in situ carcinoma in fallopian tubes. P53 was abnormal/normal/NA in 424 (94.4%)/19 (4.2%)/6 (1.3%) cases. ER was positive/negative/NA in 389(86.7%)/51 (11.3%)/9 (2.0%). PR was positive/negative/NA in 125 (27.8%)/303 (67.5%)/21 (4.7%) cases.
Conclusion: MMR loss is rare (0.5%) in T-O HGSC that may represent sporadic T-O HGSC in LS patients. In health systems with finite operational budgets, MMR IHC may need to be reserved for patients with family or personal history suspicious of LS. Other biomarkers, such as tumour mutational burden, may be more appropriate to guide immunotherapy selection.

PS-17-018
Age-related alterations in inflammaging markers in the endometrial cell cultures
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Background & Objectives: The concept of "inflammaging," introduced by C. Franceschi in 2014, describes a chronic, low-grade inflammatory state that drives systemic aging. Chronic uterine inflammation promotes endometriosis and reduces fertility. The aim of the study is to identify new markers of inflammaging and compare the expression of these markers in the endometrium of women according to reproductive age.
Methods: Endometrial tissue samples were collected via pipelle biopsy during the secretory phase of the menstrual cycle and divided into two age groups: Group 1 (under 35 years, n=10) and Group 2 (over 35 years, n=10), each group was subdivided to control and inflammaging. Cell cultures were isolated using a standard protocol developed in our laboratory. UV-C at 254 nm was used to modulate genotoxic stress.

Results: Under genotoxic stress, IL-8 levels significantly increased in both young and older reproductive age groups compared to controls: 9-fold higher in women under 35 and 13-fold higher in women over 35. When modelling inflammaging increase in IL-1α expression was observed in both age groups compared to the control. IL-6 expression was higher in the inflammaging group compared to controls, but no significant differences were found between two age groups.
In the control group, SIRT-1 expression was significantly lower in the older reproductive age group compared to those under 35. Under genotoxic stress, SIRT-1 expression decreased significantly in both age groups (3.8-fold and 4.0-fold, respectively). Similarly, SIRT-6 expression decreased significantly with age in both control and stress-exposed groups.
Conclusion: The study revealed, for the first time, that levels of IL-8, SIRT1, and SIRT6 in endometrial cell cultures significantly decrease with the transition from young to older reproductive age. At the same time, the expression of IL-1a increased significantly with the age. The IL-6 levels in the endometrium did not depend from the age.

PS-17-019
The potential prognostic value of TROP2 and FOXC1 expression in uterine leiomyosarcomas: a study of 57 cases
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Background & Objectives: Uterine leiomyosarcomas (uLMS) are malignant mesenchymal neoplasms which portend a poor prognosis with available treatments and a search for targetable therapy continues. Human trophoblast cell-surface marker (TROP2) has demonstrated increased expression and has been reported as an independent marker of poor survival in various cancers. Forkhead box C1 (FOXC1) is a transcription factor which has shown involvement in tumorigenesis in multiple neoplasms. To our knowledge, TROP2 and FOXC1 expression in uLMS has not yet been investigated.
Methods: The expression of TROP2 and FOXC1 was evaluated by immunohistochemistry in 57 uLMS. The reactivity of both markers was calculated as H-score = (1+ staining x % cells) + (2 + staining x % cells) +(3 + staining x % of cells) ranging from 1-300. Overall survival (OS) curves were obtained using the Kaplan-Meier method and comparisons were made with the log-rank test. Statistical significance was assumed at $p < 0.05$. Analysis was performed using IBM SPSS Statistics 29.0.2.0.
Results: TROP2 positivity was seen in 19% (11/57) of uLMS. The H-score ranged from 15 to 300 (mean: 130). FOXC1 reactivity was identified in 21% of cases (12/57). The H-score ranged from 10 to 230 (mean: 78). The mean survival times for TROP2-positive and FOXC1-positive tumours were lower than tumours that were negative for these markers (64.0 versus 103.5 months; 72.7 versus 109 months, respectively). The differences in OS were not statistically significant for expression of either marker (TROP2 p=0.862; FOXC1 p=0.515).
Conclusion: Although significant changes in OS with expression of TROP2 and FOXC1 were not identified, the average survival was shorter in TROP2 and FOXC1-positive tumours compared with negative cases in our small study. In light of recent trials of targeted therapy for TROP2 and FOXC1 in breast, gastrointestinal, and other cancers, further investigating the expression of these markers in uLMS would be beneficial.

PS-17-020
Placental pathology in maternal diabetes mellitus according to Amsterdam classification
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Background & Objectives: Gestational diabetes mellitus (GDM) is associated with increased risks of serious adverse outcomes: congenital anomaly, stillbirth, neonatal death, preterm delivery, large for gestational age infants and neonatal intensive care unit admission. Diabetes developing in early pregnancy affects mainly the structure of the placenta while its onset in late pregnancy disturbances mainly placental function. The aim of this study was the analysis of placental abnormalities in pregnant women with GDM and their association with the state of the foetus at birth.
Methods: 124 pregnant women with confirmed GDM and 80 non-diabetic patients were included in the study. Patients with preexisting diabetes and those with associated pathologic conditions (such as hypertension, autoimmunologic diseases) were excluded. Clinical data were obtained from medical files. Placenta was collected at the time of delivery. Macroscopic examination, sampling and microscopic examination were conducted according to guidelines of Amsterdam Placental Workshop Group Consensus.
Results: In both GDM groups majority of gestational diabetes was diagnosed in the second pregnancy. Most deliveries were in the third trimester. Gross findings included: increased placental weight, abnormal umbilical cord insertion and increased coiling. Foetal vascular malperfusions (FVM) dominated among microscopic findings being statistically significant. Impaired villous maturation: delayed villous maturation and distal villous hypoplasia were present.
Conclusion: Several abnormalities are reported in association with FVM, and these include a variety of foetal/neonatal pathologies. As FMV are reported in GDM, pathologic examination of the placenta by experienced histopathologist may direct the further management of the baby and mother.

PS-17-021
Detection of POLE mutations in endometrial carcinomas: bridging histopathology and deep learning algorithms
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Background & Objectives: Analysis of POLE mutations in endometrial carcinomas(ECs) is cost-limiting and not available worldwide. We have characterized histopathological features of the molecular classes of EC(POLEmut, MMRd, p53abn and NSMP), and performed a proof-of-concept analysis using deep learning(DL) classifier models to identify POLE mutation status from H&E images.
Methods: Anonymized whole H&E slides from 119 ECs of our institution, molecularly classified (51/42,86% NSMP, 34/28,57% MMRd, 23/19,33% p53abn, 11/9,24% POLEmut), were reviewed (glandular outlines, solid areas, squamous differentiation, atypia, giant cells, intratumoral lymphocytes, MELF, necrosis, lymphovascular invasion (ILV), atypical mitosis and aberrant differentiation) with histological diagnosis and molecular class prediction. Concurrently, we took pictures (20x) from a balanced distribution of 20 ECs per class (adding POLEmut from the public database) and created a dataset for POLEmut and POLEwt (wild type), applying supervised transfer learning using two DL free platforms (Google's Teachable Machine(TM) and Apple's Create ML(CML).
Results: Molecular groups exhibited histopathological heterogeneity, with significant distribution (p<0,05) for glands with smooth (96%NSMP/43%p53abn) or irregular outlines

(65%p53abn/24%NSMP), marked atypia (70%p53abn/16%NSMP), giant cells (57%p53abn/4%NSMP), necrosis (52%p53abn/8% NSMP), ILV (70%p53abn/27%NSMP), mitosis (70%p53abn/8%NSMP) and aberrant differentiation (27%POLEmut/2%NSMP/9%p53abn). The right histological diagnosis was reached in 82%, higher in p53abn (87%) and lower in POLEmut (73%). The molecular prediction was 50%, higher in p53abn (83%) and lower in POLEmut (18%) and MMRd (26%). Regarding DL platforms, TM achieved an overall accuracy of 0,95 (0,98 for POLEmut and 0,93 for POLEwt), with less than 10% of misclassifications. CML displayed less overall accuracy 0,88 (POLEmut:0.82 and POLEwt: 0,90) but several advantages such as ability to explore the misclassified images or many adjustable parameters.
Conclusion: ECs present histopathological features allowing a subtype diagnosis but insufficient to accurately predict molecular class. However, DL models exhibit potential usefulness and viability for POLEmut detection on H&E images that could serve as a selection approach for molecular analysis.

PS-17-022

Vulvar Squamous Cell Carcinomas (VSCC) with both immunohistochemical p16-overexpression and aberrant p53 immunostaining *"Double-Positive"* tumours molecularly belongs to HPV-independent *TP53*-mutated molecular subtype

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Background & Objectives: There is increasing impact of molecular subclassification of vulvar squamous cell carcinomas (VSCC). The molecular approach subclassifies VSCC into tumours that arise secondary to high-risk human papillomavirus infection (HPV-associated, or HPVA) and those that arise independent of HPV (HPVI), defining three molecular subtypes of VSCC (HPVa, HPVi p53 abnormal, and HPVi p53 wild type). In the majority of cases, molecular subtyping belongs on immunohistochemical staining for p16 and p53 using pattern based analysis of staining results. VSCC representing both p16-overexpression and p53-aberrant staining cannot classified into molecular subtypes by immunohistochemistry alone.
Methods: Histopathological and immunohistochemical evaluation (p16, p53) as well as mutational analysis by next generation sequencing performed on HPV high-risk DNA negative (HPVI) VSCC.
Results: Seven cases were available with a mean age of 72.6 years of age (range 43 to 8 years). All cases represented block-like overexpression for p16 as well as aberrant p53-immunoepression (parabasal/diffuse overexpression, null staining, aberrant cytoplasmatic) within the keratinising and non-keratinising invasive tumour cell nests. All tumours were negative for HPV-DNA and showed pathogenic *TP53*-mutation on NGS-analysis. Two cases represented additional pathogenic mutation of *PIK3CA*.
Conclusion: VSCC representing both p16-overexpression and aberrant (mutation type) p53-immunostaining cannot be classified by immunohistochemistry alone. Mutational analysis represent *TP53*-mutation indicating that immunohistochemical "double-positive" VSCC belongs to HPVI-VSCC, p53 abnormal subtype.

PS-17-023

Correlation of DICER1 immunohistochemistry and mutational status in a large cohort of ovarian sex cord-stromal tumours

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Background & Objectives: *DICER1* is an essential gene involved in microRNA processing via RNA interference, and its mutations are associated with a wide range of neoplastic conditions, including ovarian sex cord-stromal tumours. We analysed a large cohort of these tumours, focusing on the correlation between molecular and immunohistochemical status, assessing the potential diagnostic value of DICER1 immunohistochemistry.
Methods: We examined and correlated 249 ovarian sex cord-stromal tumours, including 214 adult granulosa cell tumours (AGCT), 5 juvenile granulosa cell tumours (JGCT), and 30 Sertoli-Leydig cell tumours (SLCT). Immunohistochemistry (IHC) was performed on tissue microarrays and verified on whole tissue sections in equivocal cases. Molecular analysis was carried out using DNA-based next-generation sequencing (NGS). Additionally, RNA-based NGS was performed in all SLCT cases, all of which were eligible for expression profiling.
Results: Among AGCT, two cases harboured *DICER1* mutations - one with positive and one with negative IHC expression. Additionally, three *DICER1*-wildtype AGCT showed positive IHC staining. All five JGCT were *DICER1*-wildtype and IHC-negative. Among the 30 SLCT, 16 (53%) had *DICER1* mutations; of these, 15 (94%) demonstrated positive IHC expression. One SLCT with *DICER1* mutation was IHC-negative. Among the 14 *DICER1*-wildtype SLCT, one case (7%) showed IHC positivity, while the rest were negative.
Conclusion: Our study supports the potential utility of DICER1 IHC as a surrogate marker in SLCT. In contrast, no consistent correlation was observed in AGCT and JGCT. These findings indicate that IHC may serve as a practical and cost-effective alternative when molecular testing is not available; however, further validation is required to confirm these results.

Funding: This work was supported by the Ministry of Health, Czech Republic (MH CZ DRO-VFN 64165 and AZV NU21-03-00238), by Charles University (Project UNCE24/MED/018, SVV 260631), and by the European Regional Development Fund (EF16_013/0001674 and BBMRI_CZ LM2023033)

PS-17-024

Decoding the molecular landscape of endometrial hyperplasia: a focus on PTEN, PAX2, P53, Ki67, and beta-catenin

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Background & Objectives: Endometrial hyperplasia (EH) is recognized as a precursor to endometrial carcinoma, with classification into typical endometrial hyperplasia (TEH) and atypical endometrial hyperplasia (AEH) based on histopathological features. Accurate differentiation between these subtypes is essential for guiding clinical decision-making and stratifying patients at risk for malignant transformation. This study evaluates the expression of PTEN, PAX2, P53, Ki67, and beta-catenin as potential biomarkers to enhance diagnostic accuracy in differentiating typical from atypical endometrial hyperplasia, specifically within the context of the Bulgarian population and its associated risk factors.
Methods: A total of 150 endometrial biopsy specimens were analysed, divided into three groups**:** Group 1 (Control, n=50)**,**consisting of normal proliferative and secretory endometrium; Group 2 (TEH, n=50), with histologically confirmed typical endometrial hyperplasia and Group 3 (AEH, n=50), comprising cases with nuclear atypia. Immunohistochemistry (IHC) was performed on formalin-fixed paraffin-embedded (FFPE) tissue to evaluate the expression of PTEN, PAX2,

P53, Ki67, and beta-catenin. Biomarker expression was semi-quantified based on staining intensity and the percentage of positive cells.
Results: Loss of PTEN and PAX2 was observed in 72% of AEH cases, compared to only 8% in TEH . The Ki67 proliferation index was significantly higher in AEH. Aberrant P53 expression, including overexpression or complete loss, was found in 24% of AEH cases, whereas TEH exhibited wild-type expression. Additionally, beta-catenin nuclear accumulation was detected in 38% of AEH cases, while no nuclear staining was observed in TEH or normal endometrium.
Conclusion: Loss of PTEN and PAX2, increased Ki67, aberrant P53 expression, and beta-catenin nuclear accumulation are significantly associated with AEH and may serve as reliable biomarkers for distinguishing atypical from typical hyperplasia, enhancing early detection and risk stratification for endometrial carcinoma.

Funding: „This study is financed by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project № BG-RRP-2.004-0007-C03"

PS-17-025

Deciphering tumour heterogeneity of ARID1A expression in Endometrial Carcinomas using histogram based digital pathology

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Background & Objectives: Beyond accurate risk stratification in endometrial carcinomas (EC) by molecular classification further biomarkers like *ARID1A* mutation emerge as potential therapeutical targets. Compared NGS and digital pathology analysis seeks to assess the most reproducible approach to biomarker quantification, reducing interobserver variability. This study aims to tackle ARID1A expression patterns with respect to intratumoral heterogeneity in EC.
Methods: A total of 63 EC cases from the University Hospital Bern with known molecular status by TSO 500 sequencing were analysed for ARID1A expression using immunohistochemistry. Staining percentages and intensity were quantified using QuPath using intensity histograms as novel interpretation tool. Cases were classified as homogeneous or heterogeneous based on the presence of a bimodal intensity distribution.
Results: Among the 60 cases, 28 (46.6%) exhibited bimodal intensity histograms, indicating intratumoral heterogeneity in ARID1A expression with this novel approach. These cases showed distinct subpopulations with varying staining intensities, suggesting potential biological differences or subclones within tumours. The remaining 32 (53.3%) cases displayed a homogeneous expression pattern with n=14 (23.3%) showing a clear loss and n=18 (30%) retained staining. As expected, concordance between *ARID1A* mutational status was higher in homogenous than heterogenous cases.
Conclusion: QuPath successfully identified tumour heterogeneity in EC through intensity histogram analysis, demonstrating its potential as a tool for refining biomarker-driven risk stratification. The detection of bimodal expression patterns may provide additional insights into tumour biology with implications for NGS testing. Future studies should focus on standardizing digital pathology protocols and expanding analyses to other biomarkers to further enhance clinical applicability.

PS-17-026

Molecular profiling of endometrial precursor lesions according to the four molecular subtypes

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Background & Objectives: Endometrial cancer (EC) ranks as the second most prevalent gynaecological malignancy. The Cancer Genome Atlas (TCGA) has identified molecular subtypes that are essential for determining risk levels and guiding treatment choices. Current insights into the molecular changes in endometrial precursor lesions are still limited in existing research, primarily due to their infrequent occurrence in pathological records and the small sample sizes.
Methods: We conducted a comprehensive histopathological and molecular examination of so far 15 precursor lesions using immunohistochemistry (p53, MSH6, PAX2, PTEN, L1CAM, PMS2), and a targeted NGS panel (POLE, PTEN, TP53, CTNNB1, MLH1, MSH2, MSH6, PMS2) on laser-capture microdissected areas and in corresponding tumour areas and metaplastic lesions, if applicable.
Results: Out of these 15, one case was POLEmut, one MMRd, 10 NSMP and 3 cases P53abn, respectively. Of note, MMR protein loss was rarely found to occur even in ciliated metaplastic epithelia prior to obvious atypia. Additionally, we discovered pathogenic PTEN mutations in 7 atypia and 2 tumour samples.
Conclusion: Our results are consistent with emerging evidence that molecular subtypes arise early in the process of carcinogenesis. Furthermore, precursor lesions contain the complete range of molecular subtypes observed in endometrial carcinoma. The predominance of PTEN alterations and the rarity of POLE mutations in our cohort suggest distinct pathways for early tumour development, with implications for fertility-preserving management strategies in future research

PS-17-027

Epithelial-mesenchymal Transition (EMT) immunophenotype is more common in the prognostic poor $p16^{-ve}/p53^{abn}$ molecular subtype of vulvar squamous cell carcinoma

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Background & Objectives: Epithelial-mesenchymal transition (EMT) is associated with increased metastatic spread. Data on vulvar carcinoma are limited. Dissociative tumour growth and strong peritumoral stromal remodelling has been shown to be associated with epithelial-to-mesenchymal transition (EMT) in VSCC (Holthoff et al. 2016, Rofrigues et al. 2013). mounting evidence that EMT plays an essential role in lymphatic spread (Campo et al. 2015). Some of the most validated markers to identify cells undergoing EMT are vimentin, e-cadherin and cyclin D1.
Methods: Thirty-two squamous cell carcinoma of the vulva were evaluated for immunohistochemical expression of EMT-markers (vimentin, cyclin D1, e-cadherin) using immunoreactive score (IRS). Overall staining scores were compared to the molecular subtypes of vulval carcinoma, defining $p16^{+ve}/p53^{wt}$ and $p16^{-}ve/p53^{mut}$ VCX.
Results: Staining for vimentin and cyclin D1 was seen within tumour cells at the front of invasion in 100% and 84.4% of the tumours, respectively. The majority of cases (68.7%) showed negative or reduced staining for e-cadherin. $p16^{-}ve/p53^{abn}$ represented higher expression of the EMT markers vimentin (4.5 versus 0; p=0.03) and cyclin D1 (7 versus 5; p=0.87) without differences in e-cadherin (6 versus 3; p=1.0) when compared to $p16^{+ve}/p53^{wt}$ VCX.

Conclusion: The present study indicates an EMT-phenotype in p16^{-}ve/p53^{mut} VCX which may represent one driver for the prognostic poor outcome in that molecular type of VCX.

PS-17-028

Multi-parameter characterisation of disseminated tumour cells (DTCs) in patients with cervical carcinoma

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Background & Objectives: While disseminated tumour cells (DTCs) are associated with an unfavourable prognosis in breast cancer [Hartkopf et al. 2021], their significance in cervical carcinoma remains unclear. Current detection methods are based exclusively on the epithelial marker cytokeratin (CK) without any clear prognostic relevance [Fehm et al. 2014].

Methods: We analysed bone marrow aspirates from 43 patients with early or locally advanced cervical carcinoma. A two-stage multiparameter immunofluorescence (IF) staining method was developed to characterise the DTCs. This allowed the five different markers CK, vimentin, p16, PD-L1 and VEGF to be analysed on the same cell. Corresponding tumour tissue samples were stained against p16, VEGF and PD-L1 and compared with the expression in the DTCs.

Results: The DTC positive rate was 74% (32/43 patients). A total of 248 DTCs were found, with a median cell count of 7 DTCs (range: 1-17) per patient. Overall, 27% (68) of the cells were CK+, 85% (211) Vim+, 20% (49) VEGF+, 11% (27) PD-L1+ and 21% (53) p16+. We were able to identify 22 different DTC subpopulations. Vim+-only DTCs (54 %) were the most frequent, followed by CK+-only (12 %), the combination Vim+/VEGF+/p16+ (7 %), CK+/Vim+/VEGF+/p16+ (4 %) and CK+/Vim+ DTCs (4 %). Spearman rank correlation showed that the presence of Vim+ was significantly negatively correlated to the presence of CK+ on the same cell ($r = -0.529$, $p < 0.001$). In addition, the expression of p16+ on the DTCs correlated significantly positively with VEGF+ ($r = 0.631$, $p < 0.001$) and PD-L1+ ($r = 0.323$, $p < 0.001$). Comparison of the expression of VEGF, p16 and PD-L1 in tumour tissue vs. DTCs (n=28) revealed discordance rates between 43-64%.

Conclusion: The majority of DTCs were of the mesenchymal type (Vim+). The prognostic relevance of individual DTC phenotypes will be analysed in more detail by correlation with clinical data.

PS-17-029

Neuroendocrine marker and thyroglobulin expression in mesonephric and mesonephric-like carcinomas: implications for diagnosis

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Background & Objectives: This study examines the expression of neuroendocrine markers (chromogranin, synaptophysin, CD56, and INSM1) and thyroglobulin in ovarian and endometrial mesonephric-like adenocarcinoma (MLA) and cervical mesonephric carcinoma (MA). As these tumours share morphologic and immunohistochemical features with other gynaecologic carcinomas, understanding their immunoprofile is important to avoid diagnostic pitfalls.

Methods: The study cohort included 14 MLAs and 5 MAs from two institutions. Immunohistochemical staining (distribution and intensity) for chromogranin, synaptophysin, CD56, INSM1, and thyroglobulin was performed on whole-tissue sections.

Results: CD56 was the most frequently expressed neuroendocrine marker, detected in 14/18 (82.3%) cases, with up to 70% expression. Synaptophysin was positive in 8/19 (42.1%) cases with up to 30% expression. Chromogranin was positive in 5/19 (26.3%) cases, with staining up to 30%, while INSM1 was expressed in 4/18 (22.2%) cases, with positivity up to 20%. Thyroglobulin expression was more uncommon, identified in only 2/13 (15.4.%) cases (2% and 5% in ovarian MLAs).

Conclusion: Similar to other gynaecological adenocarcinomas, a subset of MLAs and MAs exhibit neuroendocrine marker expression, which should be recognized and not misinterpreted as evidence of a neuroendocrine neoplasm. Rare cases exhibit focal thyroglobulin positivity and this presents a diagnostic pitfall, especially in an ovarian neoplasm exhibiting TTF1 positivity (often positive in MLA) when the differential diagnosis may include malignant struma ovarii or metastatic thyroid carcinoma.

PS-17-030

PD-1 expression in the tumour microenvironment of endometrial cancer depending on MMR status

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Background & Objectives: Endometrial cancer is a common malignancy of the female reproductive system affecting women globally. In recent years, the role of the tumour microenvironment in the development and progression of this disease has been actively studied. The aim of the study was to investigate the expression patterns of PD-1 on immune cells in the microenvironment of MMR-proficient and MMR-deficient endometrial cancers.

Methods: The study included 44 patients with endometrial cancer (34 – pMMR, 10 – dMMR). Immunohistochemical assessment of MMR status was performed on the Ventana BenchMark ULTRA platform using antibodies: MLH1, PMS2, MSH2, MSH6. Multiplex tyramide signal amplification immunofluorescence was used for tumour microenvironment phenotyping. This was performed using the BOND RXm automated stainer, primary antibodies against CD8, PD-1, CD20, CD163, FoxP3. The number of CD8+ cells, CD20+ cells, CD163+ macrophages, and FoxP3+ T-regulatory cells in the tumour stroma was quantified, along with PD-1 expression.

Results: In pMMR tumours, the predominant cell population was CD163+ macrophages, followed by CD8+ T cells, FoxP3+ T cells, and CD20+ B cells ($p=0.0001$). In dMMR tumours, the numbers of CD163+ , CD8+, and CD20+ cells did not differ, while FoxP3+ T cells were the least abundant ($p=0.0210$). PD-1 expression was equally rare and low in FoxP3+ T cells and CD163+ macrophages ($p=0.1820$, $p=0.3605$, respectively). The proportion of PD-1-expressing CD8+ T cells did not differ between MMR statuses ($p>0.05$). In dMMR endometrial cancer, there was a significant increase in PD-1-expressing CD20+ B cells compared to pMMR tumours ($p=0.0003$).

Conclusion: This study found that PD-1 expression occurs on all studied cell types in the tumour microenvironment. However, PD-1 expression on CD20+ B cells is more characteristic of MMR-deficient

tumours, which may be associated with a better response to immunotherapy. These results highlight the need for further research into the endometrial cancer microenvironment to personalize therapy and develop effective predictive biomarkers.

Funding: The study was supported by the Russian Science Foundation (grant # 20-75-10033-P)

PS-17-031

Integrative analysis of histopathological subtypes and PD-L1 status in high-grade serous ovarian carcinoma: correlations with clinicopathologic features and survival outcomes

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Background & Objectives: High-grade serous ovarian carcinoma(HGSOC) is divided into four gene expression-based subtypes. Murakami et al. created a new histopathological classification with each molecular subtype. We aimed to classify HGSOCs into histopathological subtypes and to compare the subtypes with PDL-1 status and clinicopathological prognostic parameters.
Methods: 158 cases between 2007-2021 were included in the study. Clinicopathologic findings were noted. Platinum-free interval(PFI), progression-free survival(PFS), and overall survival(OS) data were obtained from follow-up at the oncology clinic. The tumour was divided into four subtypes as mesenchymal(MT), immunoreactive(IR), solid proliferative(SP) and papilloglandular(PG) by (1)evaluating the infiltrative pattern in the desmoplastic stroma, (2)intratumoral and stromal lymphocyte count, (3)solid pattern and (4)cribriform glandular pattern. The cases were also named with a binary classification system as mesenchymal(MT) and non-mesenchymal(n-MT) subtype. Immunohistochemically, CD8/144B mouse monoclonal IgG1 and PD-L1 22C3 clone antibody kit were applied.
Results: 141 cases (34 MT,16 IR,33 SP,58 PG) were followed up at our centre. There was a significant difference between subtypes and PFI, with a higher number of MT cases in the group with PFI <6 months(p=0.012). There was no significant difference in PFS and OS among the four subtypes(p=0.100,p=0.094). In pairwise comparison analysis MT subtype had a statistically significant shorter PFS than SP subtype(p=0.022) and MT subtype had statistically shorter OS than SP and PG subtype(p=0.024,p=0.048). According to the binary histopathological classification, PFS(p=0.022) and OS(p=0.014) of the MT subtype(n=34) were significantly worse than the n-MT(n=107) subtype. A significant association was found between PD-L1 positivity and IR subtype(p=0.002).
Conclusion: Since molecular methods are difficult to access and costly, a histopathological classification that offers prognostic prediction and individualized treatment is valuable. The binary classification system (rather than four subtypes) may enhance reproducibility and improve prognostic prediction in HGSOC. This classification system and its association with PD-L1 status and IR subtype could facilitate personalized treatment strategies in future clinical practice.

Funding: This study has been supported by the 'Trakya University Scientific Research Projects Unit' under grant number: 2023/182

PS-17-032

Reclassification of endometrial carcinoma by the implementation of a 161-gene NGS panel

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Background & Objectives: Endometrial cancer (EC) comprises four TCGA-molecular prognostic groups, i.e. Polimerase-Ɛ (*POLE*)-mutant, mismatch-repair (MMR)-deficient, *TP53*-abnormal and "no specific molecular profile" (NSMP) EC. These groups are integrated into ESGO-ESTRO-ESP and WHO guidelines. The NSMP group is clinically heterogeneous and the detection of new molecular parameters is mandatory. Our objective is to evaluate this group by a Next-Generation-Sequencing (NGS) panel composed of 161 genes.
Methods: The group of study consists of endometrial biopsies from 77 women diagnosed of endometrioid, serous and clear cell EC. The patients were classified according to MMR and TP53 expression by IHC and the presence of POLE mutations by NGS in all the patients. Targeted DNA/RNA-based NGS was considered to identify single nucleotide variants (SNVs), insertions and deletions (indels), copy number variations (CNVs) and fusions using the 161-gene-panel *Oncomine™ Comprehensive.v3 (*OCAv3*), Chef-ready library panel (ThermoFisher Scientific*) with automatic workflow.
Results: We found five (6.5%), 20 (25.9%), 13 (16.9%) and 37 (48.1%) cases were of *POLE*-mutant, mismatch repair (MMR)-deficient, *TP53* abnormal and NSMP EC, respectively. Two cases (2.6%) were *MMR-deficient/TP53* abnormal. Two out of five POLE-mutant cases displayed PMS2 and MSH2 mutations detected only by NGS. In NSMP EC group, NGS helped to find nine cases (24.0%) with TP53 mutations that had not been not identified by IHC. Among the alterations detected in this group, we found PIK3CA mutations at exons 10 and 21 in 8 patients (21.6%) and 1 patient with KRAS p.Gly12Cys mutation (2.7%), actionable in other type of tumours.
Conclusion: NGS allows the detection of unexpected TP53 mutations and hence the reclassification of patients from NSMP EC group into TP53-mutant EC. It also makes possible to find additional gene variants of possible clinical value that have been proved to be of clinical value in other types of tumours, i.e. PIK3CA and KRAS G12C mutations.

PS-17-033

Endometrial cancer and mismatch repair deficiency: are we missing Lynch syndrome cases?

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Background & Objectives: Lynch syndrome is a hereditary cancer syndrome linked to mismatch repair (MMR) gene defects. MMR deficiency occurs in approximately 30% of endometrial cancers. MLH1 loss can also occur due to hypermethylation. Patients with non-methylated MLH1 loss or MSH6/MSH2 loss should be screened for Lynch syndrome. This study evaluates the effectiveness of our institutional algorithm and clinical awareness.
Methods: We reviewed biopsy reports of 970 endometrial cancer patients (between 2020–2024), analysing immunohistochemical MMR status, MLH1 hypermethylation, and Lynch syndrome genetic evaluations.
Results: Among 970 patients, 244 (25.2%) had MMR deficiency, with a mean diagnosis age of 59.8 years (26–84). MLH1 expression was preserved in 44 cases, while 200 showed MLH1 and PMS2 loss. MLH1 methylation was assessed in 120 cases, revealing 14 (11.6%) non-methylated cases.
Of 58 expected referrals, only 22 patients (8 PMS2-MLH1 loss, 7 MSH2-MSH6 loss, 4 MSH6 loss, 2 PMS2 loss, 1 MSH6-PMS2-MSH2 loss) attended genetic counselling. Genetic results were unavailable

for 5 cases. Six tested negative, one had hypermethylated MLH1, and one was under investigation. A hereditary cancer-related mutation was identified in 9 patients.
Conclusion: Among 244 MMR-deficient cases, 200 had MLH1 loss, yet 80 (40%) were not tested for MLH1 hypermethylation. Of those tested, 14 (11.6%) were non-methylated. Despite identifying MMR-deficient patients and informing clinicians, awareness regarding MLH1 hypermethylation and hereditary cancer screening remains low. This study highlights the need for improved clinician awareness and patient education, particularly in developing countries, to ensure appropriate testing and genetic counselling. Social awareness initiatives may be crucial in increasing Lynch syndrome detection and protecting future generations.

PS-17-034
Clinical, morphological and age-related features of HSIL/LSIL and cervical cancer
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Background & Objectives: The annual increase in the number of cervical cancer (CC) cases shows the urgent need to step up diagnostic and preventive measures among women of different age groups. Currently, the morphogenesis of CC has not been fully studied, modern concepts are based on the viral theory of oncogenesis, that is, the sequence of changes from dysplasia to cancer. The aim of the work was to study the clinical and morphological features of dysplasia and CC in women of different age groups.
Methods: The conclusions of pathologists from the regional pathology bureau in patients with dysplasia and CC were studied. Age groups (by decades of life), the area of the tumour and the depth of invasion were assessed.
Results: The number of cases of dysplasia and CC increases with age, with CC being 10-15 years late (dysplasia peak 30-39 y.o., CC peak 40-49 y.o.). The incidence of HSIL was about 10 times higher than LSIL. In age groups over 50 years of age, there is a decrease in the incidence of dysplasia, despite the fact that CC rates are decreasing slightly. The average size of the cancer site and the depth of invasion were almost the same in all age groups. More often these are tumours up to 2 sq.cm in size, large sizes are rare. With increasing age, this feature persists, there is no shift towards increasing the size of the tumour or the depth of invasion in older age groups.
Conclusion: The peak incidence of LSIL/HSIL is observed in the 30-39-year-old group, CC - in the 40-49-year-old group. The lesion area and depth of invasion in CC do not show the expected increase with increasing age of patients, which indicates the non-linearity of cancer development, which makes it difficult to apply screening approaches.

PS-17-035
Pseudocarcinomatous epithelial hyperplasia of the fallopian tube: a comprehensive clinicopathological study of 31 cases
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Background & Objectives: The aim of this study was to investigate the clinicopathological features of pseudocarcinomatous epithelial hyperplasia (PCEH) of the fallopian tube. We provide a detailed description of the histological and immunophenotypic characteristics of tubal PCEH to help pathologists differentiate it from its mimickers, including high-grade serous tubal carcinoma (HGSC) and serous tubal intraepithelial carcinoma (STIC).
Methods: Between January 2019 and December 2023, we identified cases diagnosed as PCEH, HGSC, or STIC from the institutional database. Clinical information was collected through a review of electronic medical records. Immunostaining for CK7, p53, and Ki-67 was performed.
Results: Twelve patients with PCEH were included in the study. The ages of the patients ranged from 20 to 45 years, with six patients having a prior history of pelvic inflammatory disease. Histologically, PCEH demonstrated significant epithelial proliferation with papillary and cribriform architecture, nuclear stratification, crowding, and mild-to-moderate nuclear atypia. An intense inflammatory response was observed in all PCEH cases. Most cases lacked mitotic figures and showed a low Ki-67 labelling index, whereas both HGSC and STIC exhibited brisk mitotic activity and high Ki-67 labelling indices. In contrast to the aberrant p53 expression seen in HGSC and STIC, all PCEH cases exhibited a wild-type pattern of p53 immunostaining.
Conclusion: Due to its rarity, the correct diagnosis of PCEH can be challenging. Key diagnostic features, including the absence of high-grade nuclear atypia, low mitotic activity, and a wild-type p53 expression pattern, can help distinguish PCEH from other entities. These characteristics should be carefully considered to ensure accurate diagnosis and appropriate management for patients with PCEH.

PS-17-036
Reevaluation of the prognostic value of CRS in the context of homologous recombination deficiency and maintenance therapies
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Background & Objectives: Ovarian cancer is the fifth leading cause of mortality in women, with high-grade serous carcinoma (HGSC) being the most common subtype. When primary surgery is not feasible, neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS) is used, allowing for the evaluation of the chemotherapy response score (CRS).
Omental CRS is the gold standard due to its lower variability and prognostic value with two categories (CRS1/2 and CRS3) proposed for better clinical applicability, although its predictive value remains debated. Approximately 50% of HGSCs exhibit homologous recombination deficiency (HRD), increasing sensitivity to platinum-based chemotherapy. Also, maintenance therapies with bevacizumab (BVZ) or PARP inhibitors (iPARP) improve survival, potentially challenging the independent prognostic value of CRS.
This study aimed to assess the prognostic value of CRS and its relationship with HRD and maintenance therapies.
Methods: A retrospective study was conducted on patients with advanced HGSC undergoing IDS after NACT between 2009 and 2023. Clinical, surgical, and histopathological variables were analysed. A univariate analysis was performed, and progression-free survival (PFS) and overall survival (OS) were assessed using Kaplan-Meier curves and logistic regression.
Results: A total of 132 patients were included. Omental CRS3 was associated with HRD tumours ($p=0.048$) and adnexal CRS ($p<0.001$). Patients with omental CRS3 had higher PFS ($p=0.003$) and OS

(p=0.006). Adnexal CRS showed no prognostic differences. BVZ had no impact on PFS (p=0.8) or OS (p=0.2). Patients with HRD or treated with iPARP had improved PFS and OS, with iPARP use being the only independent prognostic factor.
Conclusion: Omental CRS is associated with better PFS and OS, unlike adnexal CRS. Patients with HRD exhibit better pathological response and prognosis. The use of iPARP is the only independent prognostic factor, questioning the prognostic value of CRS in patients receiving iPARP after IDS.

PS-17-037
Diagnostic significance of PD-L1 and HER2 expression in high-grade serous ovarian carcinoma: an immunohistochemical analysis
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Background & Objectives: High-grade serous ovarian carcinoma (HGSOC) is the most common aggressive subtype of ovarian cancer, often diagnosed at advanced stage. PD-L1 and HER2 protein expression may have diagnostic, prognostic, and therapeutic relevance, yet their role remains unclear. Study objective is to evaluate features of protein expression of these microenvironmental markers.
Methods: Immunohistochemical reactions against PD-L1 (Dako 22C3 clone) and HER2 (SP3 clone) were performed for 97 selected high-grade serous ovarian carcinoma cases. TNM stage, patient's age, and presence of applied neoadjuvant chemotherapy were also investigated. Statistical analysis was applied (p<0.05).
Results: Mean age of patients was 64.36 (10.52) years old (y.o.) with predominant pT3c (52.1%, n=50), followed by 16.7% (n=16) in pT3b, 15.6% (n=15) in pT3a. Considering pN status, pN0 (78.1%, n=75) category was predominant among selected serous ovarian carcinoma cases. PD-L1 expression below 1% was identified in 11.3% cases (n = 11), while intermediate expression (1–49%) was observed in 12.4% cases (n = 12). HER2 1+ staining intensity was detected in 8.2% (n = 8), and strong 3+ expression was present in 4.1% cases (n = 4). Most selected cases were PD-L1-negative (76.3%, n=74) and HER2-negative (87.6%, n=85). Neoadjuvant chemotherapy was applied in 21.6% (n=21) selected cases. Younger patients were more likely to be confirmed with high-grade ovarian serous carcinoma spreading to the local lymph nodes (58.52 (9.35) y.o. vs 66.05 (10.35) y.o.; p=0.002).
Conclusion: This study highlights that the majority of high-grade serous ovarian carcinoma (HGSOC) cases lack significant PD-L1 and HER2 expression, suggesting limited utility of these markers as standalone therapeutic targets in most patients. However, a subset of cases did exhibit intermediate PD-L1 or strong HER2 expression, indicating potential relevance for personalized treatment in selected patients. Additionally, younger patients demonstrated a statistically significant association with lymph node involvement, suggesting a more aggressive disease pattern in this subgroup.

PS-17-038
The correlation of tumour-infiltrating lymphocytes and immune-inflammatory environment with progression-free survival in high-grade serous ovarian carcinoma
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Background & Objectives: High-grade serous ovarian carcinoma (HGSC) is the most lethal gynaecological malignancy, with limited improvement in survival over recent years and an urgent need for novel prognostic markers. Tumour-infiltrating lymphocytes (TILs) and systemic immune-inflammatory environment have shown potential prognostic value, but their roles and interplay remain poorly understood due to limited and sometimes contradictory evidence. Our objective was to assess TILs and inflammatory scores in HGSC and investigate their association with progression-free survival (PFS).
Methods: Forty-six patients with primary HGSC were included in the study. Intratumoral and stromal CD3+ and CD8+ TILs (iTILs and sTILs) were manually evaluated by immunohistochemistry, following the recommendations of the International Immuno-Oncology Biomarkers Working Group. The systemic immune-inflammation index (SII) and the pan-immune-inflammation value (PIV) were calculated using complete blood-count data obtained at the time of diagnosis. ROC curve analysis was performed to determine optimal cut-off values for categorizing patients into low and high groups for TILs and immune-inflammatory scores, which were then correlated with PFS.
Results: CD3+ and CD8+ sTILs were present with median percentages of 13.67% and 8.50%, with optimal cut-offs of 12.9% and 5.66%, respectively. The median levels of iTILs were below 1.67%. The median values for SII and PIV were 1,466.27 and 919.98, with cut-offs of 912.45 and 423.92, respectively. CD8+ sTILs (p=0.015) and PIV (p=0.018) were significantly associated with PFS, while CD3+ sTILs and SII did not reach significance. Notably, higher CD8+ levels were linked to worse PFS, possibly indicating functional exhaustion. No direct correlation was observed between CD8+ sTILs and either SII or PIV.
Conclusion: CD8+ sTILs and PIV emerged as significant prognostic markers for PFS in primary HGSC. Their independent predictive value underscores the importance of local and systemic immune responses in disease progression; however, larger patient cohorts and multicentric studies are needed to validate and strengthen these findings.

Funding: This research was funded by the Slovenian Research and Innovation Agency—funding code P3-0289

PS-17-040
Uterine inflammatory myofibroblastic tumour: clinicopathological and molecular study emphasizing p16 absence and CDKN2A deletion association with aggressiveness
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Background & Objectives: Uterine inflammatory myofibroblastic tumour (IMT) is a rare mesenchymal neoplasm with frequent 'leiomyoma-like' morphology associated with *ALK* gene rearrangement. Clinical outcome is uncertain, but *CDKN2A* deletion and genome complexity have been shown to be prognostic relevant. We aim to evaluate clinicopathological and molecular features of a small series of uterine IMT.
Methods: Four cases of uterine IMT were diagnosed between 2020-2025 in our archives. Clinicopathological data was reviewed. p16

and p53 IHC were performed as well as FISH for *ALK* and *CDNK2A* and CGH.
Results: Patients were aged 53-75 years old (mean age:65 years). One case presented with extrauterine disease. During a mean follow-up of 14.3 months, none of the cases recurred. Tumours' mean size was 12.2 cm. 3/4 cases (75%) showed expansive borders. An exclusive compact, leiomyoma-like, pattern was present in 2/4 of cases with the remainder showing a myxoid pattern (ranging from 60-90%). A diffuse and severe lymphoplasmacytic infiltration was present in 3/4 of cases. Ischemic-type necrosis was present in 3/4 of cases and 2/4 had moderate/severe atypia. Mitotic mean count was 2/10HPF. Based on the risk stratification score, 1 case was classified as high-risk and 3 as intermediate-risk. All cases were ALK IHC positive (diffuse or multifocal) and smooth muscle actin and desmin expression ranged from multifocal to diffuse in all cases; caldesmon was negative in one case. All cases were wild-type p53. 3/4 cases had *ALK* gene rearrangement by FISH. Only the tumour with extrauterine disease had p16 expression in <1% of cells and *CDKN2A* deletion. P16 was patchy in the remaining tumours and no *CDKN2A* deletions were found. A complex profile was found by CGH in 3 cases.
Conclusion: Some IMTs can have an exclusive 'leiomyoma-like' morphology. ALK IHC staining may not correlate with *ALK* fusions, especially using FISH. P16 IHC and *CDKN2A* deletion may be prognostic useful.

PS-17-041
PD-L1 testing in HPV-related cervical cancer: simplifying pembrolizumab access
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Background & Objectives: Pembrolizumab treatment for recurrent/metastatic cervical cancer requires PD-L1 testing, which can add cost, risk misinterpretation, and delay treatment. Given the low positivity threshold in cervical carcinomas, this study examines PD-L1 expression across the spectrum of cervical neoplasia.
Methods: In a series of cervical carcinomas, PD-L1 immunohistochemical (IHC) expression was assessed using the PD-L1 IHC 22C3 pharmDx assay. Positivity was defined as a combined positive score (CPS) ≥1. The subgroups included: HPV-associated squamous cell carcinoma (HPVa-SCC), HPV-independent squamous cell carcinoma (HPVi-SCC), HPV-associated non-SCC (HPVa-nonSCC), and HPV-independent non-SCC (HPVi-nonSCC). PD-L1 expression rates were compared across subgroups using chi-squared test and Student's t-test.
Results: The cohort included 54 HPVa-SCC, one HPVi-SCC, 15 HPVa-nonSCC (including 11 endocervical adenocarcinoma, three mixed endocervical adenocarcinomas with neuroendocrine carcinoma component, and one pure neuroendocrine carcinoma), and six HPVi-nonSCC (including two gastric type adenocarcinomas, three endocervical adenocarcinoma NOS, and one adenosquamous carcinoma). All HPVa-SCC carcinomas (n=54) and HPVi-SCC (n=1) were PD-L1 positive, while three PD-L1 negative cases were identified among the HPVa-nonSCC (1/15) and HPVi-nonSCC (2/6). The rate of PD-L1 positivity was significantly higher in HPVa-SCC when compared to the other subgroups combined ($p<0.01$). The average PD-L1 CPS in HPVa-SCC (CPS 40) was higher than the other subgroups combined (CPS 24), though this difference was not statistically significant ($p>0.05$).
Conclusion: These findings support reconsidering PD-L1 testing requirements for pembrolizumab eligibility in cervical cancer. Although the small number of HPVa-nonSCC cases limits conclusions for this group, the absence of PD-L1-negative HPVa-SCC — which accounts for most cervical cancers — suggests routine testing in this subset may be unnecessary. PD-L1 testing remains informative for HPV-independent tumours, especially given their low case numbers.

PS-17-043
Ectopic adipogenesis in uterine scar and its relation to Placenta accreta spectrum
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Background & Objectives: Placenta accreta spectrum (PAS) is a severe complication of pregnancy and believed to associate with uterine scar after caesarean section (CS). The uterine scar is a necessary but not enough factor for PAS. During histopathological observation we often find adipocyte clusters in accreta area. We have suggested that adipocytes in scars may affect the development of PAS.
Methods: Histological and immunohistochemical study of uterine samples obtained during abdominal delivery was performed. The study included women without a previous CS (group 1, n=10), with a scar in the uterine wall without complicated (group 2, n=23) and with complicated by PAS (group 3, n=22).
Results: No adipocytes were found in group 1. In group 2, clusters of adipocytes were found in 83% of cases and only in the scar zone: in serosa 40%, in the perivascular zone 28%, among muscle bundles 15%. In the 3rd group the thinned uterine wall was detected in 68% and adipocyte component in 86% of cases. Adipocytes was observed in serosa (56%), in the perivascular zone (25%) and among muscle bundles (6%). No adipocytic component was found in the uterine wall outside the scar tissue and from women without previous CS. The number of adipocyte clusters in PAS group was greater than in group 2 ($p < 0.05$). In the uterine wall outside the adipocyte clusters, a decrease in CD68 cells was detected in the groups with a scar compared to the control group ($p < 0.05$). In the zones of adipocyte clusters were revealed a decrease in CD68 cells but an increase in CD163 and CD206 in the PAS group compared to group 2.
Conclusion: Adipocyte clusters in caesarean scar indicated the disturbance of cell interactions. Differences in CD206 and CD163 cells in adipocyte clusters between groups may be indirect evidence that uterine adipocytes affect the development of PAS.

Funding: The work was carried out within the framework of FSBSI "Petrovsky National Research Centre of Surgery", 119991 Moscow, Russia, No. 123030700105-0 (FURG-2023-0046)

PS-17-044
The role of adipose tissue in the healing of rat uterine wall after a full-thickness surgical incision
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Background & Objectives: Data about the role of components of adipose tissue in the repair of damaged uterine walls are limited, although a number of authors claim that cell-based drugs from adipose tissue have a positive effect on the repair of damaged uterine walls in laboratory rodents. The aim of the study was to evaluate the adipocyte components in the uterine wall of rats in healing after a full-thickness surgical incision.
Methods: The study was on 40 female Sprague Dawley rats. The animals were subjected to a full-thickness longitudinal incision in the wall of the right uterine horn, with the left one serving as an intact control.

We carried out morphological examinations of the uterine walls daily in 5 animals from day 1 to 7 and on day 15. The sections from paraffin blocks were stained with haematoxylin and eosin and Mallory's trichrome staining. Immunohistochemistry detected FABP4+ adipocytes and CD68+ macrophages.T
Results: The period of the most active interaction of adipose tissue with the damaged horn to last from day 3 to 15 and coincide with the macrophage activation in the healing zone. The intact left uterine horn was not involved in the interaction processes with the mesenteric adipose tissue. From day 3FABP4+ cells in the uterine wall of the operated horn formed groups, creating rounded nest-like structures. Clusters of FABP4+ cells were localized in the healing zone, near the suture material, and in the perimetrium near the mesentery attachment sites. There were no FABP4+ cells in the left intact horn.
Conclusion: We characterized the morphological interaction of adipose tissue with the damaged uterine wall during the first two weeks after a full-thickness surgical incision of the rat uterine horn. The results of the study indicate that adipocytes take an active part in the healing after a surgical incision of the rat uterine wall at the earliest stages

Funding: The work was carried out within the framework of FSBSI "Petrovsky National Research Centre of Surgery", 119991 Moscow, Russia, No. 123030700105-0 (FURG-2023-0046)

PS-18 Poster Session Soft Tissue and Bone Pathology

PS-18-001
Undifferentiated small round cell sarcomas of soft tissue: insights from WHO updates and a five-case clinical experience

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Background & Objectives: The extraskeletal undifferentiated small round cell sarcomas (URCS) are an extremely rare, heterogeneous group of soft tissue tumours that usually affect young adults but have been reported from 2 months to 81 years of age with a slight male predominance. The WHO classification recognizes four main subtypes (Ewing sarcoma, EWSR1-non-ETS fusion round cell sarcoma, CIC rearranged sarcoma, and BCOR-altered sarcoma) with different behaviour and clinical course. Because of overlapping features, these invasive neoplasms have a high misdiagnosis rate. Molecular testing is often required for accurate diagnosis.
Methods: From January 2023 to date, five soft tissue URCS have been diagnosed in our laboratory: three Ewing sarcomas, one CIC-rearranged sarcoma, and one BCOR-altered sarcoma. Patient ages ranged from 3 to 25 years, with three females and two males. All cases underwent comprehensive histopathologic and immunohistochemical examination, and molecular testing was performed in three tumours to further evaluate specific genetic alterations.
Results: Involved tumour sites included the shoulder, axillary, chest wall, and pelvic-abdominal and laterocervical soft tissues. All three cases diagnosed as Ewing sarcoma showed classic morphology with strong CD99 and vimentin positivity; two of them were also confirmed by molecular testing (presence of EWSR1:FLI1 fusion). The suspected CIC rearrangement sarcoma showed WT1, myogenin and vimentin expression but was negative for CD99 and desmin. The BCOR-altered sarcoma also showed strong CD99 and vimentin positivity, and FISH analysis supported a diagnosis consistent with BCOR-ITD-associated undifferentiated round cell sarcoma. In terms of clinical outcome, four patients received treatment and remain in follow-up, while the suspected CIC rearrangement patient declined evaluation and was transferred to another centre.
Conclusion: Immunoh ntial for the diagnosis of small round cell soft tissue sarcoma, and molecular genetic testing clarifies equivocal cases. A multimodal approach (integration of clinical, radiologic, histopathologic, and molecular data) improves diagnostic accuracy and increases the chance of survival.

PS-18-002
Functional screens unravelling neddylation as a therapeutic vulnerability in soft tissue sarcoma

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Background & Objectives: Soft Tissue Sarcomas (STS) are a heterogeneous group of mesenchymal tumours with more than 70 histological subtypes. Standard treatments for the majority of STS have been limited to surgery, radiation and chemotherapy for decades without significant advances, causing poor patient prognosis. Despite recent advances in genomic landscape profiling, there is no existing targeted therapy for complex karyotype STS due to a lack of recurrent genomic aberration and high genomic instability. Moreover, the lack of well characterized patient-derived cell models (sacro-sphere models) has impeded therapeutic development. We aim to discover novel therapeutic targets with patient-derived STS models.
Methods: We firstly establish a biobank of well-characterized patient-derived STS cell models, then we perform whole genome CRISPR screens and medium-throughput drug screens with *ex vivo* cell models to uncover new targets.
Results: Through a comprehensive whole-genome CRISPR screen and medium-throughput drug screens, we have uncovered the significance of protein homeostasis regulation, especially neddylation in soft tissue sarcoma pathogenesis. Building upon our existing findings and literature, we hypothesize that STS subtypes exhibiting high genomic instability, especially with a homologous recombination deficiency (HRD), are more susceptible to proteomic stress induced cell death. More specifically, we have discovered that neddylation inhibitor MLN4924 and TAS4464, but not other protein homeostasis disruptors including proteasome, ubiquitination, heat shock protein and chaperone inhibitors, displayed differential potency towards STS that harbour HRD, possibly by activating Unfolded Protein Response (UPR) induced cell death as previously reported. We have thus investigated the cell death mechanism upon MLN4924 inhibition, with focuses on DNA damage, cell cycle arrest and UPR -induced cell death. We also found impaired cell proliferation upon CRISPR KO of key UPR genes. We are validating our results by patient-derived xenografts.
Conclusion: Our research has discovered neddylation inhibition as a therapeutic vulnerability in STS with HRD, which can potentially stratify patients and improve clinical outcome.

PS-18-003
The pivotal role of platelets in metastasis of osteosarcoma

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Background & Objectives: Treatment outcomes for osteosarcoma have improved with chemotherapy and surgery, although prognosis has stagnated for over 20 years. Recent studies have highlighted the role of the tumour microenvironment and coagulation system, particularly thrombin, in tumour growth and metastasis. Platelets activated by thrombin shield tumours from stress and immune attacks while promoting survival and proliferation during metastasis. This study investigated how platelets interact with osteosarcoma to explore their therapeutic applications.
Methods: Osteosarcoma cell lines (MG63 and 143B) were transfected with green fluorescent protein (GFP), washed human platelets were prepared from healthy volunteers, and a platelet aggregation assay was used to observe interactions. Immunofluorescence was quantified and *in vivo* experiments used BALB/c-nu/nu mice. Statistical differences were determined using Student's t-test ($p<0.05$).
Results: Platelets aggregated in high lung metastatic 143B-GFP and low metastatic MG63-GFP cells. Two-hours post-tail vein injection of 143B-GFP and MG63-GFP cells, there was no significant difference between the two cell types. However, 48 h post-injection, there were no MG63-GFP cells and significantly more 143B-GFP cells, suggesting that extravasation occurred only in highly metastatic 143B cells. In addition, a thrombocytopenia model induced with GP1b antibodies showed no difference between IgG and GP1b antibodies, 2 h post-intravenous tail injection of 143B-GFP cells. However, 48 h later, cells with GP1b antibodies were significantly reduced compared to cells with IgG antibodies, suggesting that platelets regulate extravasation. Finally, *in vivo* experiments, GP1b antibody revealed a drastic reduction in the number of microcolonies in lungs.
Conclusion: This study highlights that platelets play a key role in metastasis of osteosarcoma. Tumour platelet aggregation, which is observed in osteosarcoma, promotes metastasis. Thrombocytopenia inhibits extravasation in metastatic cells, suggesting that anti-platelet agents (e.g., aspirin and P2Y12 inhibitors) could be viable therapies. Investigating platelet-releasing cytokines and tumour podoplanin-platelet CLEC-2 interactions may inspire diagnostic and therapeutic advances.

PS-18-005
Protein expression of Glypican-3 in soft tissue sarcomas is associated with poor prognosis regardless tumour subtypes
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Background & Objectives: Glypican-3 (GPC3) is a glycoprotein of the glypican family that is overexpressed on the cell surface of hepatocellular carcinoma. It is a promising biomarker for liver cancer diagnosis and an emerging candidate for novel molecular target therapies. In contrast, the role of GPC3 in soft tissue sarcoma has not been well established. In this study, we observed the expression of GPC3 in various soft tissue sarcomas and evaluated its clinical significance using immunohistochemistry (IHC).
Methods: A tissue microarray (TMA) was constructed using 249 cases of soft tissue sarcoma collected from 2000 to 2015 at a single institute, the Asan Medical Centre. IHC with TMAs and methylation-specific PCR were performed, and clinicopathologic parameters were analysed.
Results: Malignant peripheral nerve sheath tumour (51.4%) most commonly exhibited positive GPC-3 expression, followed by myxoid liposarcoma (44.7%) and alveolar rhabdomyosarcoma (42.1%). To investigate the pathogenesis underlying the varying GPC-3 expression across subtypes, methylation-specific PCR was performed; however, most sarcomas exhibited an unmethylated status with no significant differences between subtypes. Additionally, no clinicopathologic correlation was observed except for age ($p = 0.01$). GPC-3 overexpression was associated with poor prognosis, regardless of sarcoma subtype ($p = 0.005$, log-rank test).
Conclusion: GPC3 protein expression varied among sarcoma subtypes, suggesting that selective anti-GPC3 therapeutic strategies should be applied based on tumour subtype. Moreover, GPC3 protein expression is a prognostic marker for poor survival.

PS-18-006
Clinicopathological spectrum of intimal sarcomas: diagnostic challenges and molecular insights
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Background & Objectives: Intimal sarcoma is a rare and aggressive tumour. Recently, two molecular signatures have been defined: "Copy number variation-high" involving Wnt/beta-catenin pathway and microsatellite instability-high-like with mismatch repair (MMR) protein loss. This study aims to evaluate the clinicopathological features of intimal sarcomas and assess MMR protein status and beta-catenin expression.
Methods: We reviewed 16 biopsies from 11 patients. Immunohistochemistry for MLH1, MSH6, PMS2, and beta-catenin was performed on available tissue samples or unstained slides.
Results: Of 11 patients, 3 were male, and 8 (73%) were female, with a mean age of 50 years (22–75). Six tumours were in the pulmonary artery, four in the heart, and one in both. Six had a history of pulmonary thromboembolism. The mean tumour size in 8 cases was 7.1 cm (3–10 cm). Morphologically, all had a myxoid and/or collagenized stroma. Necrosis was present in 3 cases (27%). Inflammatory cells were interspersed in 7 cases. Three cases showed prominent vascularity, and 4 had smooth muscle differentiation. Adipocytic differentiation or lipoblast-like cells were seen in 5 cases. Two distinct tumour morphologies coexisted in 3 cases. *MDM2* was amplified in all 7 FISH-tested tumours and MDM2 immunoexpression was present in 3 additional tumours. PMS2, MSH6, and MLH1 expressions were retained, and beta-catenin was negative in all tested cases. Tumours were positive for SMA (5/11), CD34 (1/10), CAM5.2 (2/8), EMA (1/2), and negative for AE1/AE3 (0/4). Eight patients died due to the disease, while three remained alive for 5, 8, and 72 months.
Conclusion: Intimal sarcomas exhibit highly variable morphologies across a wide age range. The presence of lipoblast-like cells, mature adipocytes, hemangiopericytic vascular pattern, smooth muscle differentiation, and epithelial marker positivity can complicate diagnosis in biopsies. *MDM2* was amplified in all cases tested by FISH. We were unable to show MMR deficiency or beta-catenin overexpression, immunohistochemically.

PS-18-007
Clinicopathological and molecular characterization of benign vascular lesions in adults display reproducible phenotypic-genotypic correlations and represents a valuable diagnostic surrogate
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Background & Objectives: Cutaneous and visceral benign vascular lesions in adults are heterogeneous, some of them can mimic malignant entities. Their molecular features remain underinvestigated due to their benign nature and the lack of comprehensive studies.
Methods: 64 benign vascular lesions from 64 patients exhibiting a wide range of anatomic distributions were included. The lesions included

anastomosing haemangioma (AH), capillary-venous malformations (CVM), fibro-adipose vascular anomalies (FAVA), epithelioid haemangioma (EH), intramuscular angiomatosis, Kaposiform lymphatic malformation (KLM), lobular capillary haemangioma (LCH), lipo-venous malformation, sinusoidal capillary haemangioma (SCH), as well as lesions with mixed patterns. Patients were 25 females and 39 males; all but three were adults (mean age 48yo, range: 3 to 83). All lesions have been submitted for second opinion. Molecular testing was performed on FFPE tumour DNA using custom small NGS panels that include the relevant genes (GNA11, GNAQ, PIK3CA, PTEN, RAF/RAS).

Results: GNA11 and GNAQ were the most frequently mutated genes in AH (20 of 27 cases, independent of the anatomic site). These mutations were also identified in mixed lesions that contained an AH-like component. Some of them also exhibited a second mutation in PIK3CA and rarely FANCF gene.

RAS pathway mutations (KRAS, NRAS, and MAP2K1) were most commonly found in LCH.

Alterations in the PIK3CA were frequently observed in CVM.

The least frequent mutations, PTEN and IDH1, were detected in FAVA and SCH, respectively. A wildtype status was observed across nearly all lesions with the highest frequency detected in venous malformations and LCH.

Conclusion: This study provides a detailed molecular analysis of benign vascular tumours, shedding light on their genetic landscape and the potential relevance of specific mutations in their pathogenesis. Many of these alterations represent valuable surrogate diagnostic tools on limited biopsies from unusually located lesions such as those in the breast or the retroperitoneum where well differentiated angiosarcoma is a consideration.

PS-18-009

Rare primary breast sarcomas: a case series from a tertiary cancer

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Background & Objectives: Primary breast sarcomas account for <1% of all breast cancer cases, typically affecting patients aged >55 years. They are difficult to differentiate from other types of breast cancer based on the clinical and imaging results and are associated with a poor prognosis. It is important to recognize them owing to differences in treatment options. We here present a series of four cases of primary breast sarcomas. The purpose of presenting this case series is to familiarize the pathologist with these rare entities as they clinically mimic epithelial malignancy of the breast but are heterogeneous and follow a different clinical course and treatment protocol.

Methods: A collection of four rare breast mesenchymal tumours is presented. The cases were worked up extensively with ancillary testing and the diagnosis was rendered.

Results: A total of four cases were identified. All cases were females with age group of presentation being 14-71 years with the mean age being 44 years. The tumour size ranged from 1.5-20 cms. A diagnosis of malignant peripheral nerve sheath tumour was rendered in one case, one was diagnosed as chondrosarcoma, one as osteosarcoma, and the last as rhabdomyosarcoma. A diverse panel of immunohistochemistry markers was used to reach the final diagnosis, including but not limited to SMA, desmin, CD34, S-100, H3k27me3, myogenin, myoD1, and SATB2 amongst others. The most common differential in all these cases was a malignant phyllodes tumour.

Conclusion: This case series describes unique cases of primary breast sarcomas. Histology plays a pivotal role in the diagnosis of these tumours along with an immunohistochemical panel that is valuable in excluding phyllodes tumours and differentiating amongst the various sarcomas. In these cases, immunohistochemistry was a major contributor in diagnosis. This study supports and builds upon global data on rare breast neoplasms, while offering valuable regional insights.

PS-19 Poster Session Uropathology

PS-19-001

Immunohistochemical profiling of mismatch repair deficiency in advanced prostate cancer: a retrospective analysis

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Background & Objectives: Mismatch repair (MMR) deficiency has been reported in prostatic cancer with a low prevalence, ranging from 0.4% to 3.5%, and is commonly associated with advanced tumour stages. The study aims to investigate the prevalence of MMR deficiency in high-grade prostatic acinar adenocarcinoma (PAA) using IHC analysis.

Methods: For this study, 26 cases of PAA with high Gleason scores (≥8) with available data on PSA levels and metastatic status were selected. Formalin-fixed, paraffin-embedded specimens, including prostatic biopsies, prostatectomies, and TUR-P samples, were evaluated by immunohistochemistry (IHC) to assess the expression of mismatch repair proteins (MLH1, PMS2, MSH2, and MSH6).

Results: Our analysis included 26 specimens, comprising 18 prostatic biopsies, three prostatectomies, and 5 TUR-P samples. Serum PSA levels ranged from 6.7 to 3090 ng/ml. Distant metastases were identified in 61.54% of cases (16 samples). All cases were evaluated by IHC for MMR protein expression, revealing an MMR deficiency rate of 23.08% (6 cases). Among the deficient cases, one showed isolated loss of MLH1 expression, two exhibited isolated loss of MSH6, and three demonstrated concurrent loss of MSH2 and MSH6. We performed a logistic regression analysis to evaluate whether PSA levels and the presence of metastases were associated with MMR status. The resulting p-value was ≈ 1.00, indicating no statistically significant correlation between the variables analysed. In this cohort, MMR status does not appear to be predicted by serum PSA levels or the metastatic status.

Conclusion: This study highlights a notable prevalence of MMR deficiency in advanced prostate cancer (poorly differentiated and high stage). Serum PSA levels and metastatic status showed no significant association with MMR status, suggesting the need to explore alternative indicators for identifying and testing cases potentially eligible for checkpoint inhibitor therapies.

PS-19-002

Liquid biopsy-based comprehensive genomic profiling in advanced prostate cancer

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Background & Objectives: Comprehensive genomic profiling (CGP) from liquid biopsy is an emerging method, and allows the assessment of hundreds of genes and genome-wide signatures in a minimally invasive manner. In metastatic prostate cancer, liquid biopsy is often the only feasible method for tumour sampling. Bone, a frequent metastatic site, is not only difficult to sample but the decalcification process also degrades the DNA. In other cases, the condition of the patient may not be suitable for invasive procedures.
Methods: Fourteen patients (aged 45-76) with advanced prostate cancer were selected as unsuitable candidates for tissue-based CGP. Cell-free DNA (cfDNA) was extracted from the patients' plasma. Trusight Oncology 500 ctDNA next generation sequencing panel test was performed, which assesses homologous recombination repair (HRR) gene mutations and genome-wide signatures, such as tumour mutational burden (TMB) and microsatellite instability. A clonal hematopoietic origin of the mutations was excluded.
Results: HRR gene mutation was found in 21% (3 out of 14) of the cases. No BRCA1 or BRCA2 mutation was identified. Other HRR gene mutation was detected in 3 cases (CHEK2, RAD51B with CDK12, and ATM). No microsatellite instability was detected in our cohort. Five patients had a tumour with high TMB (>10 mutations/Megabase).
Conclusion: HRR mutation was detected at a similar incidence reported in primary tumours, but with the notable lack of BRCA mutation. This might be due to the relatively small size of our cohort. The significance of blood TMB (bTMB) is still not well established. Recent studies suggest that TMB and bTMB correlate, but a new cut-off (probably higher than 10 mutations/Megabase) needs to be validated to predict response to immune checkpoint inhibitor. Liquid biopsy-based CGP can be an exceptionally helpful tool for identifying targetable genomic alterations, especially in cases with tissue sampling difficulties. However, further investigations are needed to predict therapeutic responses.

PS-19-003

Evaluation of incidence and histopathological findings of soft tissue sarcomas in genitourinary tract

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Background & Objectives: This study aims to assess the clinicopathological features and prognostic factors affecting survival in patients diagnosed with genitourinary sarcomas at our institution.
Methods: Patients diagnosed with primary genitourinary soft tissue sarcomas between 2014–2025 were retrospectively reviewed from our hospital's pathology archive. Sarcomas of female genital tract and retroperitoneal origin were excluded. Thirty-eight patients with clinical follow-up were included. Demographic, histopathological, and clinical data (age, sex, histologic type, tumour size, necrosis, mitotic count, primary organ, metastasis, surgical margins, and follow-up duration) were collected through literature review. Data were analysed using IBM SPSS Statistics 27 with appropriate statistical methods.
Results: The cohort included 28 males and 10 females, with 17 paediatric and 21 adult patients. The mean overall survival was 41.1 months. The kidney was the most common tumour site (42.1%), followed by the bladder (28.9%), testis/paratesticular region (23.7%), and prostate (5.2%).Rhabdomyosarcoma was the most frequent histological subtype (26.3%), followed by leiomyosarcoma (23.7%) and clear cell sarcoma (15.8%).High mitotic activity (≥20 mitoses/10 HPF) was observed in 47.4% of cases, and tumour necrosis in 78.9%. At diagnosis, systemic metastases were present in 42.1% of patients, and surgical margin positivity in 28.9%. By the end of follow-up, 55.2% of patients were alive. Tumour location significantly influenced survival (p=0.016), with kidney tumours showing the longest and prostate tumours the shortest survival. Survival also differed significantly by tumour type (p<0.001), with clear cell sarcoma having the longest and malignant peripheral nerve sheath tumours the shortest survival. Absence of metastasis at diagnosis was linked to longer survival (p=0.003).Positive surgical margins were associated with shorter survival (p=0.041).No significant association with survival was found for mitotic activity (p=0.382), tumour necrosis (p=0.077), age (p=0.069), or tumour size (p=0.754).
Conclusion: Tumour type and location, metastasis at diagnosis, and margin status are key prognostic factors for survival in genitourinary sarcomas. Recognizing these factors can guide clinical decision-making and patient management.

PS-19-004

Prognosis and tumour grading in bladder urothelial carcinomas with intratumoral grade heterogeneity

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Background & Objectives: Grade heterogeneity is one of the most debated issues in grading urothelial carcinomas. According to the 2021 World Health Organization (WHO) classification, approximately one-third of urothelial carcinomas exhibit grade heterogeneity, and a minimum of 5% high-grade component is currently required for a tumour to be classified as high-grade. However, it is also emphasized that further studies are needed to determine this threshold. In this study, we aimed to investigate the prognostic significance of the high-grade component in urothelial carcinomas exhibiting grade heterogeneity and to determine a cut-off value for the high-grade proportion based on survival data.
Methods: In this retrospective study, 180 cases of non–muscle-invasive urothelial carcinoma diagnosed via transurethral resection of bladder tumours (TURBT) between January 2019 and August 2022 were included. All cases demonstrated grade heterogeneity. The presence of lamina propria invasion, percentage of high-grade tumour, recurrence, and overall survival were evaluated.
Results: Recurrence was observed in 26.67% of the cases, and the two-year survival rate was 73.33%. Statistical analysis revealed no significant association between recurrence and the proportion of high-grade tumours. However, a significant decrease in survival was observed with increasing proportions of high-grade components. Receiver operating characteristic (ROC) curve analysis identified a cut-off value of 27.5% for the high-grade tumour component in relation to overall survival.
Conclusion: Our study demonstrated a strong association between the proportion of high-grade components and survival in non–muscle-invasive urothelial carcinomas. Considering our findings and existing literature, our results suggest that a threshold higher than 5% may be more appropriate for classifying tumours as high-grade. Large-scale, multi-centre studies are warranted to validate and refine these findings.

PS-19-007

Tumour budding in urothelial carcinoma, single institution study of 84 cases

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Background & Objectives: In Tunisia, Urothelial carcinoma is the most common genitourinary cancer in men and the second most common cancer. Approximately 20-30% of patients with newly diagnosed bladder cancer have muscle-invasive disease. Despite advances in management, predicting outcome remains a challenge due to the limitations of classical prognostic factors. Identification of novel markers, such as tumour budding (TB), may represent a promising advance.
The aim of this study was to investigate tumour budding in muscle-infiltrating urothelial carcinoma of the bladder and to analyse its prognostic significance.
Methods: We performed an analytical study including cases of muscle-invading bladder urothelial carcinoma. Tumour budding was assessed using the hot spot method, according to the recommendations of the International Tumour Budding Conference Consensus in 2016.
Results: Our study included 84 cases. The sex ratio was estimated at 11. The majority of tumours were high grade. Carcinoma in situ lesions was seen in 32.1% of cases. Vascular emboli were identified in 63 cases, lymphatic emboli in 68% and peri-nervous invasion in 58.3% of tumours. Tumours were classified as pT4a in 40.5% of cases. The presence of lymph node metastases was noted in 28.6% of cases.
Tumour budding was observed in 41.7% of cases: it was grade I: in 9.5% of cases, grade II: in 16.7% of cases, grade III: in 15.5% of cases. There was a correlation between TB and the type of invasion, the degree of parietal infiltration, the presence of vascular emboli, the presence of lymphatic emboli, the presence of peri-nervous involvement (p=0.012) and the presence of carcinoma in situ. There was no correlation with epidemiological data, tumour size, grade, histological variants or overall survival.
Conclusion: These results highlight the potential role of TB as a prognostic marker in muscle-infiltrating bladder cancer and pave the way for its use as an additional tool in patient sratification.

PS-19-009

Reporting practices in post radiation prostate biopsies among genitourinary pathologists

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Background & Objectives: Despite the widespread use of radiation therapy (RT) in prostatic adenocarcinoma, no formal, international pathology reporting guidelines exist, with only two prior studies (1987[1], 2009[2]) providing recommendations on how to assess these cases. We surveyed genitourinary (GU) pathologists to determine their reporting practice in post-RT prostate biopsies.
Methods: A 14-question survey was circulated to GU pathologists to understand annual reporting volumes, grading approach, use of immunohistochemistry (IHC) and reporting of morphologic features in the context of prior RT. Representative images of post-RT prostatic carcinomas (n=3) were included.
Results: 21/28 GU pathologists completed the survey. Annually, 24% report <10 post-RT biopsies, 57% assess 10-50 cases, and 19% see >50. Pathologists reporting ≥10 cases/annum are more likely to comment on radiation effect vs those who see <10 (86% vs 20%, p=0.055). 24% do not report Gleason score/grade group (GS/GG) if there is known prior radiation while 71% report GS/GG if radiation effect is present in background benign tissue but absent in cancer. Regarding the 3 examples of post-RT cancer included in the survey, the proportion of pathologists who said they would grade was 19%, 57% and 86%, respectively. Overall 67% comment on the degree of radiation change, including 63% of those who report GS/GG and 80% of those who do not report GS/GG. 52% always note the presence of intraductal/cribriform carcinoma, 33% note only if they provide GS/GG, and 14% never report in post-RT biopsies. 62% routinely use IHC to identify residual cancer including all who do not provide GS/GG. With respect to awareness of reporting guidelines, 58% believed there are none, and 14% were unsure.
Conclusion: There is widespread variability in reporting practice in post-RT prostate biopsies amongst GU pathologists, with variable use of IHC, reporting of intraductal/cribriform carcinoma, and GS/GG assignment. Formal, evidence-based guidelines would help standardizing reporting practice.
[1]PMID: 3595408
[2]PMID: 19117039

PS-19-010

Assessment of c-kit expression in neuroendocrine carcinomas of the genitourinary tract: an exploratory study

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Background & Objectives: De novo neuroendocrine carcinomas (NEC) of the genitourinary (GU) tract are relatively rare but increased frequency is noted in prostate cancers treated with androgen deprivation therapy. Therapeutic options are limited. C-kit (CD117) is upregulated in treatment-emergent NEC of prostate mediated via FOXA1/A2. Phase-1 clinical trials assessing c-kit antibody-drug conjugates (ADC) in NEC of multiple tumour sites have started. Our objective was to explore the pattern and frequency of c-kit expression in a real world cohort of NEC from the GU tract.
Methods: High grade NEC of prostate and bladder were identified through search of the laboratory information system. Gleason score 10/10 acinar prostatic adenocarcinomas, and high grade, muscle invasive urothelial carcinomas (MIBC) were used as controls. All were stained with CD117 antibody (DAKO, 1/400 dilution, run on Ventana Benchmark Ultra platform). Each case was assessed using H-scores (range 0-300), calculated as follows: (3 x percentage of cells with strong staining) + (2 x percentage of cells with moderate staining) + (1 x percentage of cells with weak staining).
Results: Twenty-four GU NEC were identified: 10 NEC of prostatic origin (6 de novo) and 14 NEC of bladder origin. Thirty-eight controls (18 Gleason score 10/10 prostate and 20 MIBC) were used. Expression of cytoplasmic CD117 was seen in 13/24 (54%) NEC, including 7/10 prostate cases and 6/14 bladder cases. H-scores ranged from 10 to 270. All control cases (n=38) were negative for CD117 (p< 0.0001).

Conclusion: Pharmacologic inhibition of c-kit represents a novel therapeutic target in high NEC of the GU tract. Prostate derived NEC displayed higher frequency of CD117 expression than urothelial NEC. Additional larger series should be explored to fully evaluate the frequency, patterns of expression and clinico-pathological correlates for determining future clinical utility of c-kit ADC.

PS-19-011

Expression profiles and translational relevance of transcriptional regulators of neuroendocrine differentiation in castration-resistant prostate cancer

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Background & Objectives: The acquisition of a neuroendocrine phenotype by prostate cancer cells is a known mechanism leading to castration resistance, defining the so-called "treatment-related neuroendocrine prostatic carcinomas (t-NEPCs)". While the molecular drivers of t-NEPCs remain unclear, marked epigenetic differences between t-NEPCs and non-neuroendocrine castration-resistant prostate cancers suggest a role for transcriptional reprogramming. This study aimed to investigate the expression patterns of transcription factors associated with neuroendocrine differentiation in patients with castration-resistant prostate cancer, exploring their association with the development of a neuroendocrine phenotype, pathological features, and clinical outcomes, including responses to androgen deprivation therapy (ADT) and survival.
Methods: Eighty-three prostate cancer tissue samples from patients subsequently treated with first line ADT, and later with androgen receptor pathway inhibitors (ARPI) were retrieved. Gene expression of transcriptional regulators mediating neuroendocrine differentiation (*ASCL1*, *DLL3*, *NEUROD1*, *MYCL1*, *INSM1*, *NOTCH1*, *YAP1* and *POU2F3*) were assessed using real-time PCR. Additionally, the immunohistochemical (IHC) expression of synaptophysin and chromogranin A was evaluated.
Results: Unsupervised hierarchical analysis revealed three primary transcriptional classes significantly correlated with neuroendocrine phenotype. In particular, *ASCL1* was significantly associated with *CHGA* gene expression and with positive chromogranin A and synaptophysin IHC. In terms of clinical outcomes, low *DLL3* and *POU2F3* expression, and high *MYCL1* expression, were associated with disease progression during ARPI treatment. High *CHGA* expression was associated with poor disease-free survival during both ADT and ARPI treatments. Moreover, high *ASCL1* expression correlated with shorter time-to-progression interval and overall survival during ARPI treatment.
Conclusion: Our study revealed heterogeneous expression patterns of transcriptional regulators of neuroendocrine differentiation in prostate cancer patients admitted to ADT. Moreover, it provides the first evidence of the role of *ASCL1* as a prognostic parameter in prostate cancer patients undergoing ARPI.

PS-19-012

DNA methylation profiling of urological cancers identifies novel cancer-specific and pan-cancer biomarkers, and reveals differentially activated pathways for therapeutic targeting

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Background & Objectives: DNA methylation profiling holds promise for biomarker discovery and therapeutic targeting with hypomethylating epidrugs. This study aimed to investigate the DNA methylation landscape of prostate, bladder and kidney cancer (PCa, BlCa, KCa), integrating findings with The Cancer Genome Atlas (TCGA) datasets to identify both shared and cancer-specific DNA methylation signatures with functional relevance.
Methods: DNA methylation profiles of 72 fresh-frozen tissues were histologically characterized, underwent DNA extraction and were analysed using the HumanMethylation450 BeadChip methylation array (Illumina). These included 25 PCa (acinar adenocarcinoma), 5 normal prostatic tissues (transurethral ressections, without HGPIN), 14 BlCa (urothelial carcinomas), 5 normal bladder urothelium (from cystoprostatectomies not harbouring urothelial neoplasia), 17 KCa (all clear cell RCC), and 6 normal kidney cortical tissue (from nephroureterectomies not harbouring renal cortical neoplasia). Unsupervised clustering and principal component analysis was performed. Differentially methylated CpG sites were identified, and then further analysed using the TCGA datasets [RNAseq and DNA methylation (450k)] to evaluate their impact on gene expression. Gene ontology (GO) analysis was performed to identify affected biological pathways.
Results: DNA methylation profiles distinguished tissue types, and also normal from cancer tissues within each tissue type. BlCa and KCa showed predominant genome-wide hypomethylation (suggesting genomic instability), whereas PCa was characterized by predominant promoter hypermethylation. Hypermethylation-associated gene silencing in PCa and BlCa affected genes involved in DNA repair, oxidative stress regulation, epithelial-mesenchymal transition (EMT), and immune evasion. Cancer-specific analyses revealed that PCa hypermethylation predominantly impacted metabolic and detoxification pathways, whereas in BlCa, it affected genes regulating cell fate and tissue organization.
Conclusion: This study provides new insights into the epigenetic heterogeneity of urological cancers. The identification of both shared and cancer-specific methylation patterns highlights their potential as biomarkers for early detection, disease monitoring and therapeutic targeting.

PS-19-013

Prognostic value of androgen receptor and androgen receptor splice variant-7 in prostatic adenocarcinoma

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Background & Objectives: Current research on prostate cancer focuses on the role of the androgen receptor (AR) and its variants in hormone sensitivity and resistance. Our study analyzes AR and androgen receptor splice variant-7 (AR-V7) heterogeneity, emphasizing their relationship with clinico-pathological parameters that influence tumour behaviour.
Methods: The study group comprised 86 cases of prostatic adenocarcinoma (pADK). Clinico-pathological characteristics - including age, PSA value, histological type, Gleason score, ISUP prognostic grading group, clinical/pathological staging, progression-free survival (PFS), and overall survival (OS) - were extracted from medical records. AR

and AR-V7 expression were assessed immunohistochemically. Relationships between AR and AR-V7 immunoprofiles (positive versus negative) and clinico-pathological parameters were statistically analysed.
Results: AR immunoexpression was positive in 72 cases (92.31%) and negative in 6 cases (7.69%), while AR-V7 immunopositivity was identified in only 10 out of 78 cases (12.82%). Statistical analysis of classical clinico-pathological factors and AR immunoexpression showed significant differences concerning clinical stage at diagnosis, PSA value, ISUP prognostic grading group, tumour localization in both prostate lobes, and histological type. AR-V7 immunoexpression showed a statistically significant correlation only with clinical stage at diagnosis and extensive tumour localization in both prostate lobes. Kaplan-Meier curves and Cox regression analysis indicated no statistically significant differences in OS or PFS based on AR and AR-V7 positivity or negativity.
Conclusion: The mechanisms underlying hormone sensitivity and resistance in pADK are not yet fully understood. Studies investigating AR as a prognostic factor report heterogeneous and contradictory results due to major differences in cohort structures and immunoexpression assessment methods. Our results suggest that although AR status significantly correlates with several clinico-pathological parameters, it does not influence tumour progression. The AR-V7 profile, consistent with data reported in the literature, supports its potential role in the development of antiandrogen treatment resistance in pADK patients.

PS-19-014

Comprehensive clinicopathological and immunohistochemical evaluation of mucinous tubular and spindle cell carcinoma of kidney: a multicentre retrospective study of 71 cases

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Background & Objectives: Mucinous tubular and spindle cell carcinoma (MTSCC) is a rare subtype of renal cell carcinoma and considered a low-grade neoplasm. Limited data exists regarding its clinical course, prognostic factors, defining histopathological and immunohistochemical features. This study aims to provide a comprehensive evaluation of the clinicopathological and immunohistochemical features of MTSCC through a multicentre retrospective series, explore potential diagnostic markers via tissue microarray analysis.
Methods: A total of 71 MTSCC cases were retrospectively collected from 17 institutions; patient demographics, pathological findings including tumour size, pT stage, nuclear grade, the presence of high-grade or sarcomatoid phenotype, necrosis, metastasis, were reviewed. A panel of marker expression including CK7, CK20, PAX8, RCC, AMACR, PanCK, EMA, CD10, 34βE12, other HMWK and vimentin were evaluated. 20 out of 71 cases also underwent tissue microarray analysis with immunostaining for keratin 7, CD10, AMACR, VSTM2A and YAP1. The extent and intensity of staining semi-quantitatively assessed by 2 pathologists. Results were correlated with morphological and clinical parameters.
Results: The cohort included 47 females and 24 males, with a mean age of 60 years. Mean tumour size was 58.8 mm. Most tumours were pT1 (52.1%) and grade 2 (60.6%). High-grade features were present in 16.9%, sarcomatoid differentiation in 9.8%, tumour necrosis in 7%, metastasis in 8.5% of the cases. CK7, AMACR, PAX8 were among the 3 consistently positive markers in almost all cases (consecutively, 100%, 100% and 92.3%). CD10 and RCC expressions were variable (76.9% and 61.5%). Tissue microarray confirmed high AMACR, YAP1 and CK7 expression (consecutively 95%, 95% and 75%), and weak but common VSTM2A expression (75%). CD10 was mostly negative, some cases show weak-heterogeneous staining.
Conclusion: This study represents one of the largest series of MTSCC; aims to support the diagnostic immunoprofile of MTSCC, potentially identifying novel markers (VSTM2A, YAP1) that may help differential diagnosis.

PS-19-015

Mutational profile of invasive penile squamous cell carcinoma

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Background & Objectives: Penile squamous cell carcinoma (SCC) are rare cancers that arise after transforming human papillomavirus (HPV) infection or independent of HPV. Limited knowledge about genetic alterations comes from studies of mainly small cohorts of typically mixed aetiology.
Methods: Invasive penile SCC of 133 patients from a single institution in a low-incidence country, hot spots of 50 cancer-relevant genes were analysed with targeted next-generation sequencing.
Results: 64/133 SCC were classified as HPV-induced with 20/64 (31%) carrying somatic mutations. 69/133 SCC arose independent of HPV with 61/69 (88%) featuring somatic mutations. *PIK3CA*, *FGFR3 and FBXW7* mutations occurred in both groups in similar numbers as seen in other human cancers. Mutations in *TP53* (41/69; 59%) and *CDKN2A* (30/69; 43%) with a co-occurrence in 25/69 (36%) and *HRAS* (12/69; 17%) occurred exclusively in HPV-independent SCC. Multiple genes mutations occurred in 9/64 (14%) HPV-induced SCC versus 42/69 (61%) HPV-independent SCC (Chi square; $p< 0.001$). More than one mutation per gene (multi hits) were characteristic for HPV-independent SCC (14/69; 20%) compared to 3/64 (5%) HPV-induced SCC (Chi square; $p<0.001$). The total number of mutations was significantly higher in HPV-independent (136 mutations) than in HPV-induced penile SCC (38 mutations; Welsh test; $p<0.001$). No differences were identified with age or tumour stage of the primary SCC in neither etiologic group suggesting that acquisition of driver gene mutations are early events after invasion.
Conclusion: There are characteristic differences in mutational landscapes for the two aetiologies. While genetic mutations in tumour suppressor genes drive HPV-independent penile carcinogenesis, oncogenic action of E6 and E7 substitute for mutations in HPV-induced SCC.

Only a subgroup of patients with advanced mutated HPV-positive SCC may be candidates for targeted therapy and clinical trials, while HPV-independent SCC with tumour suppressor gene mutations remain a therapeutic challenge.

PS-19-016

Genomic copy number variations in human papillomavirus (HPV) – induced and HPV – independent penile cancer

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Background & Objectives: Penile squamous cell cancer (SCC) is a rare disease that arise via two major pathways: human papillomavirus (HPV) - induced and HPV - independent. Genomic copy number variations (CNV) are observed in many cancer types, however, their role in penile carcinogenesis remain to be poorly understood. In this study, we examined CNV changes in a cohort of 122 invasive penile SCC from a single low-incidence country.
Methods: DNA was extracted from micro-dissected tumour tissues and analysed for the presence of HPV genotype-specific DNA using the LCD-Array (CHIPRON) and for CNV by shallow WGS (Agilent SureSelect). Immunohistochemical overexpression of p16INK4A served as a surrogate marker for a transforming HPV infection. A segmentation algorithm was used to identify CNV segments associated with gains (CN>2) and losses (CN<2). Statistical analysis was performed using R.
Results: The overall fraction of genome alterations - documented as percentage of genome with CN changes - did not differ significantly between 63/122 (52%) HPV-induced SCC (median: 42.6%) and 59/122 (48%) HPV-independent SCC (median: 45.2%). The most common shared alterations included gains on 1q (HPV-induced: 51%, HPV-independent: 36%) and 3q (HPV-induced: 56%, HPV-independent: 52%), and losses of 19q (HPV-induced: 37%, HPV-independent: 40%). Although HPV-independent SCC featured more losses of 19p (53% vs. 32%) and 21q (25% vs. 9%), these differences were not significant Significant differences ($p<0.05$) in HPV-independent SCC were observed for gains of 8q (69% vs. 32%), 7p (43% vs 21%) and 7q (31% vs 11%). Losses of 11p (HPV-induced: 27%, HPV-independent: 7%) and 11q (HPV-induced: 19%, HPV-independent: 2%) were characteristic of HPV-induced SCC.
Conclusion: Our results demonstrate recurrent CNV patterns in penile SCC with overlapping and distinct alterations with respect to HPV status. The data suggest involvement of both stochastic genomic instability and pathway-specific mechanisms in the development of HPV-induced and HPV-independent tumours.

PS-19-017

Heterogeneity of PSMA expression in lymph node metastases of prostate adenocarcinoma and correlation with PSMA imaging

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Background & Objectives: Prostate-specific membrane antigen (PSMA) is a widely used target molecule in the treatment and imaging of prostate cancer. PSMA-PET offers good specificity in the detection of lymph node metastases. However, literature reports vary in terms of sensitivity, ranging from 40 to 85 %. Our previous studies showed a clear intra- and intertumoral heterogeneity of PSMA expression in primary prostate cancer. To test whether the limited sensitivity of PSMA-PET-CT is due to heterogeneous
PSMA expression also in lymph node metastases, we investigated PSMA expression in lymph node metastases by immunohistochemistry in correlation with PSMA-based imaging (PSMA-PET-CT).
Methods: 216 lymph node metastases from 92 patients were included. PSMA expression was determined for lymphnode metastases and primary tumours by PSMA immunohistochemistry (Abcam, 1:50) followed by semiquantitative (immunoreactive score) and semiautomatic evaluation (QuPath). These values were correlated with histomorphological and imaging parameters.
Results: Preoperative PSMA-PET-CT showed a sensitivity of 63 % in relation to the individual lymph node metastases. False positive results (4%) were due to PSMA-expression in germinal centres of reactive lymph nodes. In addition to size, overall DAB intensity, but not membranous staining alone, differed significantly between detected and undetected lymph node metastases.
Consistent with our previous studies, we found PSMA negative areas in 28% of all primary prostate
cancers, but only 2% of patients presented with partially or completely PSMA negative lymph node
metastases. Unlike in primary prostate cancer, PSMA expression was homogeneous within metastases of the same patient.
Conclusion: Low PSMA expression is a key factor for false negative results in PSMA-PET-CT, and any PSMA staining (cytoplasmic and membranous) seems to be relevant for PSMA-PET-CT detection.
Unlike primary prostate cancer, lymph node metastases from the same patient showed uniform staining patterns underlining the clonal nature of lymph node metastases.

PS-19-018

International validation of glass slide-based and digital grading of renal cell carcinoma: reproducibility study and need for standardization

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Background & Objectives: The WHO-recommended grading system for clear cell (ccRCC) and papillary renal cell carcinoma (pRCC) was introduced in 2012 and is based on nucleolar prominence (G1-G3) and additional histological features (G4). While its prognostic relevance has been validated in glass-slide microscopy (GSM), its applicability to digital pathology (DP) remains underexplored. This study aimed to assess the reproducibility of grading across DP and GSM modalities.
Methods: A total of 197 ccRCC and 139 pRCC cases from Cologne University Hospital (UKK) and University Hospital Wiener Neustadt (WNS) (collected from 2012-2022) were digitized and independently graded on GSM and DP by 9 international genitourinary pathologists using the WHO system. A washout period of $\geq$ 3 weeks was implemented between modalities. Interrater variability was assessed using pairwise weighted Cohen's kappa. For each case, a majority vote (MV; highest frequency grade, defaulting to the higher grade in ties) and a consensus grading (CG; $\geq$50% agreement, when available) were calculated.
Results: In ccRCC cohorts, interobserver agreement on GSM ranged from 0.25–0.81 vs MV and 0.34–0.83 vs CG. For DP, this range was 0.27–0.85 (MV) and 0.29–0.84 (CG). In pRCC cohorts, interobserver

agreement on GSM ranged from 0.39–0.65 vs MV and 0.54–0.82 vs CG. For DP this range was 0.26–0.63 (MV) and 0.24–0.82 (CG). There were significant variations in intrarater agreement (DP vs GSM for single pathologists): 0.47–0.90 for ccRCC and 0.32–0.74 for pRCC. Observed trends were overgrading using DP and differences in G4 feature interpretation.
Conclusion: WHO grading showed moderate interrater agreement across modalities, with better reproducibility in ccRCC. Digital grading did not consistently replicate GSM and tended to higher grades, emphasizing the need for RCC grading standardization.

PS-19-019
Gene expression profiling in prostate cancer: a bioinformatics approach to prognostic stratification
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Background & Objectives: Prostate cancer is a highly prevalent disease and transcriptomic analysis has emerged as a valuable tool for its molecular characterization. This study performed a differential gene expression analysis in prostatic acinar adenocarcinoma to identify biological pathways associated with tumour progression.
Methods: RNA-seq data from the PRJNA237581 project, including 103 FFPE tissue samples from multiple institutions, were analysed. RNA extraction followed quality control steps, library were prepared using Illumina HiSeq2000. Data processing included quality assessment (FASTQC software), trimming (TrimGalore), and alignment to the human genome GRCh38.p14 (HISAT2). Read quantification was performed with HTSeq-count, followed by differential expression analysis in RStudio (edgeR). Genes with an FDR < 0.05 and a logFC|1| were considered significant. Functional enrichment was assessed using Gene Ontology (GO) analysis.
Results: A total of 265 differentially expressed genes were identified, with 65% downregulated in high-grade tumours (Gleason 8–10). These genes were primarily associated with urological development (p-value: 1.74e-05) and cellular adhesion pathways (p-value: 0.00018), including NET1 (logFC = 2.92; FDR = 0.013), reflecting the transition from well-formed tubular structures to the dedifferentiated morphologies. Increased glycolysis and methylglyoxal biosynthesis, linked to NF-kB activation and bone metastases, were also observed (*p*-value: 0.005). In contrast, upregulated pathways included: cell cycle regulation (*p*-value: 8.73e-05), DNA structure maintenance, and histone methylation-mediated epigenetic modifications (*p*-value: 7.1e-05). Additionally, the enrichment of neurogenesis-related pathways (*p*-value: 0.00012), for example N4BP3 (logFC = 2.6; FDR = 0.0033), suggests a role for stromal interactions in disease progression. Regulatory molecules, such lncRNA LIPT2-AS1 (logFC=-2,44; FDR=9,54e-04), which is associated with PD-L1 expression, were found to be upregulated in high-grade tumours and could represent a surrogate marker of good prognosis.
Conclusion: The pathogenesis of prostate cancer is highly complex, involving interrelated molecular mechanisms that can be deciphered using bioinformatics tools. Our findings highlight related biological pathways and provide insights for personalized patient management.

PS-19-020
B72.3 serves as a new diagnostic marker for testicular leydig cell tumour
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Background & Objectives: As two most common sex cord-stromal tumours in testis, Leydig cell tumour (LCT) and Sertoli cell tumour (SCT) may show overlapping morphological features and immunoprofile, causing diagnostic difficulty. Differential diagnosis of these two tumours is mainly based on histological features, and there is no reliable diagnostic marker to distinguish them. B72.3 is a widely used immunohistochemistry antibody which recognizes tumour-associated glycoprotein 72 (TAG-72) expressed in a broad range of normal and tumour tissues. Incidentally, we found that B72.3 can specifically stain Leydig cells, but not Sertoli cells, in testis. We hypothesize that B72.3 may serve as a new diagnostic marker for testicular LCT.
Methods: We retrospectively identified patients with testicular LCT or SCT in the MD Anderson Cancer Centre and University of Indiana from 2012 to 2022. The histological slides were reviewed by two genitourinary pathologists to confirm the diagnoses. The tissue-embedded paraffin blocks were retrieved and recut for B72.3 immunostain, which were evaluated independently by two pathologists.
Results: We identified 47 patients with average age of 47 year old (range 1-77), who were diagnosed with testicular LCT (organ confined, n=28), testicular SCT (organ confined, n=10), metastatic LCT (n=7), and metastatic SCT (n=2). B72.3 immunostain was performed in 17 testicular LCTs (12 primary and 5 metastases) and 7 testicular SCTs (6 primary and 1 metastasis). 10 of 17 (59%) LCTs showed focal to diffuse positive staining of B72.3, among which 9 of 12 (75%) primary tumours are positive while only 1 of 5 (20%) metastatic tumours is positive. By contrast, all 7 testicular SCTs were negative for B72.3.
Conclusion: Our study suggests that B72.3 is a new diagnostic marker for testicular LCT, and it can help us differentiate testicular LCT from SCT in challenging cases. In addition, high-grade testicular and metastatic LCTs tend to lose the B72.3 expression.

Funding: University of Texas MD Anderson Cancer Centre (To Dr. Jianping Zhao) and Andrew Sabin Family Fellowship (to Dr. Qingqing Ding)

PS-19-021
Navigating diagnostic complexity: AI improves pathologist accuracy and agreement in identification of intraductal carcinoma of the prostate and cribriform growth patterns
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Background & Objectives: Both ISUP and GUPS in 2019 recognised the importance of reporting the presence of intraductal carcinoma (IDC-P) and cribriform architecture in prostate core biopsies (PCB). The presence of these patterns is correlated with a higher risk of biochemical recurrence. However, the agreement between pathologists for both of these entities is suboptimal. Recent consensus meetings held by ISUP and GUPS have attempted to further refine the diagnostic criteria for IDC-P, highlighting the importance of identification This study evaluates our AI model's ability to assist pathologists in detecting these features, enhancing consistency.
Methods: We performed a clinical validation study to evaluate our AI model's ability to augment pathologists' performance identifying the presence of IDC-P and cribriform architecture on PCB specimens using ground truth data as the benchmark. Classification performance was measured using Area Under the Curve (AUC). Reader agreement on classification of clinical findings was assessed using the Intraclass

Correlation Coefficient (ICC). A two-way random effects model measured absolute agreement.
Results: AI-assisted pathologists demonstrated superior diagnostic performance. For Acinar Gleason pattern 4 carcinoma with cribriform architecture, AI-assisted pathologists achieved an AUC of 0.870 compared to 0.866 unassisted. For IDC-P, AI assistance resulted in an AUC of 0.840 versus 0.785 unassisted. Interobserver agreement also improved with AI assistance. The ICC for cribriform architecture agreement improved from 0.704 to 0.730 while IDC-P increased from 0.566 to 0.634. These findings highlight both enhanced diagnostic accuracy and increased agreement among pathologists when utilising AI assistance.
Conclusion: We demonstrate that AI-assisted pathologists achieve superior diagnostic accuracy and consistency identifying both IDC-P and cribriform architectures. Patients with IDC-P are ineligible for active surveillance (AS), and the presence of cribriform growth would dissuade some urologists from AS. Thus, increased accuracy and agreement in diagnosing these architectures may impact treatment pathways.

PS-19-022
Digital PCR analysis of FGFR3 aberrations: fast, multiplex, and reliable
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Background & Objectives: Genetic aberrations, including point mutations and fusion oncogenes of fibroblast growth factor receptor 3 (*FGFR3*) are known drivers of tumour initiation, progression and resistance, and established biomarkers for targeted therapies such as erdafitinib in urothelial carcinoma. While sequencing can detect *FGFR3* mutations, digital PCR (dPCR) offers a more affordable alternative with a simplified workflow and rapid turnaround time, suitable for repeated testing or resistance monitoring. We aimed to develop a testing method for detection of the 5 most common FGFR3 mutations and fusions using multiplex dPCR testing and validated its performance on samples collected from urothelial carcinoma cases.
Methods: We designed assays for research use only to detect 8 most common *FGFR3* genetic alterations including 5 point mutations (R248C, S249C, G370C, Y373C, G380R) and 3 fusions (FGFR3-TACC3 (E17;E11), FGFR3-TACC3 (E17;E10), FGFR3-BAIAP2L1 (E17;E2)) in a total of 4 multiplex reactions. Each reaction contained 2 primer/probe pairs for mutant and wild-type alleles, labeled with FAM, VIC, ABY, or CY5 fluorophores. Digital PCR was performed on Absolute Q instrument (Thermo Fisher Scientific). Analytical performance of the assays was assessed using engineered plasmids containing mutant and wild-type FGFR3 sequences, with varying allele frequencies (AF). Additionally, urothelial cancer research samples and synthetic samples provided through a ring trial were tested.
Results: The tested assays demonstrated 100% sensitivity in reference material for the respective mutations. FGFR3 genetic aberrations could be detected at AF of 0.1%. In total 5 samples provided through a ring trial were analysed with 100% correct results.
Conclusion: Digital PCR on Absolute Q instrument offers a rapid and highly accurate technique for *FGFR3* genetic aberrations detection for cancer research. The method is particularly suitable for analysing liquid biopsy material including urine and blood as well as formalin-fixed, paraffin-embedded tissue samples, as it demonstrates high analytical sensitivity and specificity in identifying mutational variants with low allele frequencies.

PS-19-023
The role of cancer-associated macrophages within the tumour microenvironment of bladder cancers
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Background & Objectives: New surgical methods (minimally invasive techniques and organ-preserving orientations) for treating bladder cancer (BC) have identified new ways to target the tumour environment, including tumour/caner-associated macrophages (TAM/CAM). This group of cells is heterogeneous: m1-CAM is inflammatory and antiangiogenic, m2-CAM provides a tissue remodelling function. M2-CAM is activated in hypoxic areas of tumour tissue and promotes proliferation of peritumoral capillaries. BC is divided into muscle-invasive (MIBC), muscle-non-invasive (MNIBC) and non-invasive categories, according to invasion level.
Methods: Immunohistochemistry was performed on material from 27 BCG-treated patients (1) and 40 non-treated patients (2). A study used the markers CD68 for common macrophages and CD163 for M2-CAM. The evaluation was done quantitatively, determining the mean by counting cells in 10 high-power fields (x400, HPF).
Results: Group (1) found CD163+CAM infiltration in MIBC (pT2) to be 9-fold higher than in pT1 and CD163+CAM infiltration in pT1 to be 4-fold higher than in non-invasive BC (pTa).A 2-fold increase in CAM infiltration was noted in recurrent low-grade MIBC cases from group (1) compared to the primary tumour. In recurrent group (1) with reduced stage compared to the primary, there was a 2.3-fold decrease in CD68+CAM stromal infiltration.
In group (2), CD163+CAM infiltration was 4-fold higher in high grade MIBC cases (>pT1) compared to high grade MIBC carcinomas. The results suggest that higher CAM of MIBC is linked to poorer outcomes. These findings suggest that CAM's role in regulating the immune response within urothelial carcinoma is confirmed.
Conclusion: This study shows that CAM can stimulate tumour growth and metastasis. More investigation is needed. Finding specific CAM antigens (type m2) and looking at how they link to clinical data in larger samples can update tests for diagnosing and genetic markers of urothelial carcinomas. This should be done using minimally invasive laboratory techniques.

PS-19-024
Cancer-associated fibroblasts and clinical and morphological features of prostate cancer
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Background & Objectives: Tumour microenvironment can modulate the tumour behaviour. One of the components of the tumour microenvironment is cancer-associated fibroblasts (CAFs). Fibroblast activation protein (FAP) and platelet-derived growth factor receptors α and β (PDGFR α and β) can be used as markers of CAFs. Objective: to evaluate the association between the clinical and morphological features of prostate cancer and CAFs markers, FAP and PDGFR α+β.
Methods: The study used surgical material obtained from 34 patients with prostate cancer. The surgical material was stained with FAP and PDGFRa+β. The relationship between these markers and features of prostate cancer was analysed using the RStudio.
Results: A higher Gleason grade was noted in the presence of FAP: in 81.3% of cases, prostate cancer was classified as 4+3=7 and higher,

while in the absence of FAP, only 33.3% (p=0.014). Patients with FAP were significantly more likely to have lymphatic invasion, which was detected in 43.8% of cases, while in the absence of FAP it was detected only in 5.6% (p=0.015). In the presence of FAP, patients were more likely to have lymph nodes involvement (31.2% and 5.6%), however, this parameter had a borderline significance (p=0.078). With moderate/high PDGFRa+β expression, a higher Gleason grade was noted: in 80.0% of cases, prostate cancer was classified as 4+3=7 and higher, while with no/weak PDGFRa+β expression, only 36.8% (p=0.030). In patients with moderate/high PDGFRa+β expression, there was a more frequent probability of involvement of lymph nodes and more likely to have lesions according to MRI at the borderline significance (p=0.097 and p=0.063, respectively).
Conclusion: The presence and severity of expression of stromal CAFs markers are associated with unfavourable clinical and morphological features of prostate cancer, in particular, with a higher Gleason grade, more frequent lesions on MRI and the presence of invasion into the lymphatic vessels.

PS-19-026
Spatial transcriptomic analysis of hormone-naïve prostate cancer and matched lymph node metastases to identify predictors of lymph node invasion
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Background & Objectives: Pelvic lymph node dissection (PLND) during radical prostatectomy (RPE) for primary prostate cancer (PCa) is currently guided by clinical risk assessments and nomograms, but its therapeutic benefit remains unclear. Many patients undergo PLND without confirmed lymph node (LN) metastasis, highlighting the need for a more precise molecular predictor. PCa's inherent heterogeneity complicates this effort. This study investigates spatial transcriptional changes associated with metastatic progression.
Methods: Using the GeoMx® Digital Spatial Profiler platform (NanoString, WA, USA), we analysed 299 regions of interest (ROIs) of formalin-fixed paraffin-embedded tissue microarrays of 50 PCa patients (34 metastasizing, 16 non-metastasizing). These ROIs included unifocal and multifocal primary tumour foci (n=172), matched LN metastasis (n=34) and non-cancerous prostate epithelium (n=92).
Data analysis, conducted using R Bioconductor, involved unsupervised analysis to identify patterns and relationships in gene expression levels across different inter- and intratumoral ROIs of tumour foci and metastases. Differential gene expression (DGE) analysis identified potential genes and signatures linked to LN invasion.
Results: Principal component analysis revealed significant inter- and intratumoral heterogeneity. In multifocal PCa, unsupervised hierarchical clustering using Euclidean distance enabled the identification of the likely seeding focus by comparing gene expression patterns of individual foci with matched metastatic samples. In certain patients, this allowed for the detection of potential seeding cells, providing insights into mechanisms of LN invasion. Together, this provides a novel approach to identify genes and gene signatures responsible for LN invasion in PCa, which might be used as biomarkers or future therapeutic targets.
Conclusion: Spatial transcriptomics highlights PCa's heterogeneity and the complexity of predicting LN involvement using molecular markers. Unsupervised analysis enables identification of likely seeding foci and cells, offering a novel approach to identify genes linked to LN invasion. Future efforts will focus on refining predictive models to improve LN metastasis assessment, potentially reducing unnecessary PLND and its associated risks.

PS-19-027
Detection of germ cell neoplasia in situ in testicular biopsy for male infertility: a 15-year retrospective study with OCT3/4 immunohistochemistry reflex testing
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Background & Objectives: Testicular biopsy is a useful diagnostic tool in the management of unexplained male infertility and azoospermia. As this procedure is often performed in patients with risk factors for testicular malignancy such as cryptorchidism, atrophy, testicular microlithiasis/masses or a history of malignancy, much care should be taken to detect germ cell neoplasia in situ (GCNIS) in this higher risk population.
In this long-spanned retrospective series, we focus on the detection of GCNIS with the uniform use of OCT3/4 immunohistochemistry in our academic institution.
Methods: Through a search of our pathology medical system, we included all men who underwent testicular biopsy for infertility, including cases with a simultaneous contralateral orchidectomy between 2010 and 2025. The detection of GCNIS was performed through histology and the reflex use of OCT3/4 immunohistochemistry for all patients.
Results: A total of 2,085 testicular biopsy cases met the inclusion criteria, of which 47 (2.3%) resulted in a diagnosis of GCNIS and/or seminoma. Of these, half of the cases were not clinically suspected (1.2%), meaning the patient was not known/suspected for a testicular tumour in either testis or did not show a testicular mass on ultrasound. For these 26 men, 6 (23.1%) had normal spermatogenesis in the involved testis. In all cases, OCT3/4 immunohistochemistry was positive in GCNIS. In the 21 clinically suspicious cases of biopsy with simultaneous contralateral orchidectomy or ipsilateral testicular mass, there was a high risk of diagnosing malignancy (38.9%).
Conclusion: We confirmed the prevalence of non-clinically suspected GCNIS on testicular infertility biopsy (1.2%) which was, in most cases, associated with impaired spermatogenesis. We argue that although GCNIS was indeed diagnosed in 0.29% of cases without clinical suspicion and with normal spermatic maturation, the use of OCT3/4 might be more appropriate if reserved for histologically and/or clinically suggestive cases.

PS-19-028
SPINK1 and ERG in prostate cancer: their role in renal function and chronic kidney disease progression
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Background & Objectives: SPINK1 and ERG are molecular markers in prostate cancer, often considered mutually exclusive. Their co-expression may impact renal function. This study explores the relationship between SPINK1, ERG expression, and renal impairment in patients with prostate cancer and chronic kidney disease (CKD).
Methods: We analysed 72 prostate cancer patients with CKD undergoing radical prostatectomy. Tumour samples were assessed for SPINK1 and ERG expression using immunohistochemistry. Renal function parameters, including preoperative and postoperative creatinine levels and CKD stages, were recorded. Patients were stratified into

four groups based on SPINK1 and ERG status. Correlations between molecular expression, renal function, and disease progression were statistically analysed.
Results: ERG+/SPINK1+ subgroup had the highest postoperative creatinine levels and CKD progression rates ($p = 0.02$). In contrast, ERG+/SPINK1− patients showed significantly better renal outcomes. ERG−/SPINK1+ patients exhibited distinct renal impairment patterns, suggesting SPINK1-driven CKD progression. The ERG−/SPINK1− group had moderate renal outcomes, indicating ERG absence alone does not drive dysfunction. SPINK1 expression correlated with worse renal function, while ERG presence appeared protective. Patients with SPINK1+/ERG+ tumours had higher rates of post-surgical renal decline than other subgroups. Additionally, SPINK1+ tumours were associated with increased proteinuria, linking SPINK1 to renal injury. The combination of SPINK1 and ERG expression patterns may serve as a prognostic biomarker for cancer progression and renal outcomes, highlighting the importance of molecular profiling in clinical decision-making and treatment.
Conclusion: SPINK1 and ERG co-expression defines an aggressive prostate cancer subset with an increased renal burden. SPINK1 may contribute to CKD progression, while ERG alone appears neutral. Patients with SPINK1+/ERG+ tumours exhibited worse renal function, suggesting a synergistic effect. These findings challenge the assumption of mutual exclusivity between SPINK1 and ERG. Molecular profiling could improve risk stratification and treatment selection. Targeted therapies addressing SPINK1+/ERG+ interactions may enhance oncologic outcomes and also mitigate renal dysfunction, improving overall patient management.

PS-19-029
Can we foresee grade and stage progression in mixed low- and high-grade non-invasive papillary urothelial carcinomas?
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Background & Objectives: Non-invasive papillary urothelial carcinoma (NIPUC) is currently graded in a 2-tier system, and some cases have mixed low- and high-grade morphology. This study aims to evaluate detailed morphological features of mixed NIPUC and determine the impact of histopathologic features on grade and stage progression.
Methods: A total of 106 primary and follow-up bladder specimens (range 2-13) of 28 patients with a diagnosis of mixed NIPUC were retrieved. Pathological parameters were specified as the volume of biopsy, percentages of 2-tier (low-high) and 4-tier (Grade 1-4) grades, hot-spot mitotic count and location of mitotic activity, discohesiveness, and the presence of whirling. Outcome measures were the grade trend (decline or incline) and stage progression.
Results: The mean age was 65 (range 35-81), and all patients, except for two, were male. Ten patients had a previous biopsy showing pure low-grade NIPUC. Half of the patients had more than 5% high-grade areas, with a mean of 16% (range 1-80); therefore, they were classified as high-grade according to the 2-tier grading system. The mean distributions of grades (G1 to G4) were 42%, 42%, 15%, and 1%, respectively. The mean mitotic count was 20/10BBA (range 2-86). Tumours with more than 80% grade 1 histology did not exhibit an upward trend in grade. Stage progression was observed in tumours with a total percentage of grade 3 and grade 4 (high-grade) areas exceeding 5% (p=0,031). There was no correlation between mitotic activity, discohesiveness, or the presence of whirling and either the grade trend or stage progression. Grade trend was correlated with stage progression (p=0,012).
Conclusion: Mixed NIPUC has variable clinical outcomes that depend on the amount of grade 1 areas (>80%) suggesting a non-inclining grade trend in follow-up biopsies and the presence of >5% high-grade (grade 3 and 4) morphology estimating a stage progression.

PS-19-030
Tertiary lymphoid structures in bladder cancer - current concept based on our epidemiology, histology and immunohistochemical studies
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Background & Objectives: Bladder carcinomas (BC) are common malignancies of the urinary tract in developed countries, but the role of immune responses, especially tertiary lymphoid structures (TLS), remains underexplored. TLS are organized tumour-infiltrating lymphocytic structures that play a key role in modulating the cancer immunologic response, offering potential strategies for cancer immunotherapy. To evaluate the presence and characteristics of TLS in BC, comparing TLS in non-invasive and muscle-invasive carcinomas of varying malignancy grades, and analysing their immunohistochemical profile.
Methods: We retrospectively analysed urothelial bladder carcinoma cases from 2016–2020, including 104 cases (42 low-grade, 62 high-grade). Immunohistochemical staining for CD31, CD34, CD3, CD20, CD21, S100, C-kit, smooth muscle actin (SMA), and PD-L1 was performed.
Results: TLS were categorized into 4 groups /grades. Approximately 42/104 (40.4%) of TLS in BC was 2nd grade. Also, grade 2 TLS were detected mostly in muscle invasive BC (pT2) with 21/104(44.7%) and high-grade (HG) BC with 27/104 (43.5%). An association between the stage of BC and the presence of TLS in its stroma estimated by Pearson correlation coefficients (p=0.021) was observed. Lack of PD-L1 expression in TLS was found in a larger number of the studied cases (51/104 (70.8%)) and only in 21/104 (29.2%) were positive expression. Of these, most of described cases with positive expression for PD-L1 were TLS, grade 3 (62.5%). Positive PD-L1 expression in association with PD-L1 show significant correlation, estimated by Pearson (p=0.005).
Conclusion: Patients with high-grade/moderately and/or poorly differentiated/ BC, in the early stage of invasion (pT1 and pT2) have a moderate stromal reaction (grade 2), but with weak or absent PD-L1 expression. Therefore, in these patients the positive expression is due to a greater percentage of tumour cells, and not to tumour-associated lymphoid cells, respectively, PD-L1 expression will be found in invasive HG BC with grade 3 TLS.

PS-19-032
Novel AI-assisted algorithm for prostate cancer detection and grading - preliminary findings
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Background & Objectives: The Gleason grading system remains the primary tool for prostate cancer diagnosis, but its high intra- and inter-observer variability can impact patients. In light of advancements in artificial intelligence facilitating automated analysis, we developed an algorithm for Gleason pattern detection in prostate biopsy cores. This investigation presents preliminary findings derived from the analysis.
Methods: We analysed a cohort of 274 digitized slides, each encompassing 1–2 biopsy cores: 58 with BPL, 60 in grade group 1, 25 in grade group 2, 31 in grade group 3, 57 in grade group 4, and 43 in grade group 5. All samples underwent processing utilizing the Gleason Classification 4.0 (v4.05) algorithmic tool. Two independent pathologists reviewed and rated the results on a 1–5 quality scale.
Results: Among 274 cases, 158 were concordant. Optimal assessment was achieved in 81 cases (29.6%). In 116 cases, algorithm-based adjustments were deemed unacceptable. The highest concordance was in the 4+4 (43/56) and BPL (43/58) groups, while the 5+4 (14/15) and 4+5 (17/28) groups had the highest discordance. The algorithm achieved 97.7% sensitivity and 72.4% specificity for cancer detection at a 4.68% tumour cell cutoff (AUC 0.985 [95% CI 0.949–0.990]).
Conclusion: The algorithm demonstrated high sensitivity in detecting cancer cells. However, its accuracy in determining the Gleason score of a specimen requires further improvement.

Funding: Implementation of the Project co-financed by the National Centre for Research and Development (NCBR) within the framework of the Operational Programme Smart Growth 2014-2020, 1/1.1.1/2020 Fast Track 1_2020, entitled: "Advanced diagnostics of prostate cancer using machine learning methods and deep learning"

PS-19-033

Prognostic significance of EZH2 immunohistochemical expression in urothelial bladder cancer

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Background & Objectives: Urothelial bladder cancer (UBC) is a common malignancy with a high impact on the healthcare system. The EZH2 transcriptional repressor plays a crucial role in the oncogenesis of bladder cancer. This research aimed to investigate the expression profile of EZH2 in UBC, analyse the correlation with clinicopathological features, and assess the possible prognostic significance of EZH2 expression.
Methods: Immunohistochemical analysis of EZH2 expression comprised 647 cases of UBC, including 201 non-invasive pTa tumours, 296 superficially invasive UBC with infiltration of lamina propria, and 150 muscle-invasive bladder tumours. The median follow-up of the patients was 60 months. Tissue samples embedded in tissue microarrays were analysed immunohistochemically for EZH2 expression. Expression status was correlated with clinicopathological and follow-up data.
Results: High nuclear expression of EZH2 was found in 38.9% of the tumours. High EZH2 was more frequently observed in older patients ($p<0.001$) but showed no significant association with gender or smoking status of the patients. The expression of EZH2 was strongly associated with high tumour grade and advanced stage ($p<0.001$, respectively). Moreover, there was a direct correlation between EZH2 expression and the finding of carcinoma in situ in the surrounding bladder mucosa and divergent differentiation ($p<0.001$, respectively). High EZH2 was a significant indicator of cancer specific mortality ($p<0.001$). In survival analysis, high EZH2 expression was strongly associated with shorter overall survival of the patients ($p<0.001$). Patients with EZH2 high tumours had a 24 month shorter median survival than patients with EZH2 low tumours.
Conclusion: The expression of the epigenetic silencer EZH2 may play a significant role in predicting UBC prognosis. EZH2 is an indicator of aggressive tumour behaviour and adverse prognosis in UBC. The assessment of EZH2 immunohistochemical expression may serve as a promising complementary diagnostic tool in selecting patients who require closer follow-up and has a promising role in targeted anticancer therapy.

PS-19-034

Detection of microplastics in urothelial carcinomas with varying degrees of dysplasia

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Background & Objectives: Microplastics, defined as plastic particles smaller than 7 μm, are persistent environmental pollutants that have been detected in food, drinking water, and biological systems. Given their widespread presence, concerns have emerged regarding their potential impact on human health. This study investigates whether microplastics are present in urinary bladder carcinomas and explores their possible involvement in tumorigenesis. We hypothesize that microplastics consumed through food and water may be excreted via the urogenital tract and, if retained, could contribute to pathological processes.
Methods: This study employs a novel approach to detect microplastics in formalin-fixed, paraffin-embedded tissue samples from patients with low-grade and high-grade papillary urothelial carcinoma. Tissue samples were deparaffinized and stained using Nile Red in dimethyl sulfoxide (DMSO), a technique optimized for microplastic visualization. Fluorescence microscopy was then used to identify microplastic particles, specifically those smaller than 7 μm, based on their characteristic fluorescence signal.
Results: Microplastics were detected in urothelial cells, the submucosa, and within blood vessels. Their presence was observed diffusely throughout the tumour tissue.
Conclusion: The detection of microplastics in urothelial carcinoma tissue raises important questions regarding their potential role in carcinogenesis. While our findings do not establish a causal relationship, they underscore the need for further studies to investigate possible correlations and underlying mechanisms by which microplastics may influence tumour development.

Funding: „Funded by the EU NextGenerationEU through the Recovery and Resilience Plan for Slovakia under the project No. 09I03-03-V03-00046"

PS-19-035

Confocal microscopy as a real time diagnostic tool in the Cambridge kidney one-stop mass investigation clinic. An evaluation of 54 patients

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Background & Objectives: Ex-vivo confocal microscopy (CFM) is an emerging diagnostic tool for real time histological assessment of fresh tissue. Urologists are increasingly reliant on percutaneous renal tumour biopsies (RTB) for informed management decisions. However, the yield varies, with 10-20% being non-diagnostic. Here we present a study of the use of CFM for the assessment of RTB in the setting of a one-stop clinic enabling same day treatment planning with patients. The primary objective is evaluating biopsy adequacy and diagnostic accuracy for tumour type using CFM and assessing its feasibility in a one-stop clinic.
Methods: The Cambridge kidney One-Stop Mass investigation Clinic (CkOSMIC) was established in January 2024. RTB performed under ultrasound guidance were examined using the VivaScope 2500. The specimens were then processed through conventional histopathology. Concordance between CFM and routine histological assessment was evaluated.
Results: 54 patients underwent RTB from January 2024 to March 2025 under the CkOSMIC pathway. A rapid assessment was provided whilst the patient was in the Ultrasound suite. The median time/IQR from specimen-receipt to result was 22min/18-24.5min with CFM. 9(16.6%) patients had non-diagnostic biopsies, 4 underwent immediate repeat biopsies with provision of same day results. 5(10%) cases were designated as renal neoplasms on CFM; however, tumour typing was deferred to conventional histopathology. Of the 45 cases where a provisional diagnosis was possible on CFM, there was 93% concordance for type of renal tumour. Clear cell renal cell carcinoma was the predominant tumour type (62%); 26% oncocytic tumours were identified and 12% were assessed to be other renal lesions. There were 3(5.5%) discordant cases for tumour type, with none resulting in a benign-malignant discrepancy.
Conclusion: The high concordance rates between conventional histopathology and CFM indicate that this is an accurate and reliable tool for instant histopathological evaluation and can be used safely in the setting of a one-stop kidney cancer clinic.

PS-19-036
Cracking CROCC gene in chromophobe renal cell carcinoma with sarcomatoid dedifferentiation
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Background & Objectives: Sarcomatoid dedifferentiation in chromophobe renal cell carcinoma (RCCs) does represent an adverse morphological feature, as being marker of poor prognostication. Little is known about the genomic pathway causing dedifferentiation and clinical poor outcomes.
Methods: We aimed to investigate the genomic dataset focusing on chromosomal instability from public repository, and on hot spot genes involved in the errors of the mitotic machinery. Immunohistochemistry as CROCC (Ciliary Rootlet Coiled-Coil, Rootletin) and other related biomarkers were tested from the dataset; FISH (chr 1p36) was also performed as surrogate of the hot spot pathways.
Results: Genomic public dataset mapped 122 hot spot genes, with the CROCC gene pathway involved in the correction of centrosome segregation errors. The CROCC gene was altered in 15/21 (71%) of the sarcomatoid dedifferentiated chromophobe RCCs; FISH analysis revealed loss of the 1p36 gene locus in 13/15 (86%) CROCC+ cases and in 3/6 (50%) of CROCC- cases. All findings were observed in both sarcomatoid and epithelial components of chromophobe RCCs. P53 was observed in 13/21 (62%) of cases. Parvalbumin and S100A1 were expressed in the epithelial components of all cases.
Conclusion: Altered (crack) CROCC gene is a key altered pathway involved in the genomic instability of dedifferentiated chromophobe RCCs. The crack of the CROCC gene is observable also in the epithelial component of chromophobe RCCs. Overall altered genes reveal the mechanism of low tolerance to gross mitotic errors and promoting tetraploidization. Interfering with the CROCC gene in near-diploid chromophobe cancer cells may disrupts mitotic spindle architecture, and causes altered DNA segregation errors, resulting in a highly aggressive features. Cure of the CROCC gene, after restoration in a metastatic cellular model harbouring 1p36.13 deletion, may reduce the risk of metastases. Overall, we shed light to the genomic instability of dedifferentiated chromophobe RCCs, with using CAR-T cell pioneering treatments.

PS-19-038
Impact of whole tissue submission on lymph node yield in pelvic lymph node dissections for radical prostatectomy: a retrospective study
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Background & Objectives: Pelvic lymph node dissection (PLND) is central to prostate cancer staging, yet no consensus exists on optimal specimen submission. The recently revised RCPath dataset shows a poor correlation between nodal size and metastasis, with smaller, impalpable nodes often positive. Notably, the diameter of the largest metastatic deposit is more predictive of cancer-specific survival than the number of positive nodes. Although whole tissue submission may increase node yield, its clinical value remains uncertain. This study examined whether whole tissue submission impacts lymph node yield and pathological staging in routine diagnostic practice.
Methods: 514 radical prostatectomies were performed at Cork University Hospital between 2019–2023. Of these, 183 cases included separate lymph node specimens, and 172/183 (94%) had all tissue submitted for processing. Pathology reports were reviewed for node yield, staging, and deposit size.
Results: The average lymph node yield was 18.4 (median 18, range 0–59), comprising 10.1 palpable and 8.2 non-palpable nodes. On average, 7.2 extra blocks yielded 1.1 non-palpable nodes per block. Of 183 cases, 130 were N0, 28 Nx (13 with no nodes), and 25 N1. N1 cases had an average of 25 nodes (median 24), with 2 positive nodes on average and a mean deposit size of 4 mm. All N1 cases had bilateral sampling; three were N1(mi) and four lacked deposit size data.
Conclusion: Whole tissue submission increased total lymph node yield by capturing additional non-palpable nodes. However, the yield per extra block was low, averaging only 1.1 non-palpable nodes per block. The RCPath dataset provides no definitive guidance on expected lymph node yield or on whether full embedding of PLND specimens is required. In this context, routine full embedding may not represent an efficient use of laboratory resources. These findings underscore the need for standardised, evidence-based protocols that balance diagnostic thoroughness with practical resource management in PLND processing.

PS-19-039

Morphologic, molecular and therapeutic effects of the epigenetic drug panobinostat in AVPC PDX models: advancing treatment strategies for aggressive prostate cancer

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Background & Objectives: Aggressive variants of prostate cancer (AVPC) represent an androgen-indifferent state characterized by distinct morphologic, genetic and epigenetic characteristics. The MDA PCa 144-4 (AR-negative large cell neuroendocrine carcinoma) and MDA PCa 177-B (AR-negative adenocarcinoma with a basal phenotype) are patient-derived xenograft (PDX) models, initially developed at MD Anderson Cancer Centre and now maintained at the University of Patras. These models provide a robust system for studying AVPC. In this study we utilized these models to investigate the effect of an epigenetic modulator in prostate cancer.
Methods: C.B.-17 SCID male mice (~5 weeks old) underwent subcutaneous implantation of patient-derived tumours. Intraperitoneal drug administration began when tumour volume reached ~250 mm^3. Panobinostat (20 mg/kg), a histone deacetylase inhibitor, was administered and its effects were compared to those of the chemotherapeutic drug Carboplatin (40mg/kg). Control groups received solvent solutions. Following treatment, tumour tissues were harvested for morphological and molecular (i.e. immunohistochemistry for key epigenetic biomarkers) analyses. Statistical significance was set to $p<0.05$ for all comparisons.
Results: Carboplatin treatment led to a decrease in tumour size, while panobinostat slowed tumour growth compared to placebo therapy ($p<0.05$ and $p<0.001$, respectively). Therapy did not alter cell morphology or the expression of standard markers (i.e. AR, PSA, chromogranin, synaptophysin). Analyses of the epigenetic markers are pending.
Conclusion: Our findings highlight the therapeutic potential of epigenetic modulators as a novel strategy for treating aggressive prostate cancer. Future studies will evaluate the efficacy of panobinostat in combination with standard therapies across an expanded cohort of PDX models.

PS-19-040

Prognostic tissue markers for clear cell renal cell carcinoma tumour-stroma interaction: influence on TNM staging criteria

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Background & Objectives: New biomarkers with prognostic impact are needed to explore for clear cell renal cell carcinoma (cc-RCC) due to its quick ability to develop resistance to therapy. We aim to study the impact of Chloride Intracellular Channel Protein 1(CLIC1) expression in tumour and stromal compartments on TNM staging parameters from cc-RCC cases presenting tertiary lymphoid structures (TLSs) in their stroma, compared to cc-RCC cases lacking TLSs.
Methods: CLIC1 immunohistochemistry was conducted on 60 cc RCC tissue biopsies, followed by an evaluation of CLIC1 expression in both tumour and stromal compartments, with particular emphasis on the expression patterns of tumour cells (nuclear-N, cytoplasmic-C, membrane-M, or combined), as well as its expression in the vascular endothelium of stromal vessels and TLSs. The existence and quantity of TLS were precisely evaluated for each case, aiding in the delineation of two cc-RCC subgroups. Microscopic evaluation was then incorporated into the comparative examination of the heterogeneity in TNM staging parameters for TLS-positive versus TLS-negative cc-RCC cases.
Results: The presence of TLS was mostly linked to the CLIC1-CM pattern in tumour cells. The CLIC1-CM pattern exhibited a robust correlation with the quantity of CLIC1 positive stromal vasculature (CLIC1-MVD, $p=0.026$), as well as with T ($p=0.028$) and M ($p=0.031$). CLIC1-expressing cc-RCC with an NC pattern in tumour cells contains TLSs that significantly affect the G ($p=0.026$) and M parameters ($p=0.025$), but no relationships were seen with CLIC1-MVD. The cc-RCC subgroup devoid of TLSs exhibited nuclear expression of CLIC1 in tumour cells. The distinctive significant correlation identified for the negative subgroup of TLSs was between N and M ($p=0.028$).
Conclusion: TLSs presence, CLIC1 tumour positivity and stromal vessels strongly influence TNM staging parameters highly dependent by CLIC1 expression patterns.CLIC1 CM and M pattern seems to favour metastasis but also stromal vascularization while TLS presence may be considering a worse prognostic marker.

PS-20 Poster Session Digestive Diseases Pathology - GI

PS-20-001

Neoplastic transformation of gastric hyperplastic polyps: morphological clues to malignancy

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Background & Objectives: Gastric hyperplastic polyps (GHPs) frequently arise in a background of chronic gastritis/gastropathy. They may harbour foci of dysplasia (1–20%) and, less commonly, adenocarcinoma (~2%), particularly in larger lesions. We aimed to explore clinicopathological features and immunophenotype of GHPs with dysplasia/adenocarcinoma.
Methods: The full series included 782 GHPs ≥10mm, resected endoscopically across eight Portuguese tertiary centres (2013-2024). Patients with hereditary polyposis syndromes were excluded.

Neoplastic transformation was observed in 33 polyps (4.2%); from these, 18 cases underwent central histopathological review and are reported here. Immunohistochemistry for gastric and intestinal differentiation (MUC5AC, MUC6, MUC2, CDX2) was performed.
Results: Most neoplastic GHPs were body-located (11/18, 61.1%), with a median size of 25mm (range:12-50mm). Features of mucosal prolapse were observed in eight cases, including one hamartomatous inverted polyp. Low-grade dysplasia (LGD), high-grade dysplasia (HGD) and adenocarcinoma (ADC) were found in 10 (55.6%), eight (44.4%) and six (33.3%) cases, respectively. Dysplasia extent correlated with grade and malignant transformation: focal (<10%) in seven cases (all LGD); multifocal (10–50%) in eight (LGD:n=3, HGD:n=5, ADC:n=3); diffuse (>90%) in three (all HGD+ADC). Morphological subtyping of dysplasia showed pure gastric or intestinal morphology in 11 cases (61.1%), associated with lower risk of progression (LGD:n=9/11,81.8%; HDG:n=2/11,18.2%; ADC:n=0/11,0%), whereas coexistence of gastric and intestinal morphology (seven cases, 38.9%) was associated with higher risk of malignancy (LGD:n=1/7,14.3%; HDG:n=6/7,85.7%; ADC:n=6/7,85.7%). Preliminary subtyping of eight cases by immunohistochemistry showed hybrid immunophenotype in the majority of cases (6/8,75%), encompassing LGD and HGD/ADC. All ADC showed tubular/papillary morphology (intestinal subtype by Laurén) and were low-grade.
Conclusion: The extent of dysplastic involvement - especially when diffuse - as well as the coexistence of gastric and intestinal differentiation, suggesting unstable phenotype, are key predictors of malignant transformation in GHPs. Preliminary data suggest that morphological subtyping may be more informative than immunophenotype for risk stratification.

PS-20-002
How did COVID-19 pandemic influence clinico-pathological characteristics of colorectal-cancer?
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Background & Objectives: Colorectal cancer (CRC) is a major global health concern, with early detection and timely treatment playing a crucial role in patient outcomes. The COVID-19 pandemic significantly disrupted healthcare services, potentially causing delayed CRC diagnosis and thus affecting treatment and prognosis of those patients.
Methods: In our retrospective analysis we examined clinico-pathological data of 694 patients who underwent surgery for CRC and whose surgical specimens were diagnosed at the Department of Pathology, University Medical Centre Maribor from January 2018 to January 2023. We compared demographic data, histopathological characteristics of tumours, tumour stage and treatment in two groups of patients, one diagnosed in pre-COVID-19 period and the other during the COVID-19 pandemics.
Results: Out of 694 patients included in the study, 406 (58,5 %) were labelled as pre-COVID-19 and 288 (41,5 %) cases as during COVID-19. The pre-COVID-19 group of patients had lower tumour grade χ^2 (1, N = 661) = 20.47, $p < 0.001$ and tumour stage (U = 49,325, Z = -2.712, $p < 0.05$) at the time of diagnosis compared to patients, diagnosed during COVID-19 pandemic. Additionally, in the pre-COVID19 group the number of cases diagnosed in national screening program was slightly higher than in COVID-19 group, however the difference was not significant. Similar trend was observed for the need to perform emergency surgery due to disease-related complications e.g. perforation or ileus, which was slightly higher during COVID-19 pandemic. Other histopathological and clinical data also did not significantly differ between the groups.
Conclusion: COVID-19 pandemic significantly impacted tumour grade and tumour stage of CRC at the time of diagnosis. Accessibility to screening program was also negatively affected by the pandemic and slightly more patients needed emergency surgery due to disease-related complications. Our findings thus underscore the importance of maintaining of cancer screening programs and treatment of cancer patients during healthcare crisis.

PS-20-003
Unraveling the immunopathology of celiac disease: a correlation between Marsh stage progression and IgA deposits
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Background & Objectives: This study aims to elucidate the relationship between the histopathological severity of celiac disease, as classified by the Marsh grading system, and the distribution of IgA deposits within the intestinal mucosa. Given the pivotal role of IgA in mucosal immunity, uncovering its progressive depletion in correlation with tissue damage could provide novel insights into pathophysiology.
Methods: Duodenal biopsy specimens from patients with active celiac disease were systematically evaluated through histopathological and immunohistochemical analyses. The samples were categorized according to the Marsh classification and IgA deposits were quantified using a visual analogue scale. Statistical models were employed to assess the association between increasing Marsh scores and IgA depletion.
Results: A striking inverse correlation was observed between Marsh grade severity and IgA deposition. Patients with extensive mucosal damage (Marsh 3) exhibited a profound reduction in IgA deposits compared to those with milder histopathological alterations (Marsh 1-2). For patients diagnosed with Marsh 2, 3a and 3b there were similar findings regarding IgA deposits. The most pronounced depletion was noted in cases with complete villous atrophy, highlighting a progressive impairment of mucosal immune defense mechanisms.
Conclusion: These findings underscore a direct link between escalating histological severity in celiac disease and a concomitant reduction in IgA deposits, suggesting that extensive mucosal destruction may compromise the integrity of local immune responses. This novel insight into the interplay between histopathological damage and mucosal immunity could pave the way for refined therapeutic interventions aimed at preserving mucosal defense mechanisms in severe celiac disease.

PS-20-004
Expression of HER2 in primary colorectal carcinomas
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Background & Objectives: HER2 expression represents a potential theranostic marker in cancers like breast and gastric cancer, but its role in colorectal cancer (CRC) remains unclear, with reported rates varying widely.

This study assesses HER2 immunohistochemical expression in primary CRC across all stages in Tunisian patients to determine its prevalence in this population.
Methods: This retrospective study included all CRC patients diagnosed on surgical resection specimens at Habib Thameur Hospital over 3 years. HER2 status was assessed by immunohistochemistry using the Tissue MicroArray (TMA) technique, following esophagogastric cancer standardized criteria.
Results: The study included 104 CRC patients with a mean age of 61 years and a male-to-female ratio of 1.36. Tumours were predominantly located in the descending colon (52.9%). Disease staging revealed a majority of stage II cases (44.2%), followed by stage III (29.8%), stage IV (14.4%) and stage I (11.6%).
HER2 expression analysis revealed three distinct groups: the vast majority of cases (98%, $n = 102$) were HER2-negative (scores 0/1+). No equivocal cases (score 2+) were identified, and only one tumour (0.96%) exhibited HER2 overexpression (score 3+). The sole HER2 positive case (score 3+) was classified as pT2N0M0 with low histological grade and exhibited microsatellite instability (MSI-high status). Notably, 13 cases (12.5%) showed isolated cytoplasmic staining without membranous HER2 expression.
Conclusion: Our study found lower rates of HER2 overexpression in Tunisian CRC patients compared to other populations. These findings suggest the need for larger, multicente rstudies to clarify HER2's clinical role in CRC within our region. Notably, frequent cytoplasmic HER2 staining warrants further investigation into its biological and clinical relevance.

PS-20-005
Ten-year retrospective analysis of gastric biopsies: focus indefinite for dysplasia cases
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Background & Objectives: Gastric epithelial dysplasia is a known precursor of gastric carcinoma, yet its diagnosis — particularly in indefinite cases — remains challenging. This study aimed to evaluate the prevalence and outcomes of gastric dysplasia over a 10-year period, with special emphasis on the clinical-pathological evolution of cases initially diagnosed as "indefinite for dysplasia."
Methods: A retrospective review of gastric biopsies performed between 2013 and 2023 was conducted. Polipectomies, secondary neoplastic involvement and neoplasia of gastroesophageal anastomosis were excluded. For counting purposes multiple biopsies of a patient performed on a single moment were counted as 1. A total of 11553 gastric biopsies were analysed. Only the most severe diagnosis per biopsy was considered.
Results: Out of 11553 gastric biopsies 589 (5.1%) were carcinomas, 40 (0.3%) high-grade dysplasia (HGD), 137 (1.2%) low-grade dysplasia (LGD) and 22 (0.2%) were indefinite for dysplasia (ID). Patients with ID were mostly male (15/22) with mean age of 71.3 (range 43-91). 90% of ID biopsies were targeted at an endoscopic lesion. All cases were associated with some degree of inflammation.
Eleven (50%) patients underwent follow-up (FU) biopsies (mean interval: 5.8 month, range 1–24), 5 of which multiple re-biopsies. 4/11 (36.4%) had abnormal findings: 1 LGD, 2 adenocarcinomas diagnosed at first re-biopsy (both within 2 months) and the remaining patient an intestinal-type adenoma at 8 month and adenocarcinoma at 2 years re-evaluation. 7/11 (63.6%) had normal findings on re-biopsy, including the 2 cases without endoscopic lesion.
Conclusion: Gastric dysplasia in biopsies is infrequent, but presents a significant risk of malignant progression. Cases diagnosed as "indefinite for dysplasia" show heterogeneous outcomes. Close surveillance and prompt re-biopsy are essential, particularly when endoscopic lesions are present.

PS-20-006
Establishment and application of the Operative Link on Gastric Low-grade Dysplasia assessment (OLGLD) system based on biopsy specimens
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Background & Objectives: For patients with low-grade dysplasia (LGD) detected through biopsy, identifying factors related to endoscopic treatment is crucial.We established an operative link on gastric low-grade dysplasia assessment (OLGLD) system to predict the progressive risk of LGD in biopsy specimens, in order to propose new follow-up or treatment strategies for patients with LGD.
Methods: The OLGLD system was established based on whether goblet cells were present in LGD glands, the degree of LGD involvement (including horizontal and vertical involvement) and whether LGD glands involved margins in the first biopsy specimens of 527 patients with LGD, and was set different scores based on the incidence of advanced neoplasia in second biopsy or endoscopic resection specimens.
Results: According to the OLGLD system, there were significant differences in the incidence of advanced neoplasia for different indicator scores, total scores, or risk scores, and high-risk patients were identified through risk scores. For visible LGD lesions with clear margins, although the OLGLD system identified high-risk patients, there was no significant difference in the incidence of advanced neoplasia in lesions with $\geq$ 1cm in size, lesions with medium to high-risk scores and lesions with $\geq$ 1cm in size and lesions with medium to high-risk scores. The incidence and the risk of advanced neoplasia in patients with visible and unclear marginal LGD lesions of OLGLD high-risk scores were higher than that in patients with visible and unclear marginal LGD lesions. For invisible lesions, although no patients had advanced neoplasia during follow-up, and the OLGLD scores were mainly low-risk scores, the probability of re-detecting LGD for medium-risk-score lesions was significantly higher than that for low-risk-score lesions.
Conclusion: Although gastric mucosal biopsy through endoscopy showed LGD lesions, the OLGLD system was beneficial for screening high-risk patients.

PS-20-007
Clinical insights about the diagnoses of colonic high-grade neuroendocrine tumours and neuroendocrine carcinomas
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Background & Objectives: In the recent WHO classification of Neuroendocrine neoplasms (NENs), neuroendocrine carcinomas (NECs) were separated from the category of neuroendocrine tumours (NETs) based on behaviour, morphology, molecular findings, treatment, and prognosis.
Occasionally, grade I/II NETs (GI/GII) can show progression to a GIII-NET, demonstrated by morphology, necrosis, or an increase in the Ki67-proliferative index. NECs lack (*MEN1/DAXX/ATRX)* mutations identified in GIII-NETs, harbour *TP53* and *RB1* mutations.
Methods: A 6-year retrospective review of cases diagnosed as colonic NETs and NECs was performed as a quality assurance project to determine if the diagnoses of GII/GIII-NETs was based on

morphology or KI67-proliferative index or mitoses. Our electronic medical record system retrieved the cases using a natural language search for "colon neuroendocrine" from 01/2019 to 01/2025.
The reports and slides of the GII-NETs, GIII-NETs and NECs were reviewed. Data regarding these biopsies (site, morphology, mitotic rate, Ki67-proliferative index) was recorded.
Results: One hundred nineteen specimens (NET:119/NEC:6) were identified. The details of these diagnoses and analyses are shown in Figure 1.
Figure 1
Conclusion: The most common NENs of the colon are rectal GI-NETs. Colonic NECs are rare. SCC is the most common type. The most common diagnostic pitfall was dismissing the morphology of SCC due to low KI67-indexes (30-40%), and/or mitotic rates. Patient A's had recurrent GIII-NETs but there were foci with SCC-morphology that showed loss of RB1/TP53 expression suggesting a rare progression to SCC.Morphology and no Ki67-proliferative index or mitoses is what distinguish NECs from GII or GIII-NETs. Other differentials should always be excluded, such as poorly-differentiated carcinomas with neuroendocrine features, metastatic NECs. The underlying molecular alteration of NET's progression to SCC still needs to be understood. Clinical and radiological correlation, stains (Rb, p53, INSM1) or NGS studies help in the differential diagnosis of challenging cases, and guide the clinical team toward an appropriate treatment.

PS-20-008
Evaluation of the demographical and histomorphological features and turnaround times of Bowel Cancer Screening Programme biopsies in a district general hospital in the UK – an audit
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Background & Objectives: The NHS Bowel Cancer Screening Programme (BCSP) is a UK-wide initiative aimed at early detection of bowel cancer to reduce mortality rates, offered to individuals aged 50 or above. The BCSP sets specific standards for pathologists reporting these biopsies. This audit aimed to evaluate the demographic profile of patients undergoing BCSP, the histomorphological features of detected lesions, the turnaround times (TATs) of BCSP biopsies compared to national standards, and to identify areas of excellence and opportunities for improvement.
Methods: An electronic search of the local histopathology reports from the hospital database was performed to identify the BCSP cases between January 2023 and January 2024. Reports were reviewed regarding age, gender, locations, number of polyps, diagnoses, and TATs.
Results: A total of 686 patients and 1851 specimens were identified. There were 424 males (61,8%) and 254 females (38,2%) with an average age of 66. Multiple specimens were received in 62,9%. The majority of specimens were localised in the rectosigmoid colon, followed by the transverse colon. The most common type of lesion was adenomatous polyps, with a total of 1205 lesions, constituting 67% of all lesions. Of these, 55% were tubular adenomas, 11% were tubulovillous adenomas, and <1% were villous adenomas. The high-grade dysplasia (HGD) rate in adenomatous polyps was 2,8%. Serrated lesions constituted 25% of all lesions, and all other diagnoses were detected in <10%. The average TAT was 3,18 (1,05-13,7) days.
Conclusion: The distribution of diagnoses aligns well with national BCSP data and demonstrates compliance with the national standards with excellent TATs, meeting patient management needs effectively. There is a slight underdiagnosis in HGD rates compared to the expected benchmark. To conclude, strengthening training and quality assurance measures to improve HGD detection should be performed while maintaining high standards in cancer reporting and TATs.

PS-20-009
Tumour and cytotoxic T cell proliferation patterns in colorectal cancer
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Background & Objectives: Tumour cell proliferation is a prognostic tool in many cancers, but in colorectal cancer (CRC) results have been conflicting. Recently, intratumoral T cell proliferation has been associated with longer survival, but the mechanisms are complex and poorly understood. Our aim was to thoroughly evaluate the role of proliferation in tumour and CD8+ T cells in CRC.
Methods: We performed multiplex immunohistochemistry for MKI67 (Ki-67), CD8, and CK on two large CRC cohorts (N=1839). Additionally, we utilized Single-cell RNA sequencing data (N=62) to more characterize molecular features and signalling pathways of proliferating and non-proliferating cells.
Results: Tumour cell proliferation associated with improved cancer-specific survival (multivariable HR for high vs. low 0.60, 95%CI 0.43-0.83 in the larger cohort), downregulation of epithelial mesenchymal transition, and upregulation of MYC signalling. Higher proliferation correlated with an anti-tumorigenic microenvironment, marked by high densities of T cells, M1-like macrophages, and mature monocytic cells, and low densities of M2-like macrophages and immature monocytic cells (all $p<0.05$). Amongst immune cells, proliferating CD8+ T cells showed high expression of effector molecules such as GZMB and IFNG and were more strongly associated with favourable outcome than non-proliferating CD8+ T cells (multivariable HR for high vs. low 0.49, 95%CI 0.35-0.70 in the larger cohort). Spatial analysis revealed that proliferating CD8+ T cells were located 47% closer to tumour cells than non-proliferating CD8+ T cells, and the prognostic significance for both subsets was comparable when evaluating their proximity to tumour cells.
Conclusion: Cancer cell proliferation in CRC is associated with improved survival. Proliferating CD8+ T cells emerged as a stronger prognostic marker than non-proliferating CD8+ T cells, though this difference diminishes with closer spatial proximity to tumour cells. These results highlight the complex relationships between proliferation dynamics and the immune landscape in CRC.

Funding: This study was funded by Cancer Foundation Finland (59-5619 and 69-7354 to JPV), Finnish Medical Foundation (6021 to JPV; 6259 to MK), Oulu Medical Research Foundation (to MK), Cancer Society of Northern Finland (to MK), Sigrid Jusélius Foundation (230229 to JPV), and Finnish State Research Funding (to MJM and JPV). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

PS-20-010
Is there a relationship between synchronous CD47/SIRPα and PD-L1 expression in advanced colon adenocarcinoma?
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Background & Objectives: This study aims to determine the synchronous expression of CD47/SIRPα and PD-L1 in colon adenocarcinoma and to investigate their effects on clinicopathological factors and prognosis.
Methods: Immunohistochemical synchronous expression of CD47 (D3O7P), SIRPα (D6I3M) and PD-L1 (22C3) and their association with clinicopathological factors were examined in formalin-fixed paraffin-embedded specimens of 106 primary colon adenocarcinomas. CD47 and SIRPα was scored as 0% (score 0), 1-10% (1 point), 10-50% (2 points) and >50% (3 points) in tumour cells. Combined positive score (CPS) was used for PD-L1.
Results: There was a statistically significant positive relationship between pT3 and pT4 and PD-L1 and CD47 tumour cell expressions. CD47 expression was found to be ≥1% in all clinical stage 4 ($p<0.001$) and metastatic patients ($p<0.001$). 76.9% of pT4 patients had CD47 expression ($p=0.006$). CD47 was negative in 67.3% of patients with tumour budding score 1 ($p<0.001$). CD47 staining above 1% was detected in 76.5% of the patients with lymphovascular invasion ($p<0.001$). CD47 was positive in 34 (87.2%) of 39 (36.8%) patients with PD-L1 CPS ≥ 1% ($p<0.001$). While the mortality risk of patients with CD47 staining intensity ratio of 1-10% and 11-50% was 1.4 times higher than that of patients with <1%, the mortality risk was 3.89 times higher in patients with >50%, indicating that these results were a poor prognostic factor ($p<0.001$). There was a statistically significant difference between survival rates with CD47 staining intensity >50% ($p=0.003$).
Conclusion: It was understood that synchronous expression could occur in different cells of the same tumour. If the CD47 expression rate is high, it can be thought that it indicates the patients' possible clinical stage and pT elevation, N, and M. Additionally, proving synchronous expression associations will enable us to better understand their roles in colon adenocancer, how they affect the tumour microenvironment, and how to manage their immunotherapeutic targets.

Funding: Hitit University Scientific Research Projects Coordination, Çorum, Türkiye

PS-20-011
Metastatic renal cell carcinoma in the gastrointestinal tract, an easily missed entity
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Background & Objectives: Renal cell carcinoma (RCC) usually metastasizes to lung, bone, liver, and brain. Metastasis of RCC to the gastrointestinal (GI) tract is rare. In this study, we analysed the metastatic RCCs in the GI tract.
Methods: We queried our records for metastatic RCCs in the GI tract from 1990 to 2024. Twenty cases were included. We analysed RCC types, metastatic locations, and the duration of metastasis after renal resection.
Results: Fifteen males and five females were included with an average age of 67 (ranging from 47 to 83). Sixteen cases were clear cell RCC (80%), three were chromophobe RCC (15%) and one was unclassified RCC (5%). Sixteen cases had nephrectomy in our institute. The GI metastatic incidence of RCC was 0.8% (16/2019). The metastatic sites were stomach (9/20, 45%), duodenum (7/20, 35%), and colorectum (4/20, 20%). The average duration of metastasis after nephrectomy was 80±16 months. As we expected, the lower pathological stages (pT1 and pT2) took much longer time (164±32 months, N=5) to metastasize than the higher pathological stages (pT3 and pT4, 62±13 months, N=11, $p<0.01$). Interestingly, two out of seven duodenal metastatic RCC were misdiagnosed as granulation tissue at the first diagnosis. The misdiagnosis rate of duodenal metastatic RCC was 29% (2/7). One out of nine gastric metastatic RCC was misdiagnosed as poorly differentiated gastric adenocarcinoma. The misdiagnosis rate of gastric metastatic RCC was 11% (1/9). All these three misdiagnosed cases were clear cell RCC.
Conclusion: Metastatic RCC in the gastrointestinal tract was rare (0.8%). The most common metastatic RCC was clear cell RCC (80%), and the most common locations were stomach and duodenum. The misdiagnosis rate in the duodenum and stomach was high (29% and 11%). When metastatic RCC is suspected in the duodenum and stomach, immunohistochemical stains should be performed to rule out metastatic RCC.

PS-20-012
PRMT5 regulates the proliferation of colorectal cancer by influencing NK cells
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Background & Objectives: Colorectal cancer patients still exhibit immunotherapy resistance. Protein arginine methyltransferase 5 (PRMT5) and natural killer (NK) cells play important roles in tumorigenesis and immune escape by mediating the symmetrical dimethylation of arginine between histone and nonhistone proteins. However, whether PRMT5 regulates NK cell phenotypic plasticity and functional polarization remains unknown.
Methods: Multiple immunofluorescence staining of PRMT5, CD16, CD56, IL-1R8 and TIGIT was performed on samples from a total of 180 patients with CRC. NK92 cells overexpressing PRMT5 were constructed via lentiviral transduction and cocultured with CRC cells. The cytotoxicity of NK cells against tumour cells was detected. CRC cells were cocultured with PRMT5 inhibitor NK cells, and the proliferation of NK cells was detected. The expression of CD16, CD56, PRMT5, TIGIT and IL-1R8 was detected by flow cytometry. The effect of NK cells on the proliferation of CRC cells was detected by establishing a tumour-bearing mouse model with PRMT5 overexpression or PRMT5 inhibition.
Results: The change in the NK cell phenotype that occurs in the immune microenvironment of bowel cancer is closely related to the high expression of PRMT5 in the interstitium of bowel cancer patients. We found that PRMT5 is critical for peripheral NK cell maintenance. PRMT5 overexpression significantly reduced the cytotoxicity of NK cells. After the inhibition of PRMT5, the ability of NK cells to secrete cytokines was weakened, and the cytotoxicity was significantly enhanced. NK92 cells killed colorectal cancer cells, and overexpression of PRMT5 inhibited this effect and promoted CRC cell proliferation. The cytotoxicity of NK-92 cells supplemented with PRMT5 inhibitors was reduced, and the growth of colorectal cancer tumours was significantly inhibited.
Conclusion: PRMT5-silenced NK cells were still beneficial for the treatment of CRC with an immunodeficient microenvironment.PRMT5 is a potential therapeutic target for NK cells in colorectal cancer.

PS-20-013

Exploring the relationship between histologic features and genomic profiles in gastric cancer

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Background & Objectives: Gastric cancer remains the fourth leading cause of cancer-related death. In stage IV disease, treatment decisions are guided by biomarkers such as C-erbB2, PD-L1, microsatellite instability, EBV, Claudin 18.2. However, these markers do not always accurately predict treatment response. Recent studies highlight the role of stromal components, including cancer-associated fibroblasts and tumour-infiltrating lymphocytes, in modulating drug sensitivity, though their genomic associations are not well defined. Advances in artificial intelligence-based digital pathology have enabled prognosis prediction and histology–genomic correlation in various cancers, but such integrative analyses are limited in gastric cancer. This study aims to explore the relationship between histologic features and genomic profiles to support therapeutic decision-making.
Methods: We analysed 405 patients with metastatic or recurrent gastric cancer who underwent next-generation sequencing (NGS) at Seoul National University Bundang Hospital from January 2020 to December 2023. Patients were subgrouped based on histologic type (e.g., tubular adenocarcinoma, poorly cohesive carcinoma, signet ring cell carcinoma, and others) and stromal reactions (lymphocytic infiltration, desmoplasia). Clinicopathological and molecular data were collected. Differences in NGS results among subgroups were evaluated, and associations between genetic mutations and clinicopathological or molecular features were analysed.
Results: TP53 mutation was the most common genetic alteration in all histologic subtypes except signet ring cell carcinoma, in which CDH1 mutation was predominant. BRCA2 mutations were frequently observed in the mixed adenocarcinoma (intestinal type dominant) subgroup, while KRAS mutations were common in the mucinous adenocarcinoma subgroup. Among desmoplasia subgroups, the highest-grade group showed a significantly higher frequency of CDH1 mutations compared to others.
Conclusion: This study demonstrates a correlation between histologic subtypes, genomic alterations, and clinicopathologic features in gastric cancer. Integrating histologic and molecular profiles may help predict patient prognosis and response to therapy, providing a foundation for more personalized treatment approaches.

Funding: Seoul National University Bundang Hospital grants

PS-20-014

Barrett's e-learning module leads to significant improvement of pathologists' assessment of oesophageal Barrett's biopsies with(out) dysplasia

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Background & Objectives: Assessment of Barrett's oesophagus (BE) biopsies is associated with significant interobserver variability. In the Netherlands we established an expert panel consisting of 15 quantitatively trained gastro-oesophageal (GE) expert pathologists, available for Dutch colleagues for consultation purposes but not readily accessible elsewhere. Using this panels' expertise, we built an e-learning module with which we investigated whether this module significantly improves diagnostic consensus within a large pathologist cohort.
Methods: The e-learning module consisted of an online platform containing 25 biopsy test cases (H&E and p53-slide) covering the BE diagnostic spectrum (11 non-dysplastic BE, 2 indefinite-for-dysplasia, 8 low-grade dysplasia, 4 high-grade dysplasia), followed by an evidence-based theoretical section, after which the same re-randomized 25 cases were re-assessed. All cases were selected from the expert panels' archives, with consensus of at least 75% of panel members ("gold-standard diagnosis"). Demographics of participants were recorded and concordance with the gold standard, as well as Cohen's Kappa, were calculated for pre- and postmodule results.
Results: 192 pathologists (including residents) enrolled and 124 participants finished the module (65%), 40% of which were general pathologists, 33% residents and 27% GE-pathologists. 65% of assessors had less than 10 years' experience assessing BE biopsies. Mean concordance with gold standard diagnosis was 81% pre-module and 85% post-module (p=0,0000) for dysplasia, corresponding to mean Cohen's kappa of 0,64 and 0,71 (p=0,0000). Both general pathologists and residents showed significant improvement of their BE biopsy assessment after working through the module. GE-pathologist also showed some improvement, albeit not significant.
Conclusion: This Barrett's e-learning module, built with the expertise of an expert pathology panel, leads to significant improvement of pathologists' assessment of BE biopsies. This implies that this module could be helpful in areas in which expert consultation is not readily available, in order to improve inter- and intrapathologist variability.

PS-20-015

Diagnostic variability in assessment of Barrett's oesophagus biopsies: creating awareness through laboratory-specific feedback reports

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Background & Objectives: Assessment of Barrett's oesophagus (BE-) biopsies is associated with significant inter- and intra-laboratory diagnostic variability, notably leading to overdiagnosing of dysplasia and therefore higher disease burden and health care costs. The aim of this study was to improve accuracy and decrease diagnostic variability on pathologist- and laboratory level. On pathologist-level, an e-learning was offered. On laboratory-level, feedback reports were sent out, benchmarking the individual laboratory against other Dutch laboratories. This abstract focusses on the laboratory-level results.
Methods: All protocolled reports of oesophageal BE-biopsies ± neoplasia were retrieved from the national pathology database for two six-month time periods, with the e-learning offered in between. Biopsies were classified according to the Vienna classification. For the two time periods, mean % grading per diagnostic category was calculated. An overall deviation score (ODS), representing the sum of deviations from the grade-specific overall proportions, was calculated to compare the absolute deviation for all grades at once. Case-mix correction was performed by multivariate logistic regression analyses, providing laboratory-specific ORs for non-dysplastic BE (NDBE) versus dysplastic BE. Individual laboratories received feedback reports where they were benchmarked against all other Dutch laboratories.
Results: After feedback and the offered e-learning module, no significant decrease in neoplastic diagnoses was reported on a national level

after case-mix correction (p=0,12). On individual laboratory level, 1/10 laboratories showed a significant decrease in neoplastic diagnoses (p=0,001). Comparing two time periods without case-mix correction, there is a trend towards less neoplastic diagnoses. Mean grading was 68% NDBE, 5% indefinite-for-dysplasia, 10% low-grade dysplasia (LGD), 3% high-grade dysplasia, 13% (suspected) carcinoma. ODS showed 45% versus 53% of laboratories falling within 95% confidence interval (CI) for the two time periods.
Conclusion: After laboratory-specific feedback and the e-learning, a trend towards more NDBE and less LGD diagnoses was observed. However, diagnostic grading behaviour of BE-biopsies didn't change significantly on laboratory- nor national level.

PS-20-016
Predictive value of superficial spreading feature for lymph node metastasis in T1b oesophageal squamous cell carcinoma and its implication for endoscopic resection
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Background & Objectives: Recently, endoscopic resection (ER) can be considered as the standard for care for selected T1b oesophageal squamous cell carcinoma (ESCC). It is well established that lymph node metastasis (LNM) is a key prognostic factor for T1b ESCC. Therefore, ER of T1b ESCC is suitable for lesions that have no or low risk of LNM. However, endoscopic findings for prediction of LNM are limited. Little is known about the significance of superficial spreading (SS) feature extending along the long axis of the oesophagus. This study aimed to evaluate the predictive value of SS feature for LNM and its implication for ER.
Methods: The study included 78 patients with T1b ESCC who had undergone esophagectomy with LN dissection. The incidence of LNM was compared according to SS length. We evaluated possible predictive SS length for LNM using the receiver operating characteristic (ROC) curve. We also evaluated the relationship between SS feature and other clinicopathological findings.
Results: The prevalence of LNM was 34.6% (27/78) and SS length was distributed from 1.2 cm to 10.9 cm. SS length was significantly correlated with LNM ($p = 0.043$) and marginally associated with depth of submucosal invasion ($p = 0.066$). However, SS length was not correlated with other clinicopathological findings. When we established the cutoff value for SS length (3.1 cm) by ROC curve, SS (≥3.1 cm) types tended to increase the risk of LNM than non-SS (<3.1 cm) types, but not significantly ($p = 0.057$).
Conclusion: Our data suggest that SS feature of T1b ESCC is a potentially useful marker for predicting LNM, although SS feature failed to demonstrate definitive evidence of significance. Based on these results, SS feature could be employed to decision-making by endoscopists with regard to which patients should best undergo ER. Further elucidation is needed to determine the significance before implementation into clinical practice.

PS-20-017
IgG4-related esophagitis – new kid on the block?
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Background & Objectives: IgG4-related esophagitis is a rare manifestation of IgG4-related disease and therefore not well recognized among pathologists. We hereby present six cases of IgG4-related esophagitis diagnosed at our institution between 2019 and 2025.
Methods: The institutional database was searched for all cases of IgG4-related esophagitis and the respective slides were reviewed. Diagnosis was validated in six cases (5 biopsies, 1 oesophageal resection) and correlated with clinical data.
Results: Three of the patients were female, three were male with a mean age of 61 years (range 54-74). Most patients had reflux symptoms (epigastric pain and/or regurgitation; 5/6) and dysphagia (4/6). In one case, the whole oesophagus was involved, while in the other 5/6 the lesions were confined to the distal third. Ulcerations were present in 100%, oesophageal stenosis in 50% of cases. None of the patients had any suspected or confirmed involvement of IgG4-related disease in another organ and only one had elevated serum IgG4 levels. In all cases, multiple rounds of biopsies were undertaken until diagnosis was made (mean 4, range 2-9), with the time to diagnosis ranging from 3 months to 18 years. Histologically, plasma cell dominant inflammation was present in all cases, with a range of 50 to >100 IgG4 positive plasma cells per HPF and an IgG4/IgG ratio of 30-95%. Follow-up was available for three patients, all of whom had clinical and histological remission after treatment with topical budesonide (3/3). However, 2/3 developed candidal esophagitis under therapy, and disease recurred in both patients after termination of steroid treatment.
Conclusion: IgG4-related esophagitis responds very well to corticosteroids but is easily overlooked in histology, in particular when tissue is only superficially sampled. With this case series, we want to highlight the importance of IgG4 immunohistochemistry in ulcerative esophagitis with plasma cell-predominant inflammatory infiltrate.

PS-20-018
Clinicopathological characterisation of Epstein–Barr virus-associated gastric cancer: a single-institution Polish study
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Background & Objectives: Epstein–Barr virus-associated gastric cancer (EBVaGC) is one of the four molecular subtypes of GC according to The Cancer Genome Atlas project. There is still a significant gap in understanding its clinicopathological features in geographical regions other than Asia. This study aimed to provide a characterisation of patients with EBVaGC based on postoperative material from the National Research Institute of Oncology in Warsaw, Poland.
Methods: A total of 262 cases with primary GC, who underwent gastrectomy between 2008 and 2018, were included. The tumour staging was assessed according to the 8th edition of the TNM classification. The morphology was evaluated using the Laurén and the 5th edition of the WHO classification. EBV was detected by chromogenic in situ hybridization with the INFORM EBER Probe. Stromal tumour-infiltrating lymphocytes (sTILs) were examined by a semi-quantitative method described by International Immuno-Oncology Biomarker Working Group (IIOBWG). All statistical analyses were conducted using R4.1.1 (R Core Team, 2021) package.
Results: EBER positivity was present in 12.21% of GC. Significant differences were noted in gender ($p<0.001$), age ($p=0.018$), tumour size ($p=0.039$), location ($p=0.003$), and morphological type ($p<0.001$). EBVaGC exhibited a negative association with the presence of mucous lakes ($p=0.004$), signet ring cells ($p=0.005$), tertiary lymphoid structures ($p=0.031$). EBVaGC was characterized by significantly more abundant sTILs within both the central tumour area and the invasive margin ($p<0.001$). No significant differences between EBVaGC and

EBV negative GC (EBVnGC) were found in terms of neuroinvasion, angioinvasion, and (y)pT, (y)pN, (y)pM parameters.
Conclusion: Findings suggest that Poland may excel in prevalence of EBVaGC compared to other countries. Patients with EBVaGC revealed significant clinicopathological differences from those with EBVnGC. The WHO classification proved to be more useful for morphologically categorising EBVaGC compared to Laurén's classification. It was shown that sTILs measured by the IIOBWG method are significantly more abundant in EBVaGC than in EBVnGC.

Funding: The work was co-financed by a donation from Roche company for the purchase of the INFORM EBER probe – donation number 54/D/7/8/2016

PS-20-020

Prognostic and immunological significance of stromal maturity and proportion in colorectal cancer

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Background & Objectives: Tumour-stroma ratio (TSR) and desmoplastic reaction (DR) classification are prognostic factors potentially linked with the composition of the tumour microenvironment. This study examines the prognostic and immunological significance of TSR, DR classification, and their combined assessment in colorectal cancer.
Methods: TSR and DR classification were evaluated using H&E-stained slides in two colorectal cancer cohorts (N=1,876). We introduced a three-tiered Stroma Maturity and Proportion Score (SMAPS), based on the presence of high (>50%) TSR in the tumour centre and myxoid stroma (immature DR classification) at the invasive margin. Computational assessment of Alcian Blue staining (pH 2.5) intensity was used to quantify myxoid stroma. Multiplex immunohistochemistry, combined with digital image analysis, was utilized to study immune cell densities associated with SMAPS, TSR, DR classification and Alcian blue intensity.
Results: In the study cohort (N=1,100), both TSR (HR for stroma-high vs. stroma-low: 1.49, 95%CI: 1.15-1.93; P=0.003) and DR classification (HR for immature vs. mature DR: 1.84, 95%CI: 1.39-2.45; P<0.0001) were independent prognostic factors for cancer-specific survival. SMAPS demonstrated stronger prognostic value (HR for high vs. low SMAPS: 2.01, 95%CI: 1.47-2.75; P<0.0001) compared to TSR and DR classification alone. Stroma-high TSR, immature DR, and high SMAPS were associated with lower densities of $CD3^+$ T cells, $CD20^+CD79A^+$ B cells, M1-like macrophages, $CD66b^+$ granulocytes in both the tumour centre and invasive margin (P<0.05 for all). Alcian blue staining was associated with the immature DR group identified on H&E-stained slides and showed similar immune cell associations. Validation cohort (N=776) confirmed the independent prognostic significance of SMAPS.
Conclusion: SMAPS is a promising prognostic tool that integrates stromal maturity at the invasive margin and stromal proportion in the tumour centre, both being associated here with an immunosuppressive microenvironment characterized by lower densities of antitumorigenic immune cells.

Funding: This study was funded by Cancer Foundation Finland (59-5619 and 69-7354 to JPV), Emil Aaltonen Foundation (220257P to JPV), Finnish Medical Foundation (6021 to JPV), Sigrid Jusélius Foundation (230229 to JPV), and Finnish State Research Funding (to MJM and JPV). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The first author has no personal grants to disclosure

PS-20-021

Axial margin sampling in colorectal cancer bowel resections – is it necessary?

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Background & Objectives: Adequacy of excision is an important prognostic factor in pathological examination of colorectal cancer resection specimens. Some studies advocate that sampling of axial margins is unnecessary if they are macroscopically clear. Criteria for retrospective margin sampling recommended by the Royal College of Pathologists are tumours showing aggressive morphological features such as signet ring cell morphology, extensive lymphovascular invasion and exceptionally infiltrative growth patterns. This study reviews the prevalence of axial margin involvement and associated tumour characteristics to determine whether and when sampling is necessary.
Methods: A search of the pathology department database at a single tertiary centre was performed for colorectal adenocarcinoma resection cases received over a 6 year period (January 2017 to December 2023). These were reviewed for tumour characteristics (TNM stage, lymphovascular invasion, perineural invasion) and margin status.
Results: 1015 colorectal adenocarcinoma resection cases (835 colonic & 180 rectal) were identified, of which 58(5.7%; 45 colonic, 13 rectal) had only circumferential (radial) margin involvement, and four (0.4%; 2 colonic, 2 rectal) had both circumferential and axial margin involvement. None had involved axial margin(s) without concurrent radial margin involvement. Tumour was macroscopically more than 3 cm from an involved axial margin in three (2 colonic, 1 rectal) cases. All were moderately differentiated, and showed serosal involvement, lymphovascular and perineural invasion and extensive nodal disease.
Conclusion: Axial margin involvement in colorectal resections is uncommon (<1%), which supports selective sampling of axial margins for carcinoma with high-risk features when tumour is macroscopically more than 3 cm away. The high-risk features identified in our study were circumferential margin involvement with simultaneous serosal involvement, lymphovascular invasion, perineural invasion, and extensive nodal disease. Poor differentiation such as signet ring cell morphology did not appear to be associated with axial margin involvement.

PS-20-022

Histological signature for risk stratification of lymph node metastasis in early-stage colorectal cancer (pT1)

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Background & Objectives: In pT1 colorectal cancer (CRC), there are no specific histopathological features that accurately predict lymph

node metastasis (LNM) to guide treatment after endoscopic resection. The aim of this study was to define a histological signature by combining various morphological parameters to predict regional LNM.
Methods: A total of 223 pT1 CRC cases from 223 patients (94 women and 129 men) were selected, 89 of whom had LNM at diagnosis. The parameters analysed included tumour grade differentiation (GTD), angiolymphatic invasion (ALI), perineural invasion (PI), tumour budding (TB), poorly differentiated clusters (PDC), vertical resection margin (VRM), and submucosal invasion (ISM). A univariate significance test was first performed to assess each parameter's relationship with LNM. Then, GTD, ALI, PDC, VRM, and ISM were analysed together in a multivariate analysis, considering all possible variable combinations into four risk categories: Very High Risk (VHR), Moderate High Risk (MHR), Moderate Low Risk (MLR), and Very Low Risk (VLR).
Results: The univariate analysis revealed that GTD, ALI, TB, PDC, and ISM had a statistically significant association with LNM, but each variable alone predicted less than 60% of LNM cases. When combining these parameters into risk groups the analysis showed a better predictive power (87% vs. 59.6%) compared to single variables. Statistically significant differences were found between metastasis proportions across the risk groups (VHR: $p<0.001$, MHR: $p<0.01$, MLR: $p=0.05$, and VLR: $p<0.01$). However, when the most favourable value combination was used, 10% of patients with LNM were missed (false negatives).
Conclusion: The combination of multiple high-risk parameters demonstrated better predictive power than individual markers alone and provided a four-group risk classification based on metastasis proportions. However, to avoid false negatives cases new technologies are needed to identify biomarkers in pT1 CRC that can better stratify the risk of LNM.

Funding: Project TED2021-131248B-I00 funded by MCIN/AEI /10.13039/501100011033 and by the European Union NextGenerationEU/ PRTR

PS-20-023

Gastric cancer whole-genome sequencing identifies peculiar mutational profile in Northeast Brazil

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Background & Objectives: Gastric cancer (GC) is a heterogeneous disease. Next-Generation Sequencing (NGS) has improved our understanding, but the molecular classifications currently proposed are based on European and Asian patients, such as the TCGA network and the ACRG, respectively. Thus, the aim of this study was to evaluate the most commonly mutated genes in GC samples from Brazil and compare it to the TCGA database.
Methods: Exome sequencing of 62 patients from Northeast Brazil was performed using the Illumina NextSeq 1000 platform. The exome library was prepared using SureSelect All Exon V8. Copy number alterations were identified using PURPLE. For somatic variant analysis, raw sequencing data were processed using the nf-core/sarek 3.4.2 pipeline. Reads were aligned to the GRCh38 reference genome using BWA-MEM, followed by duplicate marking and base quality score recalibration (BQSR) with GATK. Somatic variant calling was performed using a combination of tools integrated into the pipeline, including Mutect2, Strelka2, and Lancet, ensuring high sensitivity and specificity.
Results: We identified 10 top-mutated genes (*TTN, MUC4, EPPK1, PKD1, MUC12, MUC19, ZBED3, MUC5AC, MUC16* and *DST*, respectively). Comparing to TCGA network, most of these genes presented a divergent mutational profile. Mutations in *TTN* was observed in 82% of our sample comparing to 51% of TCGA. Likewise, *MUC16, MUC4, EPPK1, PDK1* and *MUC12* were much more commonly mutated in our population (45%, 81%, 58%, 56% and 50%, respectively, compared to 31%, 6%, 5%, 7% and 0% in the TCGA database, respectively). On the other hand, commonly mutated genes in the TCGA, such as *TP53* and *ARID1* (46% and 27%, respectively), were rarely abnormal in our sample (11% and 15%, respectively).
Conclusion: This data suggests that the GC mutational profile in Northeast Brazil is unique, with some important divergence from the TCGA network, and highlights that a broader global evaluation would contribute to a better understanding of GC.

PS-20-024

Comparison of PD-L1 assays in oesophageal squamous cell carcinoma

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Background & Objectives: Oesophageal squamous cell carcinoma (ESCC) comprises 84% of oesophageal cancers, with poor prognosis due to late diagnosis and limited treatment. Immunotherapy targeting programmed death-1 (PD-1) and programmed death-ligand 1 (PD-L1) has demonstrated improved survival outcomes, yet variability in PD-L1 testing platforms and scoring methods presents challenges. This study aims to evaluate the concordance between PD-L1 immunohistochemistry (IHC) assays, specifically 22C3 and 28-8, in ESCC using tumour proportion score (TPS) and combined positive score (CPS) methodologies to address inconsistencies in testing approaches.
Methods: PD-L1 expression in 200 ESCC cases at Asan Medical Centre was assessed using whole-slide sections from biopsy or surgical resection specimens. Two standardized PD-L1 assays (Dako 22C3 pharmDx and Dako 28-8 pharmDx) were evaluated following manufacturer protocols. Staining was independently scored by two pathologists using TPS with $\geq$1%, $\geq$10% and $\geq$50% cut-offs, and CPS with $\geq$1%, $\geq$10% and $\geq$50% cut-offs.
Results: Both assays showed similar distributions at lower cutoffs. At CPS $\geq$50%, positivity was higher with 28-8 (31%) than 22C3 (23%). Similarly, at TPS $\geq$50%, 28-8 showed more positive cases (24%) than 22C3 (18%), indicating potential differences in assay sensitivity at higher PD-L1 expression levels. Concordance on a continuous scale among the assays was good for CPS [intraclass correlation coefficient (ICC) range 0.76–0.85] and TPS (ICC range 0.78–0.87). Stratification by variable cut-offs demonstrated moderate to good agreement between the two assays, as analysed by Gwet's AC1. No statistically significant correlations between PD-L1 expression and clinicopatholoic parameters were identified. Non-significant trends emerged for tumour differentiation status with 22C3 (TPS, $p = 0.054$) and survival outcomes with 28-8 (TPS, $p = 0.073$), indicating potential biological associations requiring validation in expanded datasets.
Conclusion: Notable concordance was found among 22C3 and 28-8 assays, suggesting their potential interchangeability in selecting patients with ESCC for immune checkpoint inhibitor.

PS-20-025

Spatial transcriptomics reveal lineage complexity of gastric incomplete intestinal metaplasia and its association with gastric cancers

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Background & Objectives: Incomplete intestinal metaplasia (Inc IM) is a precancerous lesion associated with an increased risk of gastric cancers (GCs); however, its molecular characteristics remain inadequately defined. This study aimed to elucidate the unique molecular phenotype and lineage complexity of Inc IM.
Methods: We utilized single-cell resolution spatial transcriptomics (Xenium) on gastric tissue samples—including normal mucosa, various IM subtypes, and GCs—using a customized panel of 294 organ-specific genes for enhanced cellular characterization. Pure organoid lines derived from human gastric tissues representing normal mucosa, complete IM (Com IM), and Inc IM were generated. Single cell RNA sequencing (scRNA seq) was performed to assess in vitro differentiation with Bone Morphogenic Protein (BMP) treatment.
Results: Inc IM exhibits mixed lineage features with distinct populations expressing both gastric and intestinal markers, whereas Com IM closely resembles small intestine architecture. A minute gland consisted of Inc IM cell clusters, representing very early Inc IM was identified in chronic gastritis, showing the upregulation of intestinal markers (e.g., DMBT1 and REG4) alongside downregulation of gastric markers. Interestingly, mixed gastric and intestinal phenotype was observed in both surface differentiated cells and stem/progenitor cells in Inc IM. When assessing the cell types in GCs, Inc IM cell clusters were more frequently associated with GC, particularly in MSS/TP53– and MSS/TP53+ molecular subtypes, underscoring its potential origin in gastric carcinogenesis. The BMP-induced expression changes in organoid models recapitulated in vivo observations, validating their utility for studying gastric metaplasia.
Conclusion: We demonstrated unique molecular phenotype and lineage complexity of Inc IM, emphasizing its significance as a precancerous lesion in gastric tissues. Our IM organoid lines lay the groundwork for future investigations into the epigenetic and transcriptional dynamics of metaplastic changes, highlighting the critical role of Inc IM in GC development.

Funding: This research was supported by a grant of the MD-Phd/Medical Scientist Training Program through the Korea Health Industry Development Insti ute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (RS-2024-0043931)

PS-20-026

Interobserver variability of histopathological risk factors for lymph node metastasis in pT1 colorectal carcinoma

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Background & Objectives: Colorectal carcinoma (CRC) diagnosed at stage pT1 presents a unique challenge in pathological evaluation, which is crucial for guiding treatment and determining patient's prognosis. This study aimed to assess the interobserver variability in the histopathological evaluation of pT1 CRC.
Methods: This retrospective multicentric cohort study included 2,208 pT1 CRC patients diagnosed at 33 tertiary hospitals between 2007 and 2018 (EpiT1 consortium). A task force comprising 20 experienced pathologists conducted the histopathological evaluation using digitalized haematoxylin-eosin (HE) slides. A pilot study was performed with 10 cases, and after a consensus meeting 70 new cases were assessed (concordance study). We used percentage agreement and Gwet's AC1 for categorical variables, and intraclass correlation coefficient (ICC) for continuous variables.
Results: In the pilot study, histological grade, perineural invasion (PNI), and lymphovascular invasion (LVI) demonstrated 100% agreement, with moderate to good concordance for tumour budding (TB), poorly differentiated clusters (PDC), and margin assessment. The concordance study showed high agreement (≥90%) on histological grade, TB, PDC, PNI and LVI. Submucosal invasion depth showed excellent reliability in the concordance study (ICC=0.97). Lower concordance was observed on tumour infiltrating lymphocytes (TILs) and status of muscularis mucosae. Notably, the agreement of PDC was higher than for TB on both sub-studies.
Conclusion: Our results emphasize the need for standardization in evaluating pT1 CRC. Defining the evaluation criteria of pT1 histological features can improve the concordance among pathologists for most features. Moreover, the addition of PDC assessment in pT1 CRC diagnostic guidelines could help to improve the accuracy of risk stratification and reliably predict prognosis.

PS-20-027

Comparison of three different Claudin18.2 IHC assays in gastric and gastroesophageal junction (G/GEJ) cancer

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Background & Objectives: Immunohistochemistry (IHC) for Claudin18.2 (CLDN18.2) is a novel biomarker for treatment with zolbetuximab in gastric and gastroesophageal junction (G/GEJ) cancer. The aim of the study was to compare the staining patterns of two different CLDN18.2 IHC assays on the Dako Omnis platform with the approved VENTANA CLDN18 (43-14A) RxDx Assay, as not all diagnostic pathology laboratories have access to a Ventana BenchMark staining platform required for the approved IHC assay.
Methods: Optimized staining protocols for two different commercially available concentrated antibodies for CLDN18.2 were initially

developed on the Dako Omnis platform using TMAs comprising various normal tissues and G/GEJ cancers. Subsequently, each antibody was validated on TMAs comprising 67 G/GEJ cancers and 39 other neoplasias. To evaluate the accuracy, all neoplasias were also stained using the approved VENTANA CLDN18 (43-14A) RxDx Assay.
Results: The two optimized IHC assays provided comparable levels of diagnostic sensitivity and specificity to the approved assay with an overall diagnostic accuracy of 97% and 98,5% in G/GEJ cancers using a cut-off ≥75% of tumour cells demonstrating moderate-to-strong membranous staining. In the 39 tested non-G/GEJ cancers, only 1 (of 2) pancreas adenocarcinoma and 1 large cell neuroendocrine carcinoma showed positive staining reaction.
Conclusion: The two tested CLDN18.2 antibodies and the approved assay exhibited comparable staining patterns in both normal and neoplastic tissues. However, implementing CLDN18.2 IHC as predictive marker requires a rigorous optimization and validation process to ensure appropriate diagnostic accuracy of the assay. This study indicates that CLDN18.2 testing can be done on alternative IHC platforms, which is important for laboratories without access to the approved assay and platform from Ventana. This pilot study included 67 G/GEJ cancers (22 % positive). Further studies on larger cohort of G/GEJ cancers are needed to confirm our findings.

PS-20-028

The relationship between the expression of cancer-associated fibroblast markers and T-killers with characteristics of colorectal cancer

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Background & Objectives: Cancer-associated fibroblasts (CAFs) represent a heterogeneous group of cells in the tumour stroma that regulate tumour progression, and metastasis. This implies that CAFs hold significant prognostic and clinical importance for tumours of various localizations, including colorectal cancer.
Methods: Immunohistochemical analysis was performed on samples from 56 patients with colorectal cancer using antibodies against FAP and CD-8 to identify correlations with tumour stage, morphological characteristics, overall survival, and recurrence-free survival. The assessment was conducted based on quantitative parameters (area, percentage) of FAP and CD-8.
Results: A negative correlation was observed between the number of lymphocytes and perineural invasion (968 [488; 1748] vs. 548 [430; 607], $p = 0.019$). A negative correlation was also found between the number of lymphocytes and metastatic involvement of lymph nodes: patients with N1 had significantly less tissue infiltration compared to N0 (449.5 [253.25; 594.75] vs. 892.5 [560.25; 1691.75], $p = 0.013$). No correlation was found between the quantitative values of FAP and CD-8 lymphocytes with vascular invasion, gender, age, tumour localization, TNM staging, or Grade.
Conclusion: The influence of CAFs on tumour progression and invasiveness is a relatively new concept in medicine. Currently, there are conflicting data on whether this group of cells contributes to a more aggressive course of colorectal cancer. In our study, no association was found between the number of CAFs and the degree of lymphocyte infiltration in tumours or other clinical-demographic characteristics of patients. At the same time, a strong inverse correlation between tumour lymphocyte infiltration and perineural invasion, as well as the tumour`s tendency to metastasize was observed as expected. This area requires further research.

PS-20-029

Clinicopathological evaluation of oesophageal endoscopic resection (ER) specimens in a UK tertiary care centre

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Background & Objectives: Endoscopic resection (ER), including endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR), is an established treatment for early oesophageal cancer, particularly in Eastern countries. While its use in the UK remains limited, ER is a preferred approach for early-stage disease in tertiary care centres. This study evaluates the histopathological features and clinical outcomes of oesophageal cancers treated with ER at our institution, assessing adherence to the Royal College of Pathologists (RCPath) dataset and European Society of Gastrointestinal Endoscopy (ESGE) guidelines.
Methods: We retrospectively analysed 40 consecutive oesophageal ER specimens (24 ESD, 16 EMR) from patients with oesophageal malignancies (26 intramucosal, 14 submucosal) over an eight-month period (January–August 2024). Pathological parameters included tumour morphology, differentiation grade, dysplasia, lymphovascular and perineural invasion, depth of invasion, staging, and margin status. Follow-up data included endoscopic surveillance (n=14), endoscopic biopsies (n=14), and multidisciplinary team (MDT) outcomes. Poor prognostic factors were defined as poor differentiation, depth of invasion, positive margins on ESD, and metastasis on imaging.
Results: A male predominance (n=35) with a mean age of 73 years was observed. Among submucosal cancers (n=14), six were adenocarcinomas and four were squamous cell carcinomas. Poor prognostic features were identified in six cases (15%), including poor differentiation, lymphovascular invasion, submucosal invasion (pT1b), tumour budding, tubulo-infiltrative histology, and positive margins. All six had positive deep margins, and four required additional treatment.
Conclusion: Our findings support ESGE guidelines regarding high-risk pathological features necessitating further therapy in oesophageal cancer. All cases met RCPath dataset parameters, reinforcing the role of ER in early-stage disease management.

PS-20-030

Heterogeneous mismatch repair protein expression in gastric cancer: prevalence and clinicopathological implications

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Background & Objectives: Heterogeneous mismatch repair (hMMR) status, noted in colorectal and endometrial cancers, remains underexplored in gastric cancer (GC). This study investigates hMMR prevalence in GC and its clinicopathological correlates, aiming to elucidate its role in tumour progression and potential implications for immunotherapy responsiveness.
Methods: We analysed surgical specimens from 159 GC patients (2010–2018) without neoadjuvant therapy. Immunohistochemistry targeted MMR proteins (MSH2 [79H11], MSH6 [EP49], MLH1 [ES05], PMS2 [EP51]). hMMR was defined as ≥20% unstained areas amid strongly stained regions, classified per Joost et al. (modified) as intraglandular, clonal, or mixed patterns. MMR status was correlated with sex, age, tumour site, macroscopic type, size, histologic subtype, differentiation grade, vascular invasion, TNM stage, and clinical stage. Statistical analysis used χ^2 or Fisher's exact tests in Statistica 12.5.192.7 ($p<0.05$).
Results: hMMR was observed in 37/159 cases (23.3%), MMR-proficient in 104 (65.4%), and MMR-deficient in 12 (7.6%). Among MMR-deficient cases, 6 (3.8%) exhibited hMMR of retained markers (MMR-deficient/hMMR). Dual-marker heterogeneity, predominantly MLH1/PMS2 (n=17), was common. hMMR was enriched in

papillary vs. discohesive subtypes (p=0.031), while MMR-proficient tumours prevailed in the latter. Both hMMR and MMR-deficient/hMMR statuses were linked to intestinal subtype (p=0.006, p=0.036) and well-differentiated tumours (p<0.05, p=0.014). hMMR predominated in macroscopic types 3–4 vs. MMR-deficient/hMMR (p<0.001). No significant correlations emerged with sex, age, or tumour size.
Conclusion: hMMR affects 23.3% of GC cases, often involving MLH1/PMS2, and correlates with papillary and intestinal subtypes, well-differentiated tumours, and advanced macroscopic types, suggesting clonal evolution with implications for prognosis and immunotherapy.

PS-20-031
Favorable immunohistochemical prognostic factors for gastric cancer
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Background & Objectives: Gastric cancer remains a leading cause of cancer-related mortality globally, characterized by high incidence and heterogeneous outcomes necessitating reliable prognostic markers. This study aims to identify independent immunohistochemical (IHC) predictors of survival in gastric cancer patients untreated with immunotherapy, using the Cox proportional hazards model to assess intrinsic tumour biology.
Methods: We evaluated 310 patients with gastric cancer who underwent surgical resection as primary treatment, without prior or subsequent immunotherapy. Tumours were histologically classified per Lauren: 119 intestinal, 114 intermediate, and 77 diffuse. A panel of 21 IHC markers—including mismatch repair proteins (MSH2, MSH6, MLH1, PMS2), PD-L1 (SP142 clone), E-cadherin, β-catenin, and others (e.g., HER2, p53)—was analysed alongside Epstein-Barr virus (EBER) small RNA expression. Clinicopathological variables (age, sex, TNM stage, Lauren type) were correlated with survival outcomes using Cox regression analysis.
Results: Male gender was associated with a 2.02-fold higher mortality risk (p<0.001), each additional year of age increased risk by 1.02-fold (p=0.02), N-stage (lymph node metastasis) by 1.61-fold (p<0.001), and M-stage (distant metastasis) by 2.52-fold (p<0.001); other clinicopathological traits were non-significant (p>0.05). Notably, MMR-negative status reduced mortality risk twofold (p=0.05), possibly due to increased tumour immunogenicity from elevated mutation burden. PD-L1 positivity (SP142) lowered mortality risk 4.35-fold (p=0.005), potentially by modulating immune suppression in the tumour microenvironment. In contrast, aberrant E-cadherin (p=0.019) and β-catenin (p=0.001) expression emerged as adverse prognostic factors, likely linked to Wnt pathway activation driving tumour aggressiveness. These findings highlight novel prognostic roles in untreated patients.
Conclusion: Among gastric cancer patients not receiving immunotherapy, positive PD-L1 (SP142) and negative MMR status independently predict significantly better survival outcomes, whereas aberrant E-cadherin and β-catenin expression indicate poorer prognosis. These insights enhance risk stratification and suggest new avenues for personalized therapeutic strategies in future research.

PS-20-032
Prognostic significance of tumour-infiltrating lymphocytes in gastric carcinoma
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Background & Objectives: Tumour-infiltrating lymphocytes (TILs) are a crucial component of the tumour microenvironment that reflects the host's antitumor immune response. They have been investigated as a prognostic factor in several cancers. This study aimed to assess the prognostic value of TILs in gastric carcinoma (GC).
Methods: The study included all patients diagnosed with GC who underwent surgical treatment without prior chemotherapy over nine years. TILs were assessed by two pathologists following the recommendations of the International TIL Working Group (ITWG), and inter-rater reliability was evaluated. Cases were stratified based on TIL density using the median, 75th percentile, and ITWG thresholds as cut-off points.
Results: A total of 98 patients were included in the study. The mean overall survival (OS) was 44.1 ± 5.3 months, with a median OS of 24.7 ± 5.1 months. The mean relapse-free survival (RFS) was 45.8 ± 6.1 months, with a median RFS of 25.8 ± 7.2 months. Using the median as a cut-off point, 34 GCs were classified as low TILs (<10%), while 64 were classified as high TILs (>10%). TIL density was significantly correlated with the histological subtype and TNM stage ($p < 0.05$). In univariate analysis, TILs were significantly associated with OS and RFS. Low TIL density was linked to poor survival, whereas high TIL density was associated with a better prognosis (mean OS: 22.6 months for low TILs vs. 51.7 months for high TILs; $p < 0.001$ / mean RFS: 25.4 months for low TILs vs. 52.8 months for high TILs; $p = 0.006$). In multivariate analysis, TILs, the presence of metastases, and lymph node involvement (pN+) were independent prognostic factors for OS, while only TILs and pN+ were independent prognostic factors for RFS.
Conclusion: These findings suggest that TILs may serve as an independent prognostic factor for OS and RFS in GC.

PS-20-033
Evaluation of current and future theranostic biomarkers in gastric cancers
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Background & Objectives: Gastric carcinoma (GC) is one of the leading causes of cancer-related mortality worldwide. Identifying relevant biomarkers is crucial. The aim of this study was to evaluate the 5 known theranostic biomarkers in surgical specimens of GC, and to compare 2 of them, Claudin18 and FGFR2b, with their respective preoperative biopsy.
Methods: This retrospective study included a cohort of 46 patients with GC. Five biomarkers were analysed: Claudin18, FGFR2b, HER2, PD-L1 and mismatch repair deficiency (dMMR). Positive expression was defined as: a score of 2 to 3+ in ≥75% of tumour cells for Claudin18, a score of 2 to 3+ in ≥10% of tumour cells for FGFR2b, a score of 3+ or 2+ with gene amplification in ≥10% of tumour cells for HER2, a combined positive score of >10% for PD-L1, and loss of expression of MLH1/PMS2 or MSH2/MSH6 proteins for dMMR.
For Claudin18 and FGFR2b, preoperative biopsies were compared with their respective surgical specimen.
Results: Forty-six GC surgical specimens were analysed, corresponding to 30 men and 16 women, with a mean age of 68 years (range 35-90).
Biomarkers were positive in 16 cases for Claudin18 (37%), in 8 cases for FGFR2b (19%), in 8 cases for PD-L1 (19%), in 7 cases for HER2 (16%), and in 4 cases for dMMR (9%). When comparing surgical specimens to biopsies, discordant results were found in 6 cases for Claudin18 and in 4 cases for FGFR2b. Biomarker overlap is presented in a Venn diagram.
Conclusion: This is, to our knowledge, the first description of the 5 known theranostic biomarkers in gastric carcinomas. The overlap between the 5 GC biomarkers was low, allowing a clear therapeutic strategy. The discordances observed with Claudin18 and FGFR2b between surgical specimens and biopsies were likely due to tumour

heterogeneity, emphasizing the importance of multiple biopsy sampling for histological diagnosis and biomarker assessment.

PS-20-034

Phosphohistone H3 expression in gastroenteropancreatic neuroendocrine tumours

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Background & Objectives: Neuroendocrine neoplasms (NENs) primarily originate in gastroenteropancreatic system and are classified by 2022 WHO classification into well differentiated neuroendocrine tumours (NETs), poorly differentiated carcinoma(NECs) and mixed neuroendocrine- non-neuroendocrine neoplasms(MiNENs) based on histopathological differentiation, mitotic index and Ki-67 proliferation index. Phosphohistone H3 (PHH3), a mitotic marker crucial for tumour grading is well studied in other malignancies but its prognostic value in GEP-NENs is still under evaluation. This study aims at evaluating the expression of PHH3 in gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs).
Methods: A retrospective study was performed on all patients diagnosed as GEP-NENs from January 2016 to December 2023 in the Department of Pathology, Kasturba Medical College, Mangalore. Immunohistochemistry with PPH3 and Ki-67 was done on available paraffin blocks according to standard staining protocols.
Results: 72 cases of GEP-NENs with patients age range between 13-88 years (mean 55.8 years) and a slight male predominance(1.18:1) were evaluated. Duodenum was the most common site (41.7%) followed by stomach (15.3%). Most tumours were well differentiated NETs (82%), and predominantly grade1 (59.7%). PHH3 had higher predictive accuracy (76.4%) than Ki-67(72.2%) for mitotic activity and showed a strong correlation with necrosis (p value-<0.001), reinforcing its utility in identifying aggressive tumours. Discrepancies between the two markers were particularly observed in high grade cases, where Ki-67 indices were disproportionately higher than PHH3. The findings underscore PHH3 as a valuable adjunct to Ki-67 for accurate tumour grading and prognostication of GEP-NENs, with ROC analysis further confirming its diagnostic strength (AUC=0.829, $p<0.001$). No significant associations were found between PHH3 and lymph node status, lymphovascular or perineural invasion.
Conclusion: PHH3 outperformed ki-67 as a precise proliferation marker in GEP-NENs, offering stronger correlation with aggressive features like necrosis. While Ki-67 remains valuable for overall proliferation, PHH3 specificity may help prevent over grading particularly in high grade neuroendocrine tumours.

PS-20-036

Tumour-infiltrating immune cells are more abundant in lung metastases from colorectal cancer than in paired primary tumours and their prognostic value depends on adjuvant chemotherapy

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Background & Objectives: The immune microenvironment plays a crucial role in the progression of colorectal cancer (CRC), but its variation across primary tumours and metastatic sites remains incompletely understood. In this study, we compared the composition and prognostic significance of the immune microenvironment in lung metastases, paired primary tumours, and liver metastases from a retrospective cohort of patients with metastatic CRC (mCRC) who underwent pulmonary metastasectomy.
Methods: A total of 216 mCRC patients treated at a single Swedish institution were included. Immunohistochemistry was applied to evaluate CD3+, CD8+, CD20+, FoxP3+, and PD-L1+ immune cells, as well as tertiary lymphoid-like structures (TLLSs), on tissue microarrays constructed from lung metastases, paired primary tumours, and liver metastases.
Results: Lung metastases exhibited significantly higher infiltration of all immune cell subsets compared to both primary tumours and liver metastases. FoxP3+ cell density was lower in liver metastases than in primary tumours. Immune cell infiltration in lung metastases was largely unaffected by neoadjuvant chemotherapy, except for lower FoxP3+ cell infiltration in treated cases. None of the immune markers bore prognostic significance in the overall analysis. However, high infiltration of FoxP3+, CD20+, and PD-L1+ immune cells, and the presence of TLLSs in lung metastases, was associated with improved overall survival in patients receiving adjuvant chemotherapy, with a significant prognostic treatment interaction. None of the immune markers were prognostic in primary tumours or liver metastases.
Conclusion: These findings underscore a distinct, more immunologically active immune microenvironment in CRC lung metastases compared to primary tumours and liver metastases, that suggestedly also predicts response to adjuvant chemotherapy. Immune profiling of lung metastases may thus pave the way for improved personalized treatment of these patients.

PS-20-037

A comparative analysis of microsatellite instability and mismatch repair protein deficiency in colorectal carcinoma cases with a review of diagnostic challenges

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Background & Objectives: Microsatellite instability (MSI) and mismatch repair (MMR) deficiency are important prognostic as well as predictive biomarkers in colorectal cancer (CRC). The DNA MMR system recognizes short insertions, deletions, and single base mismatches during DNA replication and recombination. Deficiency in MMR proteins, leads to frameshift mutations in microsatellite repeats and microsatellite instability (MSI). This analysis delves into the concordance between MSI and MMR protein expression in CRC, highlighting diagnostic challenges and proposing solutions to enhance diagnostic accuracy.
Methods: Between January 2018 to January 2024, a comprehensive study was conducted involving 522 colorectal carcinoma (CRC) cases analysed for mismatch repair (MMR) protein expression using immunohistochemistry (IHC), and 640 CRC cases assessed for microsatellite instability (MSI) through polymerase chain reaction (PCR) targeting frameshift mutations. A subsequent comparison followed to evaluate the concordance and the diagnostic difficulties were reviewed.
Results: In our study, mismatch repair (MMR) deficiency was identified in 20.31% (106/522) of colorectal carcinoma (CRC) cases with the loss of PMS2 being most prevalent (72.64%), followed by MLH1 loss (59.43%), MSH6 (24.53%), and MSH2 (19.81%). Microsatellite instability (MSI) testing revealed 27.19% (174/640) cases as unstable, with BAT21 marker demonstrating highest instability

(86.78%), followed by BAT26 (83.91%), NR21 (81.03%), NR27 (79.89%), and NR24 (76.44%). High MSI (MSI-H) was observed in 3.45% cases, while low MSI (MSI-L) was seen in 1.15%. Concordance between MMR and MSI showed an 88.82% agreement. In addition, we evaluated the challenges pathologists encounter when assessing MMR and MSI status such as pre-analytic variables, interpretative pitfalls, and reporting complexities.
Conclusion: Accurate assessment of MSI and MMR protein status is pivotal in the management of colorectal carcinoma, influencing both prognostic evaluations and therapeutic decisions. Our study demonstrated a high concordance between the two tests. However, to further enhance diagnostic precision and improve patient outcome, we recommend standardization of testing protocols and continuous quality control.

PS-20-038

Aberrant occludin and claudin-1 expression in intestinal mucosa associates with inflammatory bowel disease activity and response to biologic therapy

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Background & Objectives: Tight junction (TJs) proteins, occludin and claudin-1 are essential for gut barrier homeostasis. We aimed to assess the expression of occludin and claudin-1 in the intestinal mucosa of patients with inflammatory bowel disease (IBD) in relation to clinical parameters and disease outcomes.
Methods: A total of 189 IBD patients were enrolled in the study (male: 59%, age: 45.5±18 years), including 92 with Crohn's disease (CD) and 97 with ulcerative colitis (UC), as well as 61 healthy controls (HC). Follow-up biopsies (>6 months) were available for 100 patients. Clinical, laboratory, histology, and endoscopic data were retrieved for all patients with available colonic or ileal biopsies. The expression of TJ proteins occludin and claudin-1 was assessed by immunohistochemistry (IHC) (H-score).
Results: Patients with active CD (CDAI>150) demonstrated increased cytoplasmic occludin expression in both the crypts (72.9±63.8 vs. 42.4±37; p=0.033) and surface epithelium (75.7±50.6 vs. 52±46.2; p=0.01), and higher cytoplasmic claudin-1 levels in the crypts (70.2±63.6 vs. 43±43.6; p=0.02), compared to HC, where both proteins showed mainly membranous localization. Patients with active UC (Mayo Score>6) showed increased cytoplasmic occludin expression in the crypts (58.3±43.1 vs. 42.4±37; 0.049) and the surface epithelium (78.7±57.8 vs. 52±46.2; p=0.009) compared to HC. Occludin expression in the crypts correlated with systemic inflammation markers, including CRP (r=0.4; p=0.001) and PLT (r=0.23; p=0.023), disease activity indices such as CDAI in CD (r=0.33; p=0.003) and the Mayo Score in UC (r=0.42; p<0.001) and histologic activity, as assessed by the Nancy index (r=0.21; p=0.008). In follow-up biopsies, patients receiving biologic therapy experienced a greater reduction in crypt cytoplasmic occludin levels versus biologic-naïve patients (-39.3±73.8 vs. -9.2±43.8; p=0.038).
Conclusion: Aberrant expression of claudin-1 and occludin in active IBD supports an important role of the intestinal barrier's dysfunction in the disease.

PS-20-039

Significance of tumour-infiltrating lymphocytes and macrophages before and after neoadjuvant chemo-radiotherapy for rectal cancer

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Background & Objectives: In rectal cancers TNM classification is of major importance but gives limited prognostic information and no prediction on the benefit of a chosen therapy.
In the present study we provide evidence that the type, the density, and the location of immune cells within tumour strongly influence the evolution of the tumour and the effect of neoadjuvant chemo-radiotherapy for the patients.
Rectal cancer is one of the most common gastrointestinal cancers. Neoadjuvant chemo-radiotherapy (nCRT) followed by surgery has been accepted to be standard treatment procedure for locally advanced rectal cancer (LARC). Furthermore, the anti-tumour immune response contributes to the response of nCRT.
Methods: We aimed to investigate the participation of T lymphocytes subsets (CD8, FoxP3, IL-17, RORγt) and type 1 macrophages ($CD163^+$) in the characterization of tumour microenvironment (TME) before and after nCRT in 22 patients with LARC.
Results: Density of $CD8^+$ TILs in the invasive front (IF) (41.61±4.43 v.s 74.98±60.27) and in tumour stroma (TS) (30.91±2.04 v.s 66.71±56.19) has been found to be increased after nCRT compared to the same locations in pre-therapy biopsies. The FoxP3 Tregs decreased in number in IF and TS (31.40±3.07 v.s 29.76±27.83 and 29.45±38.33 v.s 21.37±21.53, respectively) in post-nCRT treatment biopsies. The number of $CD163^+$ macrophages, IL-17^+ cells and RORγt^+ cells has been increased in post-nCRT treatment samples.
Statistically significant difference is found in the number of $CD8^+$TILs in the IF in post-nCRT as compared to the probes before nCRT (p=0.001, $\chi 2$=2.87).
Conclusion: The current study suggests that local antitumor immunity could be enhanced by increased numbers of $CD8^+$ and $CD163^+$ immune cells after nCRT. Concerning other T helper cells such as IL-17 (RORγt) and FoxP3, their numbers are modulated in the TME probably by nCRT and other factors such as intestinal microflora and the intestinal immunosuppressive milleu.

PS-20-041

Assessing FABP4 and CD36 expression in gastrointestinal cancer cell lines co-cultured with mature adipocytes in context with SARIFA

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Background & Objectives: The histological biomarker SARIFA (Stroma AReactive Invasion Front Areas), recently introduced by our group, marks regions where tumour cells directly interact with

adipocytes without intervening connective tissue. Easily identifiable, SARIFA holds strong prognostic potential for guiding gastrointestinal cancer (GIC) therapy. Lipid metabolism in tumour cells is key in this context, as tumour-adipocyte interactions at the invasion front correlate with altered fat metabolism protein expression, including elevated FABP4 and CD36. Our research examines how the SARIFA microenvironment both drives and responds to these metabolic shifts.
Methods: We analysed RNA expression in GIC cell lines co-cultured with adipocytes. Preadipocytes, isolated from patient tissue, were seeded and differentiated for 14 days, confirmed by lipid droplet formation. GIC cell lines (HCT116, COLO205, 23132/87) were then seeded into transwell inserts. Co-culturing continued over 15 days with media changes and passaging of GIC cell lines every 72 hours. Cells were collected at each passage and at four post-co-culture time points for analysis.
Results: Co-culturing GIC cell lines with mature adipocytes led to altered FABP4 and CD36 expression levels, which became evident after three days of co-culture. Over a prolonged 15-day co-cultivation period, FABP4 expression exhibited fluctuations ranging from 2- to 5-fold, depending on the cell line and time point. In contrast, CD36 expression steadily increased over time, reaching 6- to 20-fold upregulation, with expression peaks varying across cell lines. All cell lines lost their overexpression one to two passages post-co-culture. Findings were reproducible across experiments.
Conclusion: Using a simplified in vitro SARIFA model, we showed that mature adipocytes influence FABP4 and CD36 expression in nearby cancer cells, significantly increasing CD36 levels over time. These findings support the idea that direct adipocyte contact activates lipid metabolism in tumour cells. Further adjustments are needed for FABP4 experiments.

Funding: BZKF

PS-20-042
Transfer of SARIFA-status of colorectal cancer into metastases
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Background & Objectives: SARIFA (Stroma AReative Invasion Front Areas) has recently emerged as an independent negative prognostic H&E-based biomarker for colorectal carcinomas. SARIFA is primarily characterized by direct tumour adipocyte interaction without intervening collagenous stromal reaction. It has not yet been shown whether the SARIFA-status of colorectal cancer exhibited at the primary tumour site is carried to metastatic sites.
Methods: So far 16 cases of patients with colorectal carcinomas and at least one metastasis in a site containing fatty tissue were identified from the archive of the pathology department of the University Augsburg. Metastatic sites included peritoneal or intraabdominal metastases in 15 cases and 1 case with a pleural metastasis. SARIFA-status of the primary tumour site and the metastasis was determined and compared on all available H&E-stained tumour slides. Fisher exact test was used for hypothesis testing.
Results: Among the 16 cases, 12 exhibited SARIFA at the primary tumour site of which 10 also showed SARIFA-positive metastases, with 2 cases remaining negative for SARIFA at the metastatic site. All 4 cases with SARIFA-negative primary tumours were also negative at the secondary site. This shows that the SARIFA-status of the primary tumour site and metastatic sites is highly significantly correlated (P=.008).
Conclusion: The apparent transfer of the SARIFA-status between different tumour sites suggests that the presence of SARIFA is determined by a tumour-host interaction that is not necessarily site specific. Further studies on larger collectives should be conducted to confirm this finding and to determine the specific tumour or microenvironment characteristics leading to this phenomenon.

PS-20-043
Histopathological study of endoscopic biopsies of upper gastrointestinal tract in children with inflammatory bowel disease
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Background & Objectives: Changes in the upper gastrointestinal tract (UGI) are observed in both Crohn's disease (CD) and ulcerative colitis (UC). This study aims to identify UGI histological characteristics that effectively distinguish CD from UC.
Methods: A cross-sectional study was conducted on 67 paediatric patients diagnosed with IBD (43 with CD and 24 with UC) from 2020 to 2024. Histopathological analysis of UGI biopsies assessed FAG (lymphohistiocytic infiltrate with neutrophils around foveolae or glands), FEG (lymphohistiocytic infiltrate without neutrophils), IELosis, dyskeratosis, and the presence and distribution of eosinophils and neutrophils, comparing these features between groups.
Results: FAG was detected in 45,9% of CD patients, significantly higher than the 5,3% observed in UC (p=0,022). Additionally, CD patients exhibited a greater presence of neutrophils within the epithelial structures of the antrum, both in the wall and lumen (p=0,012). Contrarily, the presence of FEG showed no significant differences between CD (43,2%) and UC (42,1%), but the presence of lymphocytes within the epithelial structures of the antrum was significantly more common in CD (p=0,001). Notably, the presence of neutrophils within the duodenal crypt epithelium (p=0,006) and lamina propria eosinophils (p=0,033), as well as oesophageal dyskeratosis (p=0,03) and oesophageal intraepithelial lymphocytes (LyE) (p=0,019), were more frequently observed in CD patients.
Conclusion: The study underscores the importance of defining FAG and FEG, highlighting that the presence of FAG in the gastric antrum primarily suggests CD. Furthermore, it emphasizes the significance of inflammatory cell distribution (lymphocytes, neutrophils) within the epithelial structures of the oesophagus, stomach, and duodenum, often indicative of CD rather than UC.

PS-20-044
Implications of the tumour immune microenvironment of advanced Epstein-Barr virus-associated gastric cancer for immunotherapy response
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Background & Objectives: Although evidence suggests that some Epstein-Barr Virus-associated gastric cancer (EBVaGC) patients may benefit from immunotherapy, the effectiveness of anti-PD-1 antibody as a biomarker in EBVaGC remains controversial. We aimed to comprehensively analyse the immune microenvironment of advanced EBVaGC and its association with the response to immunotherapy.
Methods: With multiplex immunohistochemistry staining, the expression of immune markers (PD-L1, LAG3, FoxP3, CD8, CD4, PanCK, CK+/PD-L1+, CD8+/PD-L1+, LAG3+/CD8+, CD4+/

FOXP3+) was evaluated retrospectively in tumour sections from 12 cases of advanced EBVaGC patients who were treated with immunotherapy. Computational image analysis was used to quantify the density of each markers within the tumour and stromal region.
Results: Higher PD-L1+, CK+/PD-L1+ levels in the tumour region were significantly associated with better response to immunotherapy (P=0.04545 and 0.03788). Higher CD4+, CD8+/PD-L1+, CD4+/FoxP3+ levels in the stromal region were significantly associated with better response (P=0.04798, 0.04545, and 0.0101), whereas higher LAG3+ levels in the stromal region was significantly associated with worse response (P=0.01894). Within combined regions of the tumour and adjacent stroma, higher PD-L1+, CD4+, CD8+/PD-L1+, CD4+/FoxP3+ levels were significantly associated with better response (P=0.04798, 0.04798, 0.02904, and 0.005051). For LAG3, lower expression levels in total region was significantly associated with better response (P=0.01894).
Conclusion: This study highlights several immune markers other than PD-L1 as potential biomarkers in predicting the response to immunotherapy in EBVaGC. Future studies are required to confirm their potential to predict tumour responses to immune therapy.

PS-20-046
Claudin 18.2 expression as a biomarker in gastric cancer: clinicopathological correlations and therapeutic implications
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Background & Objectives: Gastric cancer (GC) continues to pose a significant clinical challenge due to its high mortality and limited targeted therapies. Claudin 18.2 (CLDN18.2), a protein primarily expressed in gastric epithelium, has emerged as a promising biomarker and therapeutic target. This study investigated CLDN18.2 expression in GC and gastroesophageal junction (GEJ), assessing its clinicopathological associations and prognostic significance to better understand its potential therapeutic relevance.
Methods: An observational cohort analysis of 112 patients with GC/GEJ diagnosed between 2013 and 2024. CLDN18.2 expression was evaluated via immunohistochemistry, with positivity determined by membranous staining intensity and percentage of stained tumour cells. Cases were considered positive if they had ≥75% positive tumour cells with moderate and high intensity. We also assessed H-SCORE for these cases. Statistical associations were explored between CLDN18.2 expression and clinicopathological features including specimen type, tumour site, stage, histological subtypes (Lauren and WHO), molecular markers (HER2, PD-L1, MMR status, Epstein-Barr virus [EBER]), and clinical outcomes.
Results: CLDN18.2 positivity was significantly associated with metastatic specimens compared to primary tumours (29.41% vs. 6.41%; OR=0.16; CI[0.051–0.53]; p=0.002) and advanced TNM stage IV disease (p=0.046). A significant correlation was found between CLDN18.2 expression and EBER positivity (23.53% positive vs. 0% negative; p=0.002). Median tumour size was smaller in CLDN18.2-positive tumours (30 mm vs. 42.5 mm), though not statistically significant (p=0.156). No significant correlations emerged between CLDN18.2 expression and HER2 amplification, mismatch repair deficiency, or PD-L1 scores (TPS and CPS). Survival analyses showed no statistically significant differences in recurrence-free or overall survival between CLDN18.2-positive and negative groups.
Conclusion: CLDN18.2 expression is notably associated with metastatic disease and advanced GC/GEJ stages, highlighting its potential as a therapeutic target. Its strong association with EBER positivity suggests biological specificity that may guide treatment selection. Despite lacking a direct prognostic impact, these findings emphasize CLDN18.2's therapeutic promise, advocating further investigations.

PS-20-047
Quantitative image analysis of tumour-infiltrating lymphocytes in rectal cancer: preliminary data on therapeutic response prediction
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Background & Objectives: Locally advanced rectal cancer (LARC) is routinely treated with neoadjuvant therapy (NAT), followed by surgery. However, responses to NAT are heterogeneous. The "watch-and-wait" strategy, aims to preserve organ in good responders, but requires reliable biomarkers to predict treatment response. Tumour-infiltrating lymphocytes (TILs) reflect the host immune response and have been linked to a more favourable tumour microenvironment. Objective quantification of TILs in pretreatment biopsies may help stratify patients and guide clinical decisions.
Methods: Clinical and pathological data were collected from patients diagnosed with LARC and treated with NAT. Pretreatment biopsies were immunohistochemically stained for CD3, CD4, CD8, and CD15. Slides were scanned and analysed using the QuPath software. The density of positive immune cells was automatically quantified (cells/mm²) in the manually selected hotspot areas. Pathological response was evaluated using the Mandard Tumour Regression Grade (TRG) system. Six patients (3 women and 3 men) with LARC who received NAT were included in this preliminary study. Five patients underwent surgical resection with TRG 3, and one with TRG 4. Descriptive statistics and one-way ANOVA were used to compare the mean cell densities between TRG groups. Due to the limited sample size, the results were interpreted as exploratory.
Results: Preliminary analysis revealed inter-individual variability in the densities of CD3+, CD4+, and CD8+ cells, with no statistically significant differences observed between TRG groups. In contrast, CD15+ cell density was higher in TRG4 compared to TRG3, both in hotspot and global areas, with a trend toward statistical significance in the global analysis *($p = 0.060$).*
Conclusion: Preliminary data suggest that a high density of CD15+ cells may be associated with an immunosuppressive tumour microenvironment and a poorer response to neoadjuvant therapy. Further analysis is in progress to explore the role of TILs as key modulators of treatment response.

PS-20-048
Clinicopathological features and prognostic implications of High-grade Appendiceal Mucinous Neoplasm (HAMN): a multicentre study
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Background & Objectives: High-Grade Appendiceal Mucinous Neoplasm (HAMN) is a term, introduced in 2016 to describe tumours exhibiting pushing-type invasion similar to low-grade appendiceal mucinous neoplasms (LAMNs), but possessing high-grade cytological features. Data regarding the behaviour of these rare tumours is quite limited. This multicentre study aims to investigate the clinicopathological features and behaviour of HAMNs, the impact of focal high-grade features on prognosis.
Methods: Slides from cases diagnosed as HAMN or LAMN with focal high-grade atypia in seven centres were reviewed by an experienced gastrointestinal pathologist. Thirty-four cases met inclusion criteria. Clinical details and follow-up data were collected from hospital records.
Results: The mean age was 57 years, female-to-male ratio was 1.83. Diffuse appendiceal enlargement occurred in 25 cases. High-grade features were focal (≤10%) in 10 and extensive(>75%) in 15 cases. The most frequent architectural pattern was micropapillary, which is not observed in LAMNs, followed by undulating, villous, cribriform, flat patterns. Serosal perforation was observed in 18 cases; 9 had periappendicular acellular mucin, and other 9 had cellular mucin. Three cases of the latter had grade 2(G2) and six had grade 1(G1) pseudomyxoma peritonei (PMP), while six cases presented with peritoneal acellular mucin. No tumours confined to the appendix recurred. PMP developed in one patient during follow-up. Among the two cases with 10% high-grade histological features, one was associated with PMP-G2, and one with PMP-G1. Among nine patients who presented with PMP, one died of disease, one died due to postoperative complications, and four were alive with disease at last follow-up.
Conclusion: HAMNs appear to have a stage-dependent behaviour similar to LAMNs. Prognosis is good in cases limited to appendix. However, when they spread to the peritoneum, may produce PMP-G2, which can be associated with worse prognosis. Cases showing focal high-grade histology also should be reported as HAMN due to potential association with PMP-G2.

PS-20-049

Molecular profiling of RAS and BRAF mutations in colorectal carcinoma: a comparative study between pT1-pT3 and pT4 stages

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Background & Objectives: Colorectal carcinoma (CRC) is the third most prevalent cancer and the second leading cause of cancer-related deaths worldwide. Molecular alterations play a critical role in tumour behaviour and therapeutic strategies. Mutations in RAS (KRAS, NRAS) and BRAF genes have been widely studied for their prognostic and predictive implications. Although these mutations have been thoroughly investigated in CRC, their variation in prevalence and distribution across different tumour stages is not well established. This study aims to analyse and compare the molecular profiles of RAS and BRAF mutations in different TNM stages of CRC.
Methods: This is a retrospective study including cases of CRC referred to our department for molecular testing of KRAS, NRAS and BRAF genes. Tumours were classified into two groups based on TNM staging: pT1-pT3 group and pT4 group. Molecular analysis was performed using polymerase chain reaction (PCR) and sequencing techniques.
Results: Our study included 496 cases. The mean age of patients was 59 years. Mutations in KRAS gene were detected in 243 cases (49%) while NRAS and BRAF mutations were detected in 20 cases (4%) each. A single case (0.1%) exhibited a dual NRAS and BRAF mutation. There was a significant association between pT4 stage and higher prevalence of KRAS G12A, NRAS codon 61, and BRAF V600E mutations (p=0.046).
Conclusion: Our findings suggest a significant association between tumour stage and specific molecular alterations in CRC. The higher prevalence of KRAS and BRAF mutations in advanced-stage tumours indicates their potential involvement in tumour proliferation and disease progression.

PS-20-051

B7-H3 expression in gastric cancer and its correlation with CD8+ T cell infiltration

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Background & Objectives: The majority of patients diagnosed with gastric cancer (GC) present at advanced stage. Immunotherapy has changed the management of GC, however its efficacy is limited, associated with severe side effects and significant costs. There is a high demand for new biomarkers. B7-H3 (CD276), an immune checkpoint molecule with both immune and non-immune functions, is currently investigated as a potential therapeutic target. Data on expression in GC are limited. We aimed to investigate B7-H3 expression patterns in a large therapy-naive cohort of GC.
Methods: Formalin-fixed, paraffin-embedded whole tissue sections (n=354) were analysed using immunohistochemistry. The level of B7-H3 intensity was divided into B7-H3-low (0-1) and -high (2-3) groups, correlated with clinicopathological variables, and overall survival (OS). Density of CD8+ cells was assessed using whole slide digital imaging. To address the spatial distribution of CD8+ cells, ratios between tumour centre and invasive margin were calculated.
Results: High B7-H3 expression was observed in tumour stroma (51.7%) and parenchyma (12.7%). High stromal B7-H3 expression was associated with sex (p<0.001), tumour localization (p=0.001), Lauren phenotype (p<0.001), HER2-status (p=0.001) and CD8-ratio (p<0.001). Significant differences between median CD8-ratios were observed (1.21, B7-H3-low vs. 0.62, B7-H3 high, p<0.001). No significant differences in OS could be demonstrated between cases with low and high stromal expression, or low *vs.* high median CD8-ratios. Parenchymal B7-H3 expression correlated with Lauren phenotype (p<0.001), pN-status (p=0.007), HER2-status (p=0.001) and OS (p=0.009). When subdivided by sex, the prognostic effect was seen only in females (17.1 months, B7-H3 low *vs.* 3.3 months, B7-H3 high, p<0.001).
Conclusion: B7-H3 is overexpressed in GC, making it a promising target for immunotherapy. An association between B7-H3 stromal expression and spatial distribution of CD8+ cells was observed, suggesting the potential role of B7-H3 in tumour microenvironment (TME). Further studies are needed to investigate the impact of sexual dimorphism in TME and immunotherapy-strategies of GC.

PS-20-052

Surgery for Crohn's disease: histopathological predictors of recurrence at the proximal resection margin

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Background & Objectives: Surgical intervention is required in 80% of Crohn's disease patients during their lifetime. Patient and disease-related factors have been established as potential risk factors for post-operative recurrence (POR). However, the role of microscopic inflammation at the resection margins as a predictor of POR remains unclear. The aim of this study was to assess the predictive value of histological parameters at the proximal ileocecal resection margin for disease recurrence.
Methods: A retrospective study on patients undergoing ileocecal resection for Crohn's disease between 2000 and 2020 was conducted. Pathology reports were reviewed, and slides pertaining to proximal surgical margins were reexamined. Histological findings were correlated to endoscopic, clinical and surgical recurrence.
Results: In total, 70 patients were identified with a median follow-up of 10.7 years. Thirty-three patients developed endoscopic recurrence within the first year. Clinical and surgical recurrence were observed in 35 and 9 cases respectively. Histological examination of the proximal margin found cryptitis and neutrophils in chorion in 10% and 25.7% of cases respectively. Myenteric and submucosal plexitis were found in 47% and 20% of cases respectively. Granulomas were found in 10% of cases. The Kaplan Meier analysis identified that the presence of myenteric and submucosal plexitis at the proximal resection margin was associated with shorter time to surgical recurrence (p=0.007, 0.046, respectively).
Conclusion: Submucosal and myenteric plexitis at the proximal ileal resection margin after ileocecal resection identifies a patient group at high risk for an earlier second surgical intervention. These patients have a different and more aggressive natural history of disease. Therefore, pathological evaluation of plexitis at the proximal resection margin should be implemented in the current pathological practice after ileocaecal resection for Crohn's disease.

PS-20-053

Usage of modifying phrases in pathology reports on gastric dysplasia: can we improve diagnostic accuracy by expressing the degree of certainty?

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Background & Objectives: The biopsy report, based on biopsy findings, is a complex form of communication that incorporates standardization, objectivity, and accuracy while also reflecting the pathologist's professional expertise. Modifiers indicating the degree of certainty are essential for clarity, as endoscopic biopsy results for stomach mucosal dysplasia often lack precision, leading to uncertainty in grading. This inherent limitation underscores the challenge of providing a clear and reliable diagnosis in clinical practice.
Methods: A list of 16 frequently used words and phrases, formulated after analysing more than 800 biopsy pathology reports, included terms like "not reliably determined," "doubtful signs," "suggestive of," "similar to," "cannot be excluded," "suspicious in," "similar to," "typical picture," "probable," "the most probable," "most consistent," and "reliably determined," which help to convey uncertainty and variability in diagnostic conclusions.
Results: The study utilized a simple questionnaire to evaluate the confidence levels of 12 specialized pathologists and 28 clinicians across various specialties using a 10-point ranked scale (0 - absence to 10 - 100% presence). The research identified significant variability in confidence/validity scores for each phrase, with "reliably determined" scoring 3 and "similar to..." scoring 7. This chaotic, inconsistent use of heterogeneous terms and modifiers significantly disrupts professional communication between pathologists and clinicians, leading to potential misunderstandings and inaccuracies in diagnostic conclusions. This high variability in how uncertainty is perceived and expressed poses a significant challenge in ensuring clear and consistent diagnostic reporting.
Conclusion: To improve this situation, the study proposed several solutions, including strictly limiting the use of these terms in separate sections of the report, creating a standardized list of modifying phrases, introducing algorithmic interpretations, transitioning to a more formalized synopsis format with minimal variability, and incorporating quantitative parameters to reflect certainty levels. These measures aim to enhance clarity, reduce uncertainty, and improve the reliability of diagnostic communication in biopsy reports.

PS-21 Poster Session Electron Microscopy

PS-21-001

Spleen and lymph node morphology in CLL/SLL: a comparison between histology and scanning electron microscopy

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Background & Objectives: Chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) is a type of B-cell lymphoma characterized by small, mature B cells that affect the peripheral blood, bone marrow, lymph nodes, and spleen, often resulting in splenomegaly. The infiltration of the white pulp is particularly prominent, leading to a loss of distinction between red and white pulp.
Methods: We examined a spleen from a 51-year-old patient diagnosed with CLL/SLL (weight: 2400 g; dimensions: 27×17×12 cm). Histological analysis included haematoxylin-eosin staining, along with an immunohistochemical panel for lymphomas. Additionally, samples from the spleen and hilar lymph nodes were prepared and analysed using a Zeiss 600 scanning electron microscope (SEM) to evaluate ultrastructural changes.
Results: Histological analysis revealed a diffuse proliferation of small lymphoid cells with scant cytoplasm and small nuclei, interspersed with medium-sized cells featuring dispersed chromatin and small nucleoli. These cells expressed markers including CD20, CD79a, PAX5, BCL2, CD5, and CD23. SEM demonstrated neoplastic infiltration that disrupted the splenic stroma and compromised the normal connective framework. The remaining stroma appeared as thin fibrous strands trapped among irregularly shaped neoplastic cells, forming a dense mass that completely altered the spleen's architecture. In the metastatic lymph node, the tumour cells created an even denser mass that replaced the entire tissue. The remaining connective structures were barely recognizable, and the neoplastic cells appeared more cohesively packed together.
Conclusion: Ultrastructural evaluation is a valuable approach to studying lymphoma morphology. SEM, in particular, reveals structural details that may not be visible with light or transmission electron microscopy. The combination of SEM and histological analysis

provides new insights into the infiltration patterns of CLL/SLL within the spleen and lymph nodes. Notably, SEM highlights differences in the three-dimensional organization of neoplastic cells in the spleen compared to metastatic lymph nodes, as well as their distinct interactions with connective tissue.

PS-21-002

The detection of ultrastructural features on electron microscope images of renal samples using deep learning

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Background & Objectives: Chronic kidney disease (CKD) affects over 10% of the global population, with diagnosis relying heavily on the analysis of renal biopsy images, including transmission electron microscopy (TEM). Manual analysis is time-consuming and prone to interobserver variability. This study leverages YOLOv8-OBB deep learning models to automate the detection of six ultrastructural features in renal biopsies—glomerular basement membrane (GBM), mesangial folds, deposits, normal podocytes, podocytopathy, and subepithelial deposits—to reduce diagnostic variability and enhance efficiency.
Methods: We developed five YOLOv8-OBB-based models with different training strategies: a "From Scratch" model, a pretrained model, and models with grayscale channel enhancements (GSch), additional feature extraction layers (4FExL), or both. An ensemble method combining predictions from these models was also tested. The dataset included 607 TEM images, augmented to 1652 images using grayscale conversion and brightness adjustments, annotated for six features. Model performance was evaluated using mAP@0.5, mAP@0.5-0.95, and F1-scores.
Results: Pretrained models consistently outperformed the "From Scratch" approach, with mAP@0.5 scores ranging from 0.927 to 0.936 vs. 0.877. The Pretrained+GSch+4FExL model excelled in detecting small features (confidence scores ≥30% for GBM, podocytopathy, and mesangium deposits). The ensemble method achieved high confidence thresholds (>60% for mesangial deposits, >70% for mesangial folds, and > 80% for podocytopathy, > 50% for normal podocytes, and >30% for GBM), demonstrating robust and consistent detection across features and reducing false positives by 15–20%.
Conclusion: Pretrained YOLOv8-OBB models, enhanced with grayscale and feature extraction, significantly improve ultrastructural feature detection in renal biopsies. The ensemble method boosts accuracy, streamlining pathology workflows. A web application, *RENAL AI*, was developed for diagnostics. Future work will expand feature regions, incorporate segmentation methods, and integrate detected features with patient history and blood work (e.g., proteinuria, serum creatinine) for precise disease classification (e.g., membranous nephropathy, lupus nephritis), enhancing clinical decision-making in nephrology.

PS-21-003

Mitochondria-ER Contact Sites (MERCS) in Human Glioblastoma Stem-like Cells and Differentiated Glioblastoma Cells

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Background & Objectives: Understanding the characterization of Mitochondria-ER Contac Sites (MERCS) in Glioblastoma Cells, could be important for the therapeutical approach.
Methods: MERCS ultrastructure of Glioblastoma Stem-like Cells (GSC) and Differentiated Glioblastoma Cells (DGC) in surgical specimens from human astrocytic neoplasms were studied.
Results: MERCS in Glioblastoma like-Stem Cells (GSC) are scarce. In Differentiated Glioblatoma Cells (DGC) are numerous.
Conclusion: Two remarkable cell types were observed with respect to MERCS: GSC or "MERCS deficient cells" and DGC or "MERCS rich cells". Conspicuous contrast in MERCS amount between GSC and DGC could be represent a differential metabolic phenotype. Therefore, an effective therapy seems to be a metabolic-multifaceted strategy.

PS-22 Poster Session History of Pathology

PS-22-001

Historical evolution of pathology autopsy in 1923–1970: experience of local Lithuanian pathology centre

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Background & Objectives: Extensive study of a pathology autopsy data trends in different historical periods reflects a validated historical data on evolution of clinical medicine in different regions, also assisting in standardizing the control of disease frequency evaluation. Study objective is to determine trends of autopsies in 1923 – 1970 of local Lithuanian pathology centre.
Methods: Archival documents of pathology autopsy of 2128 patients who died in 1923-1925, 1930, 1935, 1940, 1945, 1950, 1960, and 1970 in local Lithuanian pathology centre were selected. Data parameters of age, sex, and main disease diagnosed after pathology autopsy were collected from archival protocols. Descriptive statistics and $\chi 2$ test were applied ($p<0.05$). Bioethical committee approval no. BEC-MF-342.
Results: Rate of adult pathology autopsies was 88.1% in 1923-1925, 82.9% in 1930, 88.7% in 1935, 71.1% in 1940, 88.7% in 1945, 45.6% in 1950, 62.4% in 1960, and 79.1% in 1970. Average patient's age of selected cases increased from 35.6 years old in 1923-1925 up to 57.4 years old in 1970. More than 60% of pathology autopsies were performed for men in 1923-1925, whereas 55.4% of selected cases were men autopsies in 1970. Infectious diseases were predominant in 1923-1925 (22.3%), which continued to decrease up to 4.9% in 1970 ($p<0.05$). Neoplasia were diagnosed in 16.5% cases in 1923-1925, and increased up to 35.4% in 1970 ($p<0.05$). Rate of cardiovascular diseases was 14.7% in 1923-1925 and increased up to 30.2% in 1970 ($p<0.05$).
Conclusion: Significant trends of pathology autopsy of local Lithuanian pathology centre in 1923-1970 was characterized in the study. Rates of adult pathology autopsy, changes in patient's age and sex, as well as main disease reflects the impact of historical events on sociodemographic and clinical medicine trends, emphasizing the role of pathology autopsy as an effective tool to monitor accurate and timely status of clinical medicine situation in local region.

PS-22-002

History of pathology in Tunisia: a tribute to the country's pioneering pathologists

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Background & Objectives: The history of pathology can be traced back to the earliest application of the scientific method to medicine.

Rudolf Virchow is generally recognised as the father of microscopic pathology. In Tunisia, the history of pathology is relatively recent, beginning shortly after independence.
Methods: In that context, we carried out a bibliographical research on the country's first pathologists.
Results: Professor Amor Chadli was the first Tunisian pathologist to head the Institut Pasteur in Tunis from 1963 to 1988, and was also the founding Dean of the first Tunisian medical school. He was appointed Head of the Pathology department at Pasteur Institut in Tunis, the only Tunisian department i until 1972. In 1963, During his tenure, the Pasteur Institute of Tunis played its part in the country's health progress, the training of managers and biomedical research. In 1985, Professor Amor Chadli obtained a revision of the status of the scientific staff of the Tunisian Pasteur Institute and builb the first molecular biology department.
Among the pioneers in pathology, we also cite Professor Chedly Bouzakoura, as the first pathologist in Tunisia central region, dean of Sousse medical school and director of Regional Public Health Department under his leadership, pathology as well health sector has achieved prodigious success.
The list is long, but unfortunately we can't be exhaustive, we cite also Dr. Mouhamed Moncef Zitouna, former head of pathology department of Rabta hospital, in Tunis, who is a distinguished as academic author and researcher His extensive body of work spans various features of pathology. We cite also Pr Sarra Ben jilani as the first female pathologist in Tunisia, and head of Charles Nicolles hospital in Tunis.
Conclusion: To these inescapable icons, we are grateful. This tribute is a recognition and gratitude for the exemplary career of the doctors and their colossal work of leadership.

PS-22-003
Pathology Museum's conjoined twins collection from Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra
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Background & Objectives: Conjoined twins incidence is approximately 1 per 200,000 births, but is probably underestimated, representing one of the rarest forms of congenital anomalies. This type of anomalies can emerge in case of monochorionic-monoamniotic pregnancies and are characterized by fused twins, with at least 9 different types described in literature. Despite the most common accepted theory for its aetiology is partial fission or secondary fusion, not plainly explain every possible conjunction.
It is in this scenario that the Pathology Museums shows its important role of preserving these infrequent specimens.
Methods: We have documented the specimens preserved in Pathology Museum from Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, through macroscopic evaluation and description of type of fusion, associated external malformations and estimated gestational age.
Results: The present collection comprise 10 specimens: 4 cephalopagus (joined from head to umbilicus), 5 thoraco-omphalopagus (joined thorax and abdomen) and 1 craniopagus (cranium fusion). We only identified leporine lip as another congenital malformation present in 1 twin of the craniopagus case, and in both twins in one of the thoraco-omphalopagus cases.
All cases were acquired during the 20th century and the estimated gestational age ranges from 25th to 31st weeks.
Conclusion: Pathology Museums plays an important role in preserving rare specimens and rare pathologies as happen in this type of congenital malformation. They provide current pathologists and other interested audience an opportunity to see and study this cases.

PS-22-004
The specimens of syphilitic aortitis of the Pathology Collection of the University of Turin
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Background & Objectives: There are 9 specimens of syphilitic aortitis among the 395 wet specimens of the Pathology Collection of the University of Turin which derives from the Royal Pathology Museum of University of Turin dating back to the XIX and XX century. This pathology condition was the study field of Professor Pio Foà and his successor Ferruccio Vanzetti. During the conservation intervention of the Pathology Collection the preservative liquids of these specimens have been sampled to check for the presence of mercury and arsenic. These substances are related to possible drug treatment. One case of syphilitic aortitis collected by Professor Foà was histologically sampled to evaluate the morphology.
Methods: The analysis of the heavy metals is carried out after mineralization (ICP-OES) on a sample of the preservative liquid of each specimen. All the specimens have original labels on the jar and this allows to know when they date back. Haematoxylin-Eosin, histochemical staining for elastic fibres and immunohistochemical staining Vimentin and Factor VIII were performed.
Results: The presence of arsenic and mercury correlates with their time, in view of the spread of Salvarsan since 1910. The absence of significant arsenic content in the era prior to the spread of Salvarsan shows that these values are attributable to the drug treatment. This is confirmed by the fact that no known fixative had arsenic in its composition. Histochemical and immunohistochemical stains show endarteritis obliterans and the formation of capillaries.
Conclusion: The study of some wet specimens belonging to the Pathology Collection of the University of Turin shows their historical and paleopathological value once again. Chemical analyses show that this value is not limited to the specimens but extends to the preservative liquid. The histological analysis supports the potential of studying historical wet specimens with modern techniques.

PS-22-005
Fluid toxicity of ancient wet specimens: a safe proposal for the Pathology Collection of Turin
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Background & Objectives: The wet specimens from ancient museum pathological collections are kept in liquids whose composition is often unknown. However, they may also contain formalin for filling operations due to evaporation of the original liquid over time. Formalin is known to be carcinogenic, therefore it is necessary to safeguard the safety of the exposure environment of the specimens. The historical Pathology Collection of the University of Turin includes 395 wet

specimens. During the recent conservation intervention, it was made safe by a sealed closure of the jars.
Methods: Formalin content was tested in a small sample of the original fluids of 49 wet specimens with the kit Specroquant ®. Their jars were then sealed using rosin lute or vaseline and the presence of formaldehyde in the room was tested using an environmental tester
Results: 47 specimens contain 0.2-2.5% free formaldehyde, due to subsequent refills and not to the initial fixation procedure. Just 2 specimens dating back to the 1930s contains 3.5-4.5% free formaldehyde, due to the fixation procedure. This data is consistent with the time of preparation of the oldest wet specimens of the Pathology Collection between 1898 and 1923. It also shows that the traditional set-up continued at University of Turin even in subsequent years up to the 1930s. Environmental tests for formaldehyde in the ambient air of the exhibition room did not detect any formaldehyde.
Conclusion: Despite the scant presence of formalin, the closure of the jars prevents the spread of volatiles in the environment. The museum collection is therefore safe for the exhibition visitors.

PS-23 Poster Session Infectious Diseases Pathology

PS-23-001
Advanced technology for efficient tuberculosis, NTM, and drug resistance detection using Genes2Me OnePCR and Rapi-Q platforms

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Background & Objectives: Tuberculosis (TB) remains a major global health challenge, further complicated by drug-resistant TB (DR-TB) and the need to differentiate it from non-tuberculous mycobacteria (NTM). The **Genes2Me OnePCR POCT** and **Rapi-Q platforms** offer a **SAMPLE IN-RESULT OUT** solution for rapid TB, NTM, and drug resistance detection, targeting **RIF-1 to RIF-4**, **katG (codon 315)**, and **inhA (C-15T)** mutations. This study aims to evaluate their performance and compare it with the MIGIT and CBNAAT **MTB/RIF assay**.
Methods: Clinical samples, including sputum, culture, and other pulmonary specimens, were processed using a proprietary **Inactivation & Liquefaction (IL) buffer**, which breaks down the mucin matrix, reduces viscosity, and releases trapped bacteria for efficient nucleic acid extraction. The **OnePCR POCT platform** is a compact, automated system designed for point-of-care use, delivering results in **100 minutes**. It employs a **four-tube assay** for TB detection, NTM differentiation, and drug resistance analysis, making it ideal for decentralized diagnostic settings. In parallel, the **Rapi-Q platform** offers a high-throughput solution combined with the **Rapi-X16 extraction unit**, processing up to **16 samples simultaneously**.
Results: When tested with **100 MGIT-positive** and **100 MGIT-negative** clinical samples, the assays demonstrated an overall **clinical sensitivity of 95-96%** across MTB, MTB-NTM, and TB-MDR targets, outperforming the **Cepheid Xpert MTB/RIF assay** in multiple external centres. The platforms exhibited **specificity of 97-98%**, effectively distinguishing MTB from NTM and accurately identifying drug-resistant strains. The analytical performance showed a **Limit of Detection (LOD) of 50-70 rfu/mL** for both wild-type MTB and NTM strains, and 100rfu/ml for MDR with no cross-reactivity observed with common pathogens or interference from substances such as **human genomic DNA, tobacco**, or tuberculosis drugs.
Conclusion: The **Genes2Me OnePCR POCT and Rapi-Q platforms** provide a **rapid, accurate, and reliable** solution for TB diagnosis, NTM differentiation, and drug resistance detection.

PS-23-002
Visceral leishmaniasis in bone marrow biopsies: analysis of four tertiary hospitals

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Background & Objectives: Leishmaniasis is a disease caused by Leishmania spp., primarily affecting bone marrow, liver, and spleen, particularly in immunosuppressed patients. Histopathology, histochemical techniques and immunochemistry, including Giemsa and CD1a staining, play a crucial role in diagnosis. This study aims to analyse clinical presentation, diagnostic findings, and outcome of bone marrow involvement in visceral leishmaniasis.
Methods: We conducted a retrospective descriptive study across four tertiary hospitals in Spain, analysing nine cases diagnosed between 2014 and 2024. Clinical characteristics, diagnostic methods, risk factors, and complications have been assessed.
Results: The median age of patients was 49 years (r: 35-70), with a predominance of males (89%). Most patients were from Spain (78%), followed by Portugal (22%) and Georgia (11%), all residing in Spain at the time of diagnosis.
Histological examination revealed amastigotes within histiocytes dispersed in the bone marrow in all cases, without granuloma formation. Giemsa staining was positive in 89% of cases, PAS in 22%, and CD1a expression was detected in 67%.
HIV infection was the most common risk factor (67%), followed by intravenous drug use (56%), hepatitis C (33%), alcohol consumption (22%), and hepatitis B (11%). Clinically, most patients had no recent travel history, but hepatomegaly and splenomegaly were frequently observed. Complications included membranoproliferative glomerulonephritis (22%) and one fatal case (11%).
Conclusion: Haematoxylin H-E, staining is the most useful technique for evaluating bone marrow samples, while Giemsa remains the most effective histochemical method for diagnosing visceral leishmaniasis, particularly in immunosuppressed patients. CD1a serves as a valuable complementary marker. Although PAS has a lower positivity rate, it can still provide additional diagnostic support.
The presence of severe clinical complications, such as glomerulonephritis and mortality, underscores the potentially fatal course of the disease in immunosuppressed individuals. Additionally, common manifestations like hepatomegaly and splenomegaly reinforce clinical suspicion and highlight the need for comprehensive patient evaluation.

PS-23-003
Trends in hydatidiform mole incidence during the pandemic: should we worry?

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Background & Objectives: Whether partial or complete, hydatidiform moles (HM) are pre-malignant gestational trophoblastic diseases represented by trophoblastic over-proliferation without normal foetal development. Adverse pregnancy outcome, especially HM pathogenesis was theorized to be related to the hostile inflammatory environment characteristic to viral pandemics, as COVID-19 pandemic was. This study aimed to determine whether an increase in HM incidence trend could be observed during the pandemic.

Methods: An observational analitical study was conducted. The total number and percentage we reffered to was of the pregnant women registered on the Obstetrics Department of the Emergency Clinical County Hospital of Targu-Mures, who gave birth or suffered a misscariage between January 2019-December 2023. We decided upon this study period considering two years prior to and two years after 2021, the highest pandemic peak-year in Romania. Medical disorders of pregnancy were included, with emphasis on HM. HM were diagnosed only on histopathological examination without performing any molecular tests.
Results: Of a total 8155 registered-pregnancies, 62 (0.76%) were HM diagnosis. The annual incidence rate of registry-identified HM has increased from 0.72% 12-50 years-old patients in 2019 to 1.24% in 2023. Partial HM had higher incidence rate between 2019-2023 (0.39%, 0.11%, 0.43%, 0.86% and 0.83%) with a total incidence of 0.51%. HM was associated with extreme maternal age (=< 18 years-old (20.96%) and >=35 years-old patients (29.02%), p<0.0001). The highest HM incidence rate was seen among nulliparous women (58.06%, p=0.0607). The mean gestational age of the embryo at the time of diagnosis was 9 gestational weeks. Endometritis (74.19%) and abundant vaginal bleeding (38.70%) were associated (p<0.0001).
Conclusion: In crisis periods, such as COVID-19 pandemic was, nulliparous women are more susceptible to a HM diagnosis given the associated poorer inflammatory function, suggesting a possible causative association of COVID-19. Further studies and comparison with non-pandemic data are necessary to get more insight into this relation.

PS-23-004

Human papillomavirus's influence on proteasome-mediated immune stimulation in cervical and oropharyngeal cancer

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Background & Objectives: The proteasome is an essential cellular component which degrades and recycles proteins. One of its key functions is to generate antigenic peptides for presentation via MHC Class-I. In virally-infected or transformed cells, antigens derived from viral or tumour-associated proteins can activate cytotoxic T-lymphocytes. Stimulated by IFNy and TNFα, the proteasome undergoes a conformational change in which some of its subunits are replaced by 'immunosubunits', creating a more diverse array of antigenic peptides to incite an immune response.
Proteasomal function is tightly regulated. PSME4 is a negative regulator of proteasome/immunoproteasome activity. PSME4 depletion enhances antigen presentation, while the ratio of PSME4 to immunosubunit PSMB10 correlates with immunotherapeutic response.
This project aims to evaluate the impact of HPV infection on proteasomal and immunoproteasomal expression.
Methods: SiHa (cervical, HPV16+), C33a (cervical, HPV-), SCC154 (oropharyngeal, HPV16+) and SCC4 (oropharyngeal, HPV-) cell lines were grown following standard cell culture procedures. The expression of PSME4 and PSMB10 was evaluated in HPV+ and HPV- cervical and oropharyngeal cancer cell lines by Western blot. Immunofluorescence for PSME4 was performed on SiHa and C33a cell lines to evaluate protein intracellular localisation.
Results: *Western blot:* Strong PSME4 in all cell lines, with increased expression in C33a and SCC4 (both HPV-). Increased PSMB10 (immunosubunit) expression in C33a and SCC4 compared to HPV+ cell lines (SiHa and SCC154).
PSME4 Immunofluorescence: Intense staining of SiHa, with preferential nuclear localisation. Strong staining of C33a cells in both nuclear and cytoplasmic compartments.
Conclusion: Our understanding of HPV's ability to alter proteasomal function as a mechanism of immune escape is limited. These results suggest that HPV alters the expression and localisation of regulatory subunit PSME4 and reduces expression of immunosubunit PSMB10. This may contribute to viral and tumour immune escape in HPV infected cells, and may serve as a potential target for future immunomodulatory therapies.

PS-25 Poster Session Other Topics

PS-25-001

Rising workload and diagnostic complexity in histopathology and the impact on turnaround times in Ireland

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Background & Objectives: The Irish National Histopathology Quality Improvement (NHQI) Programme collects data in the form of procedure codes (P codes), quality codes (Q codes) and metrics regarding workload, turnaround times and other key quality indicators (KQIs) relating to histology, cytology and autopsy cases. The Programme recommends turnaround time (TAT) targets of 5-10 days depending on specimen type.
Methods: A review of national histopathology data (January 2013–December 2023) examined workload in 28-33 laboratories which included the number of cases, specimens, special stains, immunohistochemical stains, and TAT figures. Statistical analysis was performed using SPSS Statistics, utilizing linear regression, compound annual growth rate and Pearson correlation analysis. Statistical significance was set at $p < 0.05$.
Results: Over the 11-year period from 2013 to 2023, case numbers increased by 34.4% (420,790 to 565,669). The average specimen number per case increased from 1.6 to 1.8 ($R^2 = 0.977$, $p<0.01$), and the average block numbers per case increased from 2.7 to 2.9 ($R^2 = 0.709$, $p<0.01$), reflecting a significantly increased workload per case.
Cases requiring immunohistochemical (IHC) stains increased by 123% (43,865 to 97,593). Additionally, the total number of IHC stains performed rose by 102.7% (285,660 to 579,035). The compound annual growth rate (CAGR) of IHC stain number (7.3%) significantly outpaced that of total cases (3.0%).
The percentage of cases meeting TAT targets declined from 78.4% in 2015 to 56.4% in 2023. A significant negative correlation was observed between TAT compliance and specimen numbers ($r = -0.872$, $p = 0.002$).
Conclusion: This review of the NHQI Programme data highlights a significant increase in workload, with a shift towards more complex diagnostic work reflected in the doubling of IHC use over 11 years. The burden of increasing workload and case complexity is having a significant negative impact on TATs.

PS-25-002

Reticulin framework changes in poorly differentiated carcinoma metastases compared to large-cell lymphomas

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Background & Objectives: Reticulin fibres are responsible for maintaining the functional integrity of tissues and also have a role in the

patterns of invasion seen in various neoplasms. The aim of this study is to evaluate the changes that occur to reticulin fibres in poorly differentiated carcinoma metastases to lymph nodes and large-cell lymphomas, in order to identify shortcuts for immunohistochemical diagnosis.
Methods: We included, in a retrospective study, 13 patients with lymph node metastases from poorly differentiated carcinomas of the gastrointestinal tract, 11 patients with lymph node metastases from poorly differentiated breast carcinomas and 10 patients with large-cell lymphomas. Reticulin framework patterns were assessed with Gomori silver reticulin stain and the density of the reticulin fibres was calculated as the ratio of total fiber area to overall tissue area using the Fiji image analysis software.
Results: In the case of poorly differentiated carcinomas, the reticulin fibres were long, dense, thick and were distributed around islets of cells with a lot of branches, while in lymphomas the fibres were shorter, thinner and had an uneven distribution with numerous scattered fragments. The density of the reticulin framework had a mean value of 6.1% in lymphomas, while the values for poorly differentiated carcinoma metastases were very close at 10.5% for gastrointestinal metastases and 10.6% for breast metastases.
Conclusion: In the era of expensive immunohistochemistry, using the Gomori silver reticulin stain can prove to be useful as a first step in distinguishing between poorly differentiated carcinomas and large-cell lymphomas. Routine histologic evaluation using this stain can aid further immunohistochemical studies to be better targeted.

PS-25-005
Real-time FFPE NSCLC block stability using PD-L1 IHC 22C3 pharmDx
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Background & Objectives: PD-L1 IHC 22C3 pharmDx is intended for use in a qualitative immunohistochemical (IHC) assay to detect PD-L1 expression in formalin-fixed, paraffin-embedded (FFPE) human specimens routinely processed for diagnostic evaluation. Guidelines for use of FFPE blocks vary, with limited data to support their extended shelf life.
A real-time stability study on non-small cell lung cancer (NSCLC) blocks was performed to assess if the age of the blocks, stored over time, impacted PD-L1 expression.
Methods: NSCLC specimens were used to evaluate PD-L1 expression in FFPE blocks aged over time. A cohort of 188 NSCLC blocks were commercially procured and populated to include the full dynamic range of PD-L1 expression. In addition, an enrichment of near-cutoff specimens for both TPS 1% and 50% cutoffs were included. All specimens were prepared as FFPE blocks, properly stored in the dark at room temperature until time of sectioning. PD-L1 IHC 22C3 pharmDx (SK006) staining was performed at Time 0, 3 years and 5 years. PD-L1 expression was assessed for any changes in TPS over time compared to the initial Time 0 staining.
Results: A concordance correlation coefficient (CCC) with 95% CI was calculated to be 0.954 (0.938, 0.966) demonstrating strong alignment in TPS between staining results at Time 0 versus 5 years. The diagnostic agreement for TPS 1% and TPS 50% cutoffs both generated overall agreement 95% percentile bootstrap CI lower-bound values >90%. Our results showed no significant change in PD-L1 expression in sections from aged FFPE NSCLC blocks stored in the dark at ambient conditions over time, supporting a shelf life of at least 5 years.
Conclusion: NSCLC FFPE tissue blocks may be stored at ambient temperature for at least 5 years, where the PD-L1 antigen is well preserved and stable for evaluation with PD-L1 IHC 22C3 pharmDx.

PS-25-006
Centers for experimental animal pathology occupy a small but valuable niche in translational medicine – time for a change?
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Background & Objectives: Since CRISPR/Cas9 systems can be easily used to establish new genetically engineered mouse models, application of these models to explore predictive and therapeutic topics for human diseases is rising. Centers for comparative histopathology bridges the veterinary and human pathology fields and can combine optimally the technical, research, and diagnostic expertise for phenotyping, evaluation and interpretation of complex animal models in the context of human pathology to reach meaningful study results.
Methods: In 2016, the *Centre for Model System and Comparative Pathology (CMCP)* was established at the Institute of Pathology of the University Hospital Heidelberg to cover the demand for tissue processing and expertise in comparative pathology. Besides the *Comparative Experimental Pathology (CEP)* in Munich, the CMCP is the second centre in Germany pursuing such an integrative propose. An overview of the experience gained in handling of more than 450 animal projects with more than 40.000 processed tissue specimens is given.
Results: Centers for experimental animal pathology as the CMCP enable optimal tissue processing of large sample cohorts. They offer a broad spectrum of standard and specialized tissue-based technologies including tailored immunohistochemistry and animal model evaluation, phenotyping and scoring. The expertise in veterinary pathology allows detection of species-specific background lesions and individual spontaneous lesions to avoid misinterpretations. By providing essential prerequisites for high-quality, reproducible and sustainable research in the translational medicine, the requirements for publications in top-class professional journals were ideally fulfilled.
Conclusion: The importance of animal models reflecting human diseases will increase in future but the need for high-quality animal tissue processing and animal model evaluation cannot be met by single facilities in a niche position. To cover the existing gap and the expectable rising demand in the German and European translational research landscape, further facilities for experimental animal pathology that are integrated in the human pathology environment should be established.

PS-25-007
Pilot evaluation of a formalin recycling system in pathology: efficacy, environmental impact, and cost-benefit analysis of a sustainable alternative to single-use fixatives
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Background & Objectives: Climate emergency requires healthcare decarbonization. In Pathology laboratories, formalin, widely used for tissue fixation, is a single-use harmful reagent. We previously showed that reusing "nearly new" formalin from biopsies (season 1) reduces consumption without compromising quality and security (doi:10.1016/j.pathol.2024.12.639). This study aimed to i) test a formalin recycler for soiled formalin, ii) evaluate its impact on annual consumption alone (season 2) and combined with previous measures (season 1+2), and iii) quantify the environmental impact of this reduction.

Methods: We selected soiled formalin following manufacturer's guidelines using an in-house colour chart. A gravity-based recycler with activated carbon filter was used (doi:10.1093/ajcp/aqac062). Recycled formalin was tested for pH and formaldehyde concentration, and validated through the entire specimen pathway including immunohistochemical and molecular analyses. Formalin consumption was compared before and after recycler implementation and against 2021 reference. Environmental impact (CO_2 equivalent emissions (CO_2eq), human toxicity, and freshwater ecotoxicity) was assessed using ADEME and Ecoinvent v3 databases.
Results: Recycled formalin met all quality standards with no abnormalities detected in specimen analyses. Implementation in the second half of 2024 reduced consumption by 25% compared to 2023 (same period). Overall strategy (season 1+2) reduced formalin consumption by 54% compared to 2021 (4081 versus 1889 liters), resulting in 5 tons of CO_2eq avoided, €12,500 saved, and reduced human and aquatic toxicities (242.5 and 152.5 kg 1,4DBeq respectively). The laboratory also gained operational autonomy.
Conclusion: Pathology laboratories can effectively mitigate their environmental impact by reducing formalin consumption through recycling strategies, representing a valuable opportunity until more sustainable fixation alternatives are developed.

PS-25-008
Rapid tissue sectioning system for real-time histopathological diagnosis
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Background & Objectives: Traditional histopathological techniques such as paraffin-based microtomy and frozen sectioning present significant drawbacks, including long processing times and the generation of artifacts like ice crystals. The objective of this work is to develop a novel device that enables the production of ultra-thin tissue sections (3–5 μm) rapidly, without paraffin embedding or freezing, thereby facilitating rapid histopathological diagnosis.
Methods: The system employs a perforated tissue stabilization plate integrated with a vacuum mechanism to securely fix the tissue, eliminating distortions during cutting. A synchronized movement mechanism aligns the tissue with a microscope slide that features a low-friction, cooled surface (0–4 °C). A rotary cutting blade with adjustable thickness control enables precise sectioning, after which the tissue slice is automatically transferred onto an adhesive-coated slide. Immediate fixation and staining protocols are applied to the section, which can then be directly integrated with a digital slide scanner for real-time analysis.
Results: The system is expected to consistently produce high-quality tissue sections with adjustable thickness between 3 and 5 μm. The integrated process minimizes preparation time and eliminates the freezing artifacts commonly seen in traditional methods. Furthermore, its compatibility with digital tissue scanners supports imaging analysis, potentially accelerating diagnostic workflows.
Conclusion: This tissue sectioning system offers an alternative to existing histopathological methods by delivering rapid, artifact-free tissue sections. Its potential integration with digital imaging technologies underscores its value as a tool for enhancing diagnostic efficiency and accuracy, particularly in time-critical scenarios.

PS-25-009
Influence of preprocessing of stimulated Raman scattering images on the performance of deep neural networks for detecting cancer tissue
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Background & Objectives: Stimulated Raman scattering (SRS) microscopy enables intraoperative visualization of histological features similar to haematoxylin and eosin staining, known as stimulated Raman histology (SRH). Deep learning (DL) has become a powerful tool in automated cancer diagnostics. However, SRS image preprocessing remains crucial, affecting model performance and reliability. This study explores how various preprocessing methods impact six neural network architectures—VGG19, ResNet50, InceptionResNetV2, Xception, ConvNeXt, and Vision Transformer—in classifying tumoral and non-tumoral tissue in SRS and SRH images of oral squamous cell carcinoma (OSCC) and non-small cell lung carcinoma (NSCLC).
Methods: A dataset of 542 SRS and SRH images (pixel size: 467 nm), annotated by pathologists, was divided into 48,175 tiles. Five preprocessing methods were applied to SRS images: complex manipulation, histogram matching, histogram equalization, Gaussian blurring, and scaling to [0,1]. Each model was trained five times for 40 epochs. Metrics included balanced accuracy, precision, recall, F1-score, and AUC. Class activation and attention maps highlighted predictive image features.
Results: SRH images achieved the highest balanced accuracy (0.87), followed by scaled SRS images (0.85). Preprocessing techniques with higher complexity tended to produce lower accuracy and greater variability. Simple pixel scaling yielded the most consistent results. While class activation maps identified regions relevant to model predictions, their alignment with biologically meaningful structures varied across architectures. Vision Transformers appeared to focus on cytoplasmic and membrane areas for accurate classification, whereas convolutional neural networks (CNNs) showed less consistent patterns of attention.
Conclusion: Preprocessing strategies markedly affect the accuracy and robustness of deep learning models applied to SRS data. Among the tested methods, simple scaling of pixel values to [0,1] provided more stable performance compared to more complex preprocessing. Although overall classification accuracy was high, linking DL predictions to biologically interpretable features remains a significant challenge.

Funding: This research was funded by the German Federal Ministry of Education and Research (Bundesministerium fur Bildung und Forschung, BMBF), grant number 13GW0571D

PS-25-010

An on-line training and education portal for HER2-low interpretation in breast cancer: an initiative from the International Quality Network for Pathology

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Background & Objectives: Trastuzumab deruxtecan is a treatment for metastatic breast cancer over expressing HER2 protein at a low-level (HER2-low).
Evidence shows that pathologists have difficulty in reproducibly assessing HER2-low, potentially leading to a negative impact on patient treatment outcomes.
The International Quality Network for Pathology (IQNPath) established an on-line training portal using a uniquely validated set of HER2-stained clinical cases.
The aims of the project were to:

- Provide an educational resource for the assessment of HER2-low cases
- Document the competence of portal users
- Gather information about demographics of the testing community.

Methods: A free-to-access portal was established using PathoGate platform software (PathoPulse ApS. Denmark). It went 'live' in November 2024. The cases used had previously been scored independently by 16 expert pathologists.
After registration users completed a questionnaire which gathered information about job role and relevant experience. Participants assessed a training set of 10 WSIs (matched H&E and HER2 stained) followed by one of two randomly allocated 20-case test sets.
Cohen's Weighted Kappa (CWK) statistics were generated for each participant using the consensus scores of the expert panel (SPSS, IBM, USA).
Results: In the 5-month period reported here, 132 users registered. Most were consultant pathologists (92, 63.0%), with the next largest group being biomedical scientists (24,16.4%).
Overall, 39 (26.7%) registrants had received HER2-low training; 45 (30.8%) reported HER2-low cases regularly (≥ 1 per week).
Of all those who registered, 115 (87.1%) completed the training set, and of these 61 assessed of one of the test sets.
The median CWK (range) for Test Set 1 users was 0.64 (0.29 - 0.88), for Test Set 2 it was 0.60 (0.41 - 0.75). In comparison results for the expert panel were 0.71 (0.41-0.85).
Conclusion: The portal was successfully established and was well-utilised. The CWK statistic indicated median agreement with the expert consensus that was moderate to substantial.

PS-25-011

Meeting the future: creation of multicolored, three-dimensionally printed organ models for gross examination training in Surgical Pathology residency

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Background & Objectives: Currently, gross examination is performed worldwide by Pathologists and/or grossing personnel. Training for this very important aspect of pathologic examination can potentially be enhanced by the creation of models of excision specimens. Multicolored three-dimensional (3D) printing can further aid in the understanding of different anatomic structures and borders within the models and further elevate their learning potential.
Methods: A 3D-printed model of a radical nephrectomy specimen was created. A patient's computed tomography scan of the abdomen and pelvis was analysed for the production of a 100%-scale anatomic model. A tumour-like shape was added to the initial design, in order to simulate a renal tumour. The final model was 3D printed using low-hardness thermoplastic polyurethane material. Subsequently, copies of the model were independently dissected by seven Pathology Residents. The final results, in adequacy of sampling, correct margin evaluation and measurements of margin distances was evaluated. Two different Consultant Pathologists evaluated the sections macroscopically, independently and blinded with regard to each Resident. The Residents were provided with appropriate feedback and were tested on a model with a different location of the lesion and re-evaluated. Furthermore, the Residents and the Consultant Pathologists completed a survey on the potential benefits in their training through practice on similar models.
Results: The results of the evaluation of the Resident Pathologists showed adequate sampling of different areas and margins and low divergence from margin distances as set on the designed model, with improvement on re-evaluation. The ease of use of the models was rated positively. The estimated cost of production for each model was low.
Conclusion: The potential of the application of these techniques in the training of future Pathologists is highly promising. Our study builds on previously published literature and provides a framework that can be applied independently to enhance gross examination training.

PS-25-012

Advancing archival and precision retrieval in a pathology lab while securing tissue samples

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Background & Objectives: Donostia University Hospital's histology lab processes 350,000 slides and 230,000 blocks annually. Manual archiving was labour-intensive with high sample loss risk. The Pathology Department sought automation to improve traceability, reduce labour, and streamline sample management.
Methods: The Pathology Department conducted an observational study on 08.05.2024 with the implementation of two systems: one for automated scanning, registering, and sorting blocks, and another for slides. With these systems laboratory technicians don't need to sort samples sequentially. For retrieval, the systems quickly direct lab staff to the precise location of a sample and provides detailed information about its chain-of-custody.
Results: Adoption of the new systems decreased staff-needed hours. From 120 hours per month to archive and retrieve blocks in April 2024, to 60 hours in January 2025 (a decrease of 50%). For slides, the decrease was 66,6% (from 90 hours to 30 hours in the same period).
Even though the department suffered an increase in volume of samples processed during the study period, the hospital staff saved 4.415 hours annually in tissue sample management. This time gained by automating their workflow, has enabled the hospital to reassign 2.5 FTE positions

to aid in other areas that support patient care. The workflow of archiving samples became more efficient and eliminated errors.
Conclusion: The implementation of these systems revolutionized tissue sample storage and retrieval, significantly enhancing patient care and safety. Faster, more precise access to blocks and slides allows for faster diagnosis, enabling earlier treatment. Additionally, these advancements have improved laboratory workflow, reducing stress and minimizing the risk of sample loss. Staff benefit from increased efficiency and job satisfaction, fostering a more productive work environment. Ultimately, these innovations streamline operations while ensuring better outcomes for both patients and laboratory professionals.

PS-25-013
Sirolimus-coated balloons for the ureteral strictures. Could it be an efficient alternative to paclitaxel?
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Background & Objectives: Ureteral strictures, consisting of narrowing of the ureter, may lead to obstructed urine drainage and potential renal damage. Their management is challenging due to the intricate anatomy and need for precise treatment. Drug-coated balloons, using mainly paclitaxel, offer localized drug delivery to enhance stricture resolution and minimize recurrence. This study aimed to evaluate the distribution and effect of sirolimus within the ureter using sirolimus-coated balloons (SCB).
Methods: Two female porcine models (four ureters) were used, while artificial strictures were induced with a laser at the vesicoureteral junction. Afterward, ureteral balloons were applied, comparing specimens of no-sirolimus balloon ureter at zero time and SCBs ureters at zero time, 4 hours, and 8 hours. The main endpoints were the detection of sirolimus within the ureteral layers and its effect on regional inflammation. An evaluation of the intensity of inflammation followed, aiming to identify differences in lymphocytic infiltration between those into which everolimus had been injected and those that had not received the drug. The suppression of the inflammatory response—and consequently the effect of the drug—was indirectly assessed through the detection of Cyclin D1 expression and p27 protein."
Results: Everolimus reduced the inflammatory response as well as Cyclin D1 expression. p27 did not show significant differences in expression. However, the number of samples was insufficient to yield statistically significant results.
Conclusion: The use of sirolimus on drug-coated ureteral balloons seems to constitute a feasible alternative to paclitaxel, as it may be distributed within the ureteral layers and reduce the regional inflammation. The conduction of further experimental and clinical studies may empower the safety and effectiveness of the SCBs.

PS-25-014
Leverage complete sample traceability, from accessioning to archiving, to improve laboratory workflow and save time
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Background & Objectives: With an annual volume of 150,000 paraffin blocks and 288,000 slides, the pathology department of a university hospital was spending more than 4,002 man-hours per year on sample management and was looking for a more efficient and safer workflow.
Methods: The department conducted an observational study with the implementation of three new systems (December 2022, January 2024 and April 2024). The first will automate pre- and post-processing scanning to ensure correct sample processing. The second and third systems automate the sorting, archiving and precise retrieval of tissue blocks and slides. The systems can also be integrated with the hospital's LIS, improving the complete chain of custody.
Results: In pre-processing, the new system eliminates the need to manually scan cassettes one by one, which took 350 hours per year before automated pre-processing, compared to 130 hours with the new system (57% less). The implementation of the pre-processing system saved 220 hours per year.
The implementation of the new block and slide tracking and archiving systems also resulted in a reduction in the time associated with archiving/re-archiving blocks and slides. From 320 hours per month to 150 hours per month, or 3,840 hours to 1,800 hours per year, saving an additional 2040 hours.
In addition, the three systems together eliminated 5 manual touch points.
Conclusion: Implementing these three systems has improved the entire laboratory workflow, from sample receipt to archiving and retrieval. The complete chain of custody increases patient safety by eliminating the manual touch points that contribute to misplaced and lost specimens.
In addition, laboratory workflow automation helps address the challenges associated with increasing caseloads and volumes by freeing staff from the time-consuming task of sorting blocks and slides into sequential order, allowing them to spend more time on critical activities that support patient care.

PS-25-015
Collagen I type expression changes in anterior abdominal wall hernias repair (experimental study)
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Background & Objectives: A stimulation of collagen type I synthesis in the connective tissue increases its strength. The aim of the study was to evaluate the expression level of collagen type I in the skin and aponeurosis of rats after various modifications of anterior abdominal wall hernia repair.
Methods: 36 male Wistar rats (220-250 g) were included in three study groups: in the first group (n=12) a polypropylene mesh was placed under the aponeurosis of anterior abdominal wall of rodents; in the second group (n=12) polypropylene mesh with platelet-rich plasma (30 µl) and with a platelet activator (5 µl) was applied also under the aponeurosis of rodents; in the third group (n=12) platelet-rich plasma (30 µl) with a platelet activator (5 µl) was administered under the aponeurosis. Collagen type IA2 - antibody (Elabscience, dilution of 1:400) was used. The expression was analysed by the image analysis software Aperio Image Scope [v12.4.6.5003].
Results: On the 28th day of the experiment the positivity of collagen type I expression in skin of rats of first group was 17.5 (15.0; 19.0) %, of second group – 85.5 (84.0; 88.0) % and after implantation of platelet-rich plasma – 65.5 (64.0; 71.0) %. The median positivity of collagen type I expression in aponeurosis of rats of first group was 13.5 (52.0; 61.0) %, in second group – 90.5 (89.0; 91.0) %, in thirds group – 74.5 (73.0; 77.0) %. The maximal activation of collagen type I synthesis in skin ($p = 0.0005$) and in aponeurosis tissue ($p = 0.0005$) of the anterior abdominal wall of rodents was found after implantation of a polypropylene mesh with platelet-rich plasma.
Conclusion: This study showed that the implantation of polypropylene mesh with platelet-rich plasma during hernia repair increase the

strength of both connective and scar tissue by activation of collagen type I synthesis.

Funding: This research was supported by the Belarusian Foundation for Basic Research

PS-26 Poster Session Pulmonary Pathology

PS-26-001

Immune phenotypes in patients with non-small cell lung cancer and their association with smoking

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Background & Objectives: One of the important mechanisms leading to non-small cell lung cancer (NSCLC) recurrence is changes in the tumour microenvironment and the formation of certain immune phenotypes.
Aim: To investigate the prevalence of immune phenotypes in NSCLC and their association with smoking.
Methods: An immunohistochemical study of 40 NSCLC tumour samples was conducted using anti-CD8+ antibodies. Immune phenotypes were classified based on CD8+ spatial distribution: the immune desert phenotype (low CD8+ in tumour nests and stroma), the immune-excluded phenotype (high CD8+ in the stroma but low in nests), and the inflamed phenotype (high CD8+ in both). Pearson's rank correlation coefficient was used to assess the association with smoking.
Results: Among 20 adenocarcinoma samples, 5 (25.0%) had the immune desert phenotype, 3 (15.0%) immune-excluded, and 12 (60.0%) inflamed. Among 20 squamous cell carcinoma samples, 1 (5.0%) was immune desert, 13 (65.0%) immune-excluded, and 6 (30.0%) inflamed. Smoking history was present in 13 (65.0%) adenocarcinoma and 19 (95.0%) squamous cell carcinoma patients. The inflamed phenotype was most common in never-smokers ($\chi^2 = 9.8322$; p= 0.007).
Conclusion: The inflamed phenotype predominates in adenocarcinoma, while the immune-excluded phenotype is more frequent in squamous cell carcinoma. Smoking is associated with the immune-excluded phenotype.

PS-26-002

The impact of spread through air spaces extent and morphology on prognosis in non-small cell lung carcinoma

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Background & Objectives: STAS (spread through air spaces)is defined as tumour cells spreading within air spaces beyond the edge of the main tumour. Some studies suggest that its distance and morphological patterns may have prognostic value, but this remains unclear and is not routinely reported. This study aims to evaluate the prognostic role of STAS extent and patterns.
Methods: This study retrospectively analysed the correlations between the extent of Stas and clinicopathologic characteristiscs and prognostic significance in 104 completely resected stage I-III non-small cell lung carcinomas between 2017 and 2023 at our centre.STAS was grouped as limited (<1000 μm) or extended (>1000 μm) based on distance from the tumour. Patterns were classified as single cells, micropapillary clusters, or solid nests.
Results: STAS was present in 65 cases (62.5%): 18 limited(17,3%) and 47 extended (45,2%). Single-cell pattern was seen in 7 cases (6,7%), micropapillary in 23 (22,1%), and solid in 35 (33,7%). Median overall survival (OS) and progression-free survival (PFS) were 33.5 and 27 months, respectively. Extended STAS was more frequently found in patients with adenocarcinoma and/or pleural invasion.It was associated with significantly lower OS compared to STAS negative group (p=0.028). Although 45% of patients experienced recurrence; PFS was not significantly different in this group(p=0.075).There was no significant difference between limited versus extended STAS, or between limited versus negative STAS. No recurrence or death was seen in single-cell pattern cases. Solid and micropapillary patterns were associated with poorer OS and PFS (p=0.007 and p=0.011, respectively). In multivariate analysis, extended STAS was found as an independent poor prognostic factor for survival (p=0.023).
Conclusion: In conclusion, limited or single-cell STAS did not affect prognosis,and some may represent artifacts, while extended STAS was linked to worse survival,therefore it appears to be more reliable and clinically significant.Reporting the extent and pattern of STAS may help lead pathological evaluation and treatment decisions.

PS-26-003

Interobserver variability in subtyping and spread through air spaces assessment of lung adenocarcinomas: are we seeing the same patterns?

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Background & Objectives: Invasive non-mucinous lung adenocarcinomas are classified by predominant histologic subtype, though multiple patterns often coexist. Subtyping and the evaluation of spread through air spaces (STAS) are clinically relevant for grading and prognosis, but both can be challenging. This study evaluates interobserver agreement in subtyping and STAS assessment among pathologists with varying experience and specialization.
Methods: An online survey was conducted using selected static digital images from resected non-mucinous lung adenocarcinoma cases diagnosed at our institution. Fifty-seven pathologists participated, each evaluating two different cases. For each case, they estimated the proportion of five histologic subtypes using predefined percentage ranges. STAS assessment was based on two representative images per case, with responses recorded as present, absent, or not sure. Interobserver agreement was assessed using the intraclass correlation coefficient (ICC) for subtype scoring and Fleiss' kappa for STAS. Participants were categorized into three groups based on experience: thoracic pathology specialists, pathologists with more than five years of experience, and those with less than five years.
Results: The overall ICC for subtype scoring was 0.77, indicating good agreement. Some subtypes could not be statistically evaluated due to minimal score variation, suggesting strong concordance. Frequency analysis showed consistent scoring for acinar and lepidic patterns. In contrast, papillary and micropapillary patterns—especially in Case 2—exhibited broader distributions. Fleiss' kappa for STAS was 0.48. Scoring patterns varied by experience, with specialists showing more consistency.
Conclusion: Despite overall agreement, interpretive variability in certain subtypes and STAS highlights the need for improved standardization and training, especially for diagnostically ambiguous features. The influence of experience and specialization on scoring consistency supports the value of targeted education and consensus development. Standardized criteria may improve reproducibility and diagnostic confidence, contributing to more consistent clinical decision-making in pulmonary pathology.

PS-26-004

Immune biomarkers in advanced NSCLC: the role of PDL-1 and CD8+ T Lymphocytes in survival

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Background & Objectives: Immunotherapy has transformed advanced non-small cell lung cancer (NSCLC) treatment, with PDL-1 expression as a key biomarker. Tumour microenvironment complexity suggests additional immune factors, such as CD8+ T-cell infiltration (TILs), may impact treatment efficacy. This study examines their relationship and prognostic significance.
Methods: A retrospective study analysed 50 NSCLC patients treated with immunotherapy (2016–2021, median follow-up: 43.5 months). CD8+ TILs were assessed using Donnen's classification. PDL-1 expression was determined by immunohistochemistry, and molecular profiling by next-generation sequencing (NGS). Associations with progression-free survival (PFS) and overall survival (OS) were evaluated.
Results: Higher stromal TIL density correlated with improved OS (median, $p = 0.04$), whereas intraepithelial TILs showed no survival impact. In a Cox regression model, both high stromal TILs and PDL-1 $\geq 50\%$ were significantly linked to lower mortality (HR stromal TILs: 0.46, $p = 0.037$; HR PDL-1 $\geq 50\%$: 0.49, $p = 0.046$). Molecular analysis identified EGFR, TP53, ROS1, BRAF, and KRAS mutations, though none correlated significantly with clinical response. These findings suggest that stromal TIL infiltration and PDL-1 expression serve as independent prognostic biomarkers in NSCLC patients receiving immunotherapy, highlighting their potential role in treatment stratification and outcome prediction. Further investigation of additional immune and molecular factors is warranted.
Conclusion: PDL-1 expression and stromal TIL infiltration are key prognostic markers in NSCLC patients treated with immunotherapy. Their combination identified distinct clinical outcome subgroups, supporting their relevance in personalized treatment. Despite frequent genetic mutations, no significant association with therapy response was found, underscoring the need for further research on tumour microenvironment interactions. These findings reinforce the importance of integrating immune biomarkers into clinical decision-making to optimize therapeutic strategies and improve patient outcomes in advanced NSCLC.

PS-26-005

Morphofunctional features of alveolar type II cells of offspring that developed in utero under maternal genitourinary system chronic inflammatory process conditions

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Background & Objectives: Maternal chronic inflammatory processes of the genitourinary system (GUS) often complicate the course of pregnancy and childbirth, negatively affecting the offspring health. The objective was to identify the morphofunctional features of alveolar type II cells of offspring that developed in utero under conditions of maternal chronic inflammatory process of the GUS caused by *Streptococcus pyogenes*.
Methods: An experiment was conducted on rats of the WAG population. Group 1 included 318 one-week-old, 204 one-month-old, and 214 two-month-old rats from mothers with physiological pregnancy. Group 2 included 257 one-week-old, 134 one-month-old, 121 two-month-old rats from mothers whose pregnancy occurred against on the background of a chronic inflammatory process of the GUS caused by *Streptococcus pyogenes*. Fragments of the offspring lungs were the study material. Microscope slides were stained with haematoxylin and eosin, sudan 3.
Results: During survey microscopy in group 2, compared to group 1, alveolar type II cells were characterized by focal dystrophic, necrotic and desquamative changes. In some visual fields, in areas of dystelectasis and atelectasis, alveolar type II cells were not detected or were found in the alveoli lumen. The relative number of such cells increased ($p<0.05$) with age of the rats ((11.9 ± 0.8) % in one-week-old rats, (20.5 ± 0.3) % in one-month-old rats, (32.2 ± 0.8) % in two-month-old rats). In group 2 compared to group 1, the sudanophilic layer on the alveolar cells surface, which was a surfactant, characterized by uneven thickness and were not detectable in some places.
Conclusion: Maternal chronic inflammatory process of the genitourinary system caused by *Streptococcus pyogenes* changes the morphofunctional state of the offspring alveolar type II cells. These changes increase with the animals' age and are manifested by focal dystrophic, necrotic and desquamative changes, which lead to a deficiency of surfactant as a result of its rapid destruction or insufficient production.

PS-26-006

Clinical and pathological characteristics of multiple primary malignancies in patients diagnosed with lung carcinoma: a single-centre retrospective analysis

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Background & Objectives: Multiple primary malignancies (MPMs) represent a significant clinical challenge due to their complexity in diagnosis, treatment, and follow-up. While MPMs involving breast, gynaecologic, and gastrointestinal cancers are well-documented, data regarding those associated with lung carcinoma remain limited. This study aimed to retrospectively evaluate the clinical, pathological, demographic, and prognostic features of patients diagnosed with primary lung carcinoma with additional primary malignancies.
Methods: This retrospective study included 76 patients diagnosed with MPMs between 2005-2023 at a single centre, all with a primary lung carcinoma diagnosis. Data collected included demographic characteristics, tumour locations, histopathological types, treatment modalities, comorbid conditions, prognostic indicators, and survival outcomes.
Results: Of the patients, 76.3% were male (male-to-female ratio: 3.22), with a mean age of 66.39 years (range: 33–86). Smoking history was present in 57.9% of patients. Common comorbidities included chronic obstructive pulmonary disease, diabetes mellitus, hypertension, and cardiovascular disease. The most frequent histological types were adenocarcinoma (55.3%) and squamous cell carcinoma (26.5%). Secondary primary malignancies commonly affected the bladder, larynx, breast, prostate, colon, and other sites. Twelve patients developed a third primary cancer. Synchronous tumours were observed in 26.3% of cases, with significantly shorter intervals between malignancy diagnoses ($p<0.001$). The mean interval between the first and second malignancy was 45.46 months, and between the second and third was 42.9 months. Kaplan-Meier analysis revealed a mean overall survival of 164 months. Though patients with synchronous tumours had shorter survival, the difference was not statistically significant ($p=0.191$).
Conclusion: MPMs in patients with lung carcinoma are clinically complex and limited in the literature. Recognition of associated malignancies is crucial for effective clinical management, emphasizing the importance of risk factors such as smoking and chronic diseases. Early detection, a comprehensive multidisciplinary approach, and vigilant long-term surveillance are essential for optimizing outcomes in patients with multiple malignancies including primary lung carcinoma.

PS-26-008

IgG4-related lung disease

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Background & Objectives: Immunoglobulin G4-related lung disease (IgG4-RLD) is a rare entity. We retrospectively analysed the clinical and histopathological features of patients with pathologically confirmed IgG4-RLD to increase the diagnosis rate and reduce the risk of misdiagnosis.
Methods: We examined our patients with suspected IgG4-RLD in lung surgery specimens between 2020-2024 at Dokuz Eylul University Faculty of Medicine Hospital with histopathological and immunohistochemical findings.
Results: Among 37 patients with suspected IgG4-RLD, only 3 had storiform fibrosis and lymphoplasmacytic infiltrate and a high IgG4/IgG ratio (above 40%). Inflammatory myofibrablastic tumour was diagnosed in 1 of these patients and connective tissue disease in the other. As a result, we diagnosed only 1 patient with IgG4-RLD. This patient was a 42-year-old female patient with a complaint of cough. Histopathological examination revealed abundant lymphoplasmacytic cell infiltration and stroriform fibrosis accompanied by eosinophils. Giant cells and granuloma were not observed. Immunohistochemical examination revealed an IgG4/IgG ratio of 55%. IgG4-RLD was diagnosed based on histopathological and immunohistochemical findings.
Conclusion: In our study, we found that it was quite difficult to diagnose IgG4-RLD. In conclusion, it is not sufficient to look only at the IgG4/IgG ratio when making a diagnosis for IgG4-RLD; other diseases with high IgG4/IgG ratio should also be considered in the differential diagnosis.

PS-26-009

Development of a novel integrin beta-6 IHC assay for clinical evaluation of sigvotatug vedotin in nonsquamous non-small cell lung cancer specimens

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Background & Objectives: Integrin beta-6 (IB6) is a heterodimeric integrin protein that has elevated expression in a broad range of solid tumours compared to benign epithelial tissues. This expression pattern and the localization of IB6 to the surface of tumour cells makes it a highly relevant target for potential IB6-directed therapeutics such as the antibody-drug conjugate sigvotatug vedotin (SV). We developed an optimized immunohistochemistry (IHC) assay for the detection of IB6 expression in formalin-fixed, paraffin-embedded nonsquamous non-small cell lung cancer (nsqNSCLC) specimens for investigational use in support of clinical studies conducted with SV.
Methods: The optimized Integrin Beta-6 IHC 6.2A1 pharmDx assay uses EnVision FLEX detection system on the Dako Omnis staining platform. Sensitivity was performed by conducting a survey of IB6 expression in a cohort of >600 nsqNSCLC specimens. Specificity testing investigated IB6 expression by IHC in a variety of normal and abnormal tissues, as well as western blot testing of cancer cell lines. Precision testing in nsqNSCLC specimens included IHC staining reproducibility under various laboratory conditions and scoring reproducibility.
Results: Performance testing in nsqNSCLC demonstrated high sensitivity, specificity, and precision. A dynamic range from 0-100% IB6 expression was detected in 614 nsqNSCLC specimens. Specificity testing in normal and abnormal tissues resulted in expected expression patterns and localization primarily to the cell membrane. Western blot testing using predicted IB6 positive and negative cancer cell lines confirmed specific detection of IB6. Staining precision resulted in ≥95% of scores within expected variability limits for all parameters. Scoring precision resulted in ≥90% agreement for both intra-observer and inter-observer comparisons when evaluating different IB6 expression cutoffs.
Conclusion: The novel Integrin Beta-6 IHC 6.2A1 pharmDx assay demonstrated high sensitivity, specificity, and precision for the detection of IB6 expression. The assay is suitable for testing of nsqNSCLC subjects for investigational use in an ongoing SV phase 3 trial.

PS-26-010

Multi-site external platform comparison of PD-L1 IHC 22C3 pharmDx performance on Dako Omnis and Autostainer Link 48 for non-small cell lung cancer using Tumour Proportion Score

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Background & Objectives: PD-L1 IHC 22C3 pharmDx is a qualitative immunohistochemical (IHC) assay to detect PD-L1 expression in formalin-fixed, paraffin-embedded (FFPE) tissues. This study sought to demonstrate concordance of PD-L1 IHC 22C3 pharmDx on both Autostainer Link 48 (ASL48) (Code SK006) and Dako Omnis (Code GE006) staining platforms for non-small cell lung cancer (NSCLC).
Methods: This was a three-site, blinded, and randomized study of PD-L1 IHC 22C3 pharmDx on FFPE NSCLC specimens. To investigate inter-platform performance, one pathologist at each of the three testing sites evaluated two replicate sets of 120 NSCLC specimens: one set prestained using PD-L1 IHC 22C3 pharmDx on ASL48 and one set prestained on the Dako Omnis platform. Pathologists determined the PD-L1 expression level for the NSCLC specimens using a Tumour Proportion Score (TPS) at established diagnostic cutoffs: TPS ≥ 1% and TPS ≥ 50%.
The analytical agreements of the diagnostic outcome (positive/negative) were estimated by evaluating negative, positive and overall percent agreement (NPA/PPA/OA) using SK006 as reference with corresponding percentile bootstrap confidence intervals (CIs). Ninety-six specimens were predesignated for analysis at each cutoff. The predetermined acceptance criteria for all endpoints are that the lower-bound (LB) of a two-sided 95% CI for NPA, PPA, and OA must meet or exceed 85.0%.
Results: The study met all acceptance criteria for the TPS ≥ 1% and TPS ≥ 50% cutoffs. For TPS ≥ 1%, the 95% CI LB of the endpoints were 94.2% for NPA, 96.9% for PPA, and 96.5% for OA. For TPS ≥ 50%, the 95% CI LB of the endpoints were 85.3% for NPA, 94.2% for PPA, and 91.0% for OA.
Conclusion: This study demonstrates concordance between ASL48 and Dako Omnis platforms with respect to identifying PD-L1 expression in NSCLC specimens at the TPS ≥ 1% and TPS ≥ 50% cutoffs using PD-L1 IHC 22C3 pharmDx.

PS-26-011

Immunohistochemical subtyping of small cell lung carcinoma

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Background & Objectives: Emerging concept of small cell lung carcinoma (SCLC) subtyping relies on immunohistochemical (IHC)

studies. The aim of this study was to determine expression of ASCL1, NEUROD1, POU2F3 and YAP1 in surgical samples of SCLC.
Methods: 24 surgically resected tumours from 24 different patients were included. After confirming the diagnosis of SCLC, we formed tissue microarrays (TMAs), taking 1 to 4 (median 3) samples from different parts of each tumour. TMAs were stained with haematoxylin/eosin. IHC stainings wiith neuroendocrine (NE) markers (CD56, INSM1, synaptophysin, chromogranin) and transcription factor (TF) markers (RB1, ASCL1, NEUROD1, POU2F3 and YAP1) were performed. The expression of IHC markers was evaluated semiquantitatively and expressed in percentages. Since the samples showed spacially heterogenous expression of IHC markers, we chose the ones with the highest expression as representative. Cutoff point for positive staining was 10% of tumour tissue.
Results: 91,7% of samples stained positive for CD56 and INSM1 (not the same samples). We observed lower intensity and distribution of INSM1 compared to CD56. Synaptophysin was expressed in 71% of samples. Chromogranin was positive in only one sample, possibly due to the antibody clone. RB1 was positive in only one sample. ASCL1 and NEUROD1 were positive in two thirds of samples, with 21% showing expression of both markers, 16,7% and 29,2% were positive only for ASCL1 and NEUROD1, respectively. POU2F3 was expressed in five samples (20,8%), but only three (12,5%) did not express other TF markers. YAP1 was positive in 21% of samples. IHC suptyping found 6 (25%) SCLC-A, 10 (41,7%) SCLC-N, and 3 (12,5%) SCLC-P tumours. YAP1 was negative in all the remaining five samples (20,8%) - possible SCLC-QN subtype.
Conclusion: Our study showed concordant results with previous studies, However, it also points to some challenges, such as co-expression of different TF markers and heterogenous expression in different parts of tumour.

PS-26-012
DLL3 expression in small round cell tumours: a potential therapeutic target for SMARCA4-deficient tumours
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Background & Objectives: Small round cell tumours (SRTs) comprise diverse neoplasms characterized by small, round, hyperchromatic cells with high nuclear-to-cytoplasmic ratios. Delta-like ligand 3 (DLL3), an inhibitory Notch pathway ligand highly upregulated in small cell lung cancer, may serve as a therapeutic target. We aimed to characterize DLL3 expression across SRTs to identify potential therapeutic strategies.
Methods: We analysed DLL3 expression in 128 SRTs including alveolar rhabdomyosarcoma, desmoplastic small round cell tumour, Ewing sarcoma, malignant rhabdoid tumour, olfactory neuroblastoma, synovial sarcoma, NUT carcinoma, SMARCB1/A4-deficient undifferentiated tumours, and undifferentiated small round cell tumours, using immunohisto-chemistry with 1% and 5% cut-offs. We assessed cytotoxicity of Rovalpituzumab tesirine (Rova-T) in SMARCA4-deficent lung cancer (H661), small cell lung cancer (H82), and normal bronchial (BEAS-2B) cell lines.
Results: At the 1% cut-off, 14.1% of SRTs were DLL3-positive, while 7.0% were positive at the 5% cut-off. DLL3 expression significantly correlated with tumour diagnosis (p=0.001). SMARCA4-deficent undifferentiated tumours (SMARCA4-dUT) showed the highest DLL3 positivity (50% at 1% cut-off; 41.7% at 5% cut-off, p=0.001 vs. non-SMARCA4-dUTs). Synaptophysin expression significantly associated with DLL3 positivity (p=0.011). Western blot confirmed DLL3 protein in H661 cells, and immunostainings of H661 cell block demonstrated DLL3 expression and loss of BRG-1 expression. Rova-T demonstrated dose-dependent efficacy against both H661 (IC50=0.07686 μM) and H82 (IC50=0.1061 μM), with BEAS-2B showing similar sensitivity (IC50=0.09885 μM). No significant survival differences were observed between DLL3-positive and DLL3-negative SRTs.
Conclusion: DLL3 is expressed in a subset of SRTs, with significantly higher rates in SMARCA4-dUT. The association between DLL3 and synaptophysin suggests neuroendocrine differentiation. These findings identify DLL3 as a potential therapeutic target for SMARCA4-dUTs, warranting further investigation the absence of survival differences in our clinical cohort.

PS-26-013
Peribronchiolar metaplasia: an immunohistochemical study
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Background & Objectives: Chronic irritation of the bronchial mucosa and the lung parenchyma lead to adaptation, the most common of it – the metaplasia. And if the bronchial squamous cell and stromal smooth muscle cell metaplasia are very well known to the pathologist, it's not the same with the peribronchiolar lung metaplasia (PBM). The latest is a pathological lesion, whose study has been gaining momentum in recent years, mainly due to its combination with chronic nicotine intoxication and interstitial fibrosis of the lung parenchyma, including recovering from COVID-19. The aim of this study is the immunohistochemical profile of PBM.
Methods: We investigated immunohistochemically PBM in 20 cases of lung specimens.
Results: Two immunohistochemichal profiles of PBM have been described. In the initial stages, the prevailing phenotype of PBM is Cytokeratin7-positive, TTF1-positive, p63-positive, CC16-positive and has higher proliferative activity, demonstrated by higher Ki67-index. In the more advanced stages, the cells are still Cytokeratin7-positive, p63-positive, but alter their expression to TTF1-negative, CC16-negative and have lower proliferative Ki67-index.
Conclusion: PBM is dynamic process in immunochistochemicall regard, and progresses stepwise from alveolar to bronchial phenotype. The main role in the process of the indirect epithelial metaplasia have the CC16-positive club cells.

PS-26-014
Histopathological features of pleuroparenchymal fibroelastosis based on deep learning analysis: quantification of collagen fibre and two types of elastic fibre
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Background & Objectives: Pleuroparenchymal fibroelastosis (PPFE) is classified as a rare idiopathic interstitial pneumonia, though these features are also observed in secondary interstitial lung disease. To diagnose PPFE correctly is often problematic because various patterns of fibrosis can coexist. We analysed digital images of lungs resected for transplantation using deep learning to detect the differences between PPFE and non-PPFE and between idiopathic and secondary cases, to identify histological findings useful in improving PPFE diagnosis.
Methods: Among patients who underwent lung transplantation, 174 patients with interstitial lung diseases were enrolled and classified into 14 idiopathic PPFE (IPPFE), 34 secondary PPFE (SPPFE), and 126 non-PPFE based on multidisciplinary discussion diagnosis. Altogether, 1728 slides were digitized, and elastic and collagen fibre areas were identified and quantified using deep learning. We defined strong elastic fibre as elastic fibre consisting alveolar framework,

and weak elastic fibre as faint elastic fibre found inside the strong framework.
Results: In the upper lobe, the median collagen fibre area/fibrosis area ratio in the non-PPFE was higher than that in IPPFE ($P < 0.0001$) and SPPFE ($P < 0.0001$) and that in SPPFE was higher than that in the IPPFE ($p = 0.0197$). The median elastic fibre area/fibrosis area ratio in the non-PPFE group was lower than that in IPPFE ($P < 0.0001$) and SPPFE ($P < 0.0001$). Similar trends were observed in the lower lobe except collagen fibre.
Conclusion: Fibroelastosis comprised a uniform strong elastic fibre framework with weak elastic fibres; fibroelastosis of SPPFE showed heterogeneous manifestations with a mixture of collagen fibres.

Funding: This work was partly supported by the Japan Society for the Promotion of Science, KAKENHI (grant number: 24K10145))

PS-26-015
Molecular findings in CPAM with synchronous adenocarcinoma
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Background & Objectives: Congenital pulmonary airway malformations (CPAM) are rare developmental lesions of the lung, occasionally reported in association with mucinous adenocarcinomas. The clonal relationship between these entities remains unclear. This study aimed to investigate the molecular profiles of CPAM and contiguous mucinous adenocarcinomas to assess potential neoplastic progression.
Methods: We identified six cases of adult CPAM with contiguous mucinous adenocarcinoma, validated as distinct components for histopathological and molecular analysis. The cohort included 3 women (aged 44–76) and 3 men (all aged 74), with tumour staging ranging from pT1a to pT3, and N0 (n=4) to N1 (n=1). DNA extracted from formalin-fixed paraffin-embedded tissues underwent targeted next-generation sequencing (NGS) using a 50-gene panel, applied independently to CPAM and tumour areas.
Results: Across the six cases, several oncogenic mutations were identified in both CPAM and tumour components, involving genes such as *TP53*, *KRAS*, *EGFR*, *FGFR3*, *MTOR*, *CTNNB1*, and *GNAS*. In three cases (50%), identical *TP53* mutations were detected in both lesions, suggesting a clonal relationship:

- Case 1: *TP53* c.743G>A; p.(Arg248Gln)
- Case 2: *TP53* c.524G>A; p.(Arg175His)
- Case 3: *TP53* c.524G>A; p.(Arg175His) and c.517G>T; p.(Val173Leu)

In the remaining cases, CPAM and tumour components harboured distinct mutational profiles. These findings support a potential clonal link in a subset of cases, while also highlighting genetic heterogeneity among mucinous adenocarcinomas arising in the context of CPAM.
Conclusion: Our findings provide molecular evidence supporting a potential precursor–tumour progression from CPAM to mucinous adenocarcinoma, particularly via early *TP53* alterations and loss of function. The observed mutational heterogeneity in adenocarcinomas suggests variable carcinogenic pathways. These results underscore the importance of thorough histological and molecular assessment of congenital lesions in adults. Despite the limited sample size, this study contributes to a better understanding of CPAM-associated carcinogenesis and supports the hypothesis of a neoplastic continuum.

PS-26-016
Targeting pulmonary carcinoid tumours: analysis of gene fusions using RNA-based NGS panel
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Background & Objectives: Pulmonary carcinoid (PC) tumours are well-differentiated neuroendocrine tumours, comprising 1–2% of all malignant lung tumours. PCs are classified as typical carcinoids (TCs) or atypical carcinoids (ACs) based on morphology and mitotic index. Treatment options for unresectable PCs remain limited, emphasizing the need for novel, targeted therapies. However, PC-associated gene fusions are understudied. This study aimed to analyse gene fusions in 17 lung cancer–related genes using RNA-based next-generation sequencing (NGS) in a relatively large PC cohort.
Methods: A retrospective cohort of formalin-fixed, paraffin-embedded primary tumours from Helsinki University Hospital (1990–2018) was analysed. RNA was extracted from tissue cores/scrolls, and targeted RNA-based NGS (FusionPlex Lung v2 panel) was performed to detect oncogenic fusions in *ALK, BRAF, EGFR, ERBB2, FGFR1, FGFR2, FGFR3, KRAS, MET, NRG1, NTRK1, NTRK2, NTRK3, NUTM1, PIK3CA, RET, and ROS1*.
Results: NGS was successfully performed on 65 PC tumours (49 TCs, 16 ACs), identifying 10 different gene fusions. Seven were found in local TCs (*PWWP2A::NRG1, TFG::ROS1, MUC2::ROS1, USP17L24::ALK, SFRP5::ALK, RHOBTB1::NTRK3,* and *PRPF4B::ROS1*) and two in metastatic TCs (*MMP16::FGFR2* and *CCDC89::ALK*). One TC patient harboured two distinct fusions (*MUC2::ROS1* and *USP17L24::ALK*). In a local AC, one gene fusion (*ZNF618::NTRK3*) was identified. Additionally, a BRAF exon-skipping event was detected in a metastatic AC tumour.
Conclusion: Compared to other neuroendocrine lung cancers, PCs exhibit a low mutational burden. However, in this series, 14% of the tumours harboured a gene fusion. Since targeted therapies are available for most of the identified fusions, genomic screening should be prioritized to guide personalized therapy. Additionally, some detected gene fusions are associated with aggressive disease and poor prognosis, necessitating more vigilant patient follow-up.

Funding: Cancer Foundation Finland; Helsinki University Hospital Research Funds

PS-26-017
Investigating novel therapeutic targets in NSCLC: deciphering the relationship between NTRK, PD-L1, and PD-1 expression
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Background & Objectives: Lung cancer remains the leading cause of cancer-related mortality worldwide, with non-small cell lung cancer

(NSCLC). Precision medicine has introduced immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs) as promising therapeutic strategies. However, the interplay between PD-L1 expression and *NTRK* rearrangements in NSCLC remains largely unexplored.
Methods: This study analysed a cohort of 482 NSCLC patients. Immunohistochemical (IHC) staining was performed to assess PD-L1 and pan-TRK expression, while whole exome sequencing (WES) was used to identify *NTRK* somatic mutations, copy number variations (CNVs), and gene fusions. Statistical analyses were conducted to evaluate associations with clinicopathological features and prognosis. Additionally, possible connections through cellular pathways were studied through multiple databases and using the cytoscape v 3.10.3 program.
Results: PD-L1 expression (TPS ≥1%) varied across antibody clones, with positivity rates of 41.5% for 28-8, 34.2% for 22C3, 42.7% for SP263, and 10.4% for SP142. High PD-L1 expression (TPS ≥50%) was significantly associated with poorer overall survival (OS) in NSCLC patients assessed with SP142 ($p = 0.045$). TRK expression was detected in 4.56% (22/482) of cases, predominantly in squamous cell carcinoma (72.7%). Combined expression of pan-TRK and PD-L1 across all clones was statistically significant ($p < 0.001$), with co-expression present in 4.6% of cases. WES identified 3/482 *NTRK* fusions, but no significant survival association was observed.
Conclusion: PD-L1 and pan-TRK expression demonstrate a significant correlation in NSCLC, particularly in squamous cell carcinoma and high-grade tumours. Although PD-L1 expression is a prognostic factor, TRK expression alone does not significantly impact survival. This study suggests an interplay between NTRK1 and PD-L1 that could influence therapeutic resistance. Further studies are needed to elucidate the therapeutic implications of PD-L1 and NTRK co-expression, which may aid in optimizing personalized treatment strategies in particular needed to overcome resistance mechanisms in NSCLC.

PS-26-018
Characterization of non-small cell lung carcinoma with TTF-1 and p40 co-expression
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Background & Objectives: Non-small cell lung carcinoma (NSCLC) accounts for the majority of lung cancer cases and requires precise histological subtyping for optimal therapeutic decision-making. TTF-1 and p40 are standard lineage markers used to distinguish adenocarcinoma (ADC) from squamous cell carcinoma (SCC), respectively. However, a subset of tumours co-expresses both markers, posing diagnostic uncertainty. This study aimed to characterize the clinicopathological and molecular features of NSCLCs with TTF-1 and p40 co-expression.
Methods: We retrospectively analysed 94 NSCLC cases with available TTF-1 and p40 immunohistochemistry. Co-expression of both markers was identified in 18 tumours. Clinicopathological data, survival outcomes, and molecular alterations were evaluated. Next-generation sequencing (NGS) was performed on tumour samples to assess mutational profiles.
Results: TTF-1/p40 co-expressing tumours exhibited a significantly higher frequency of solid growth patterns compared to other NSCLCs ($p = 0.028$). No significant differences in overall survival were observed ($p = 0.458$). Pathogenic mutations were present in 15 of 17 cases (88.2%), most commonly involving *TP53* (64.7%) and *KRAS* (23.5%). Alterations in *FGFR1–3* were identified in 29.4% of cases. Immunohistochemical analysis showed frequent expression of p63 and p53 across the co-expressing group.
Conclusion: NSCLCs with TTF-1 and p40 co-expression represent a biologically distinct, poorly differentiated subset frequently harbouring *TP53* and *FGFR* pathway alterations. These tumours may be more appropriately classified as non-small cell carcinoma, not otherwise specified (NSCC, NOS), rather than as classical ADC or SCC. Given their molecular complexity, broad genomic profiling should be considered even in cases with squamous-like morphology, where such testing is not routinely performed.

Funding: Medical University of Lodz Internal Grant Programme: 564/1-000-00/564-20-082 (to GS, MB) and Medical University of Lodz Internal Scientific Funding: 503/1-034-03/503-11-001

PS-26-019
Transbronchial biopsy in the diagnostic algorithm of fibrotic hypersensitivity pneumonitis: 2-year experience from a pulmonary pathology reference unit
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Background & Objectives: Hypersensitivity pneumonitis (HP) is a challenging diagnosis, particularly fibrotic HP. In the 2022 ATS/JRS/ALAT HP diagnosis guideline, whilst bronchoalveolar lavage (BAL) is considered a crucial diagnostic step, the complementary role of transbronchial biopsy (TBB) remains unclear, especially in suspected fibrotic HP. Here, we present our experience with TBB in the diagnostic approach to HP cases.
Methods: Retrospective, observational study including all consecutive cases of suspected interstitial lung disease (ILD) assessed at a reference pulmonary pathology unit (Jan/2023-Dec/2024). Clinical, radiologic, pulmonary function test, BAL, TBB and multidisciplinary meeting (MDM) outcome data were reviewed.
Results: Out of 149 TBB performed for ILD assessment, 12 (8%) cases were clinically and/or radiologically suspicious for HP. Most patients were female (58%), elderly [mean(±SD) age, years=66(±11)] and non-smokers (75%). Eleven (92%) patients had exposure to identifiable inciting agents. Most patients showed restrictive functional pattern (50%). Radiologically, traction bronchiectasis (42%), ground glass opacities (42%), and subpleural/peribronchial reticulation (42%) were the most frequent findings. Bronchoscopy with BAL and TBB was performed in all patients. Following radiologic-pathologic integration at MDM, 4 (33%) cases were diagnosed as fibrotic HP, 4 (33%) as nonfibrosing HP, 2 (17%) as non-specific interstitial pneumonia (NSIP), and 2 (17%) as indeterminate for fibrosing ILD. HP cases showed a tendency towards higher BAL lymphocyte percentages [HP vs. non-HP, mean(±SD): 25%(±19%) vs. 8%(±4%)]. On TBB, HP cases displayed higher frequency of loose granulomas (38% vs. 25%) and multinucleated cells (13% vs. 0%) compared with non-HP, with similar interstitial inflammation and organising pneumonia frequency. Fibrotic HP cases showed higher fibrosis frequency (75%) than nonfibrosing HP (25%).
Conclusion: In our experience, TBB is a useful minimally-invasive tool in the diagnostic work-up of suspected HP cases with a diagnostic yield of 66%, which was similar for fibrotic and nonfibrosing HP. We reinforce BAL diagnostic value in this setting.

PS-26-020

Histopathological and molecular features of non-small cell carcinomas in breast cancer survivors: a retrospective case series

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Background & Objectives: Non-small cell cancer (NSCC) arising in women with a previous diagnosis of breast cancer (BC) is an uncommon clinical scenario. With increasing BC survival rates and broader use of systemic therapies, characterizing subsequent malignancies is of growing interest to pathologists.

Methods: We retrospectively analysed 36 cases of NSCC in BC survivors from 2021 to 2024. Histological review included histotype, tumour differentiation, necrosis, fibrosis, vascular invasion, and spread through air spaces (STAS). Molecular profiling and PD-L1 expression were assessed in all cases. Clinical data included BC stage, symptoms, treatment, latency interval, radiological features, and follow-up.

Results: Thirty-five cases were diagnosed as lung adenocarcinoma (LUAD). Only one case was a squamous cell carcinoma. The median age at BC diagnosis was 55 years. BC was of no special type in 18 cases. Among 17 staged BCs, 15 were stage 0–II. The median interval between BC and LUAD was 11 years. Tumours were asymptomatic in 20 cases, peripheral in 22, and solid on imaging in 25. Histologically, 13 LUAD were moderately differentiated and 3 poorly differentiated; STAS was seen in 4 cases and vascular invasion in 2. The detected mutations included EGFR (9 cases, 26%), BRAF (2 cases, 6%), KRAS mutations (8 cases, 18%), ALK rearrangement (1 case, 3%), and MET alterations (2 cases, 6%). Co-mutations were observed in 3 cases (9%), including two cases with KRAS mutations combined with STK11, MTOR, and PIK3CA, and one case with MET exon 14 skipping along with TP53 and MTOR mutations. PD-L1 expression had a median of 2%, with 8 cases (23%) ≥50%. At diagnosis, 15 LUADs were stage I. At the last follow-up, 29 patients were alive.

Conclusion: In LUAD following BC, a high frequency of oncogene addiction was detected. These findings warrant further validation and investigation to better understand the underlying mechanisms.

PS-26-021

Analysis of 9 years of real-world biomarker testing and positivity rates in non-small cell lung cancer (NSCLC) from the Spanish Prospective Central Lung Cancer Biomarker Testing Registry (LungPath)

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Background & Objectives: LungPath is a Spanish on-line registry that provides the largest amount of real-world data on biomarker testing in lung cancer. We aimed to describe the testing and positivity rates of current essential biomarkers in non-small cell lung cancer (NSCLC) and analyse potential associated factors in Spain.

Methods: A retrospective observational study was conducted, including biomarker determinations of all types of NSCLC samples from 61 Spanish hospitals between March 2018 and October 2023 recorded in LungPath registry. Only adenocarcinoma and NSCLC not-otherwise-specified (NSCLC-NOS) histologies were included. Testing and positivity rates for the current essential biomarkers in NSCLC (*EGFR, ALK, ROS1, PDL1, BRAF, KRAS, MET, RET* or *NTRK1*) were calculated and multivariable logistic models developed to assess the effect of covariates on testing and positivity rates.

Results: 12,709 NSCLC samples tested for essential biomarkers were analysed. *EGFR* (86.0%), *ALK* (84.2%) and *ROS1* (72.0%) were the most commonly tested biomarkers. Testing rates were lower for other biomarkers with newer targeted therapies, such as *MET* (15.6%), *RET* (15.4%) or *KRAS* (16.4%), and these were tested more frequently in surgical specimens compared to biopsies (*MET* (OR [95%-CI]): 1.30 [1.15-1.48]; *RET*: 1.33 [1.17-1.51]; *KRAS*: 1.82 [1.61-2.05]). The positivity rates for the current essential biomarkers in Spain were in line with figures reported in the literature. PD-L1 expression was statistically more frequent in samples with alterations in *BRAF* (2.00 [1.31-3.05]), *KRAS* (1.59 [1.27- 2.01]), and *ALK* (1.39 [1.08- 1.79]). In contrast, a positive *EGFR* result was inversely related to PD-L1expression (0.64 [0.55- 0.74]).

Conclusion: Our results show that testing rates for biomarkers with newer targeted therapies are still low and their growth is low. Widespread use of comprehensive genomic profiling (GCP) is expected to increase testing rates in the coming years.

PS-26-022

Incidence of *FGFR* mutations in lung carcinomas

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Background & Objectives: Genetic alterations of FGFs in lung carcinomas, namely amplifications, mutations and translocations in the *FGFR* genes, are closely linked to the carcinogenesis, progression and resistance to therapy, suggesting targeting FGF/*FGFR* as an attractive therapeutic strategy for lung cancer prognosis. Since *FGFR* mutations (oncogenic or likely oncogenic) were described in Non-Small Cell Lung Cancer NCCN Guidelines version 1.2025, as emerging biomarkers to identify novel therapies for patients with metastatic NSCLC, we reviewed our cases with *FGFR* alterations, diagnosed in 2024.

Methods: We report 13 cases in 2024 with *FGFR* positive alterations in NSCLC. Next Generation Sequencing (Genexus, Oncomine Precision Assay Panel, Thermo Fisher Platform) after manual macrodissection was performed and nucleic acid extraction was carried out with the MagMAX FFPE DNA/RNA Ultra Kit. All cases were evaluated for oncogenic or likely oncogenic *FGFR* mutations.

Results: *FGFR*1/2/3 gene alterations were detected in 13/240 cases (5,4%). 6 cases presented SNV and 7 cases with amplification. 4/6 cases with mutations (SNVs) are classified by NCCN guidelines as emerging biomarker linked to sensitivity to Erdafitinib (*FGFR3*: D641G, R248C, G380R, and D641N) and for 2/6 (V550M and V550L) there are no therapeutic approval. In the emerging biomarker mutations identified, one case showed no concomitant targetable mutation and three cases harboured concomitant mutations namely *EGFR* L858R (2 cases) and *EGFR* E746_A750 (1 case). None of the case had isolated mutations in *FGFR* alone. Amplification is not considered as an emerging biomarker actually.

Conclusion: *FGFR*1/2/3 gene alterations are not so infrequent (5,4%). Careful interpretation is needed as concomitant mutations are frequent, some of them in targetable genes. These cases should be discussed with clinicians especially when two targetable mutations are present knowing that some *FGFR* mutations are considered as emerging biomarkers.

PS-26-023

Pulmonary carcinomas: *KRAS – EGFR – ALK* mutations and PD-L1 immunoexpression

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Background & Objectives: PD-L1 expression and *KRAS/EGFR/ALK* alterations may influence tumoral microenvironment. The association between PD-L1 expression and *KRAS/EGFR/ALK* targetable alterations are not well understood namely concerning therapeutic responses. The authors intends to evaluate the concomitance of *EGFR*, *KRAS*, *ALK* mutations with PD-L1 > 1% immunoexpression in pulmonary carcinomas.
Methods: Mutations research performed by Genexus, OPAPanel, ThermoFisher. PD-L1 scoring (22C3-DAKO) according with guidelines.
Results: 240 cases evaluated in 2024, 31 only with *KRAS* mutation, 20 with only *EGFR* mutations and 5 with only ALK fusions. For *KRAS* mutations cases we found 11/31 (35%) negative PD-L1 cases, and 20/31 (65%) positive cases where 10/20 (50%) showed PD-L1 ≥50%. For *EGFR* mutations cases we found 6/20 (30%) negative PD-L1 cases, and 14/20 (70%) positive cases where only 4/14 (28%) showed PD-L1 ≥50%. All (100%) ALK fusions cases showed PD-L1 positivity ranging from 10% to 70% (TPS score), with TPS ≥50% identified in 2 cases (40%).
Conclusion: PD-L1 expression on survival is unclear and may depend on other biomarkers including *EGFR/KRAS/ALK* alterations. Studies indicate that tumours with *EGFR*/*ALK* alterations generally have low/intermediate PD-L1 expression and do not respond well to immunotherapy, even with high PD-L1 as *EGFR* mutated tumour cells may have an immunosuppressive microenvironment, or ALK pathway activates immunosuppressive mechanisms. Studding concomitance of *EGFR*/*KRAS*/*ALK* mutations and PD-L1 expression may impact the choice of treatment in NSCLC. *KRAS* mutations especially G12C frequently presents with high PD-L1 scores. *KRAS* mutations could induce tumoral inflammation activating the axe PD-1/PD-L1. NCCN guidelines also alert that (PD-1)/PD-L1 inhibitor could be less effective as monotherapy irrespective of PD-L1 expression, in *EGFR* exon 19 deletion or exon 21 L858R, *ALK*+ NSCLC. Large studies/clinical trials are needed to understand the implications of PD-L1 expression concomitant with gene alterations, to validate combined therapies and identify groups of better responders avoiding the administration of potentially less effective therapies.

PS-26-024

Comparison of typical and atypical carcinoids using vibrational spectroscopy

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Background & Objectives: Carcinoids are tumours originating from neuroendocrine cells and belong to the family of neuroendocrine tumours (NETs) due to the presence of neurosecretory granules in their cytoplasm. Lung carcinoids make up 2% of lung tumours and can be classified as typical or atypical. In comparison to atypical carcinoids, typical ones show a much lower metastatic potential and a significantly higher survival rate. Our goal was to compare the vibrational spectra of typical and atypical carcinoids using vibrational spectroscopy and explore the potential difference as a new diagnostic tool.
Methods: Diagnosis was verified by an experienced pulmonary pathologist, and paraffin blocks with the most suitable material were selected. The tissue was stained with haematoxylin-eosin stain to identify the carcinoid areas and deparaffinized. Paraffin blocks were then cut, yielding 140 slides from 28 biopsies of 25 patients (60 typical, 80 atypical). After vacuum desiccation, FTIR spectra of 140 samples were recorded in transmission mode using a PerkinElmer Spectrum GX spectrometer (MCT detector, KBr beam splitter). Data were processed in MatlabR2010b with the Kinetics add-on and PLS Toolbox. PCA, SVMDA, and KNN were used for multivariate analysis.
Results: Not only did PCA successfully visually separate typical from atypical carcinoids, but it also showed clear grouping of atypical ones by size, recurrence, and invasiveness. SVMDA proved to be a better predictive method with 82.5% accuracy.
Conclusion: FTIR spectroscopy and PCA effectively distinguish typical carcinoids from atypical ones, with differences in size, invasiveness, and recurrence in atypical cases. Developed SVMDA model showed high accuracy in atypia classification. FTIR spectroscopy has significant potential as a diagnostic tool for automated lung carcinoid diagnosis in the future. Downside of this method is the variability in recording conditions, requiring better process standardization, along with significant investment in equipment and time for data analysis.

PS-26-025

Correlation between *TP53* mutations and p53 protein expression patterns in neuroendocrine lung carcinomas

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Background & Objectives: *TP53* mutations play a key role in various cancer types and, together with *RB1* mutations, are characteristic of small cell lung carcinoma (SCLC) and certain cases of large cell neuroendocrine carcinoma (LCNEC). This retrospective study aims to evaluate the correlation between *TP53* mutations and p53 expression patterns in SCLC and LCNEC cases diagnosed at a single centre.
Methods: We reviewed medical records to identify all lung tumours harbouring pathogenic *TP53* mutations since 2018, selecting cases diagnosed as SCLC or LCNEC. Biopsy, cytology, and surgical specimen samples were reviewed. Mutational analysis was performed using next-generation sequencing (NGS) with the Oncomine Solid Tumour DNA panel (Thermo Fisher Scientific; S5 Gene Studio). We recorded the mutation type, its location within the protein domain, and its functional impact. p53 expression was assessed by immunohistochemistry (DO7, Roche; Ventana), with a wild-type pattern defined as normal, and altered patterns classified as null, cytoplasmic, or overexpressed.
Results: A total of 18 samples (6 cytology, 4 biopsies, and 8 surgical specimens) from 16 LCNEC and 2 SCLC cases were analysed. *TP53* mutations were identified in all cases. Among the detected mutations, 15 were missense, 2 were splicing mutations, and 1 was a nonsense mutation. Mutations were distributed across exons 5 (n=6), 8 (n=6), 7 (n=5), and 10 (n=1); 17 affected the DNA-binding domain, while one involved the tetramerization domain. Immunohistochemical analysis revealed normal p53 expression in one case, null expression in two

cases, and overexpression in 15 cases. Expression patterns correlated with the identified TP53 mutations, as the two null expressions harboured splicing mutations.
Conclusion: In SCLC and LCNEC, TP53 mutations predominantly affect the DNA-binding domain, resulting to loss of protein function. Immunohistochemical analysis of p53 is a useful tool for identifying TP53 gene mutations, with expression patterns correlating with mutation type.

PS-MD-01 Poster Session Molecular Pathology Diagnostics Symposium

PS-MD-01-001
High-sensitivity methylation profiling in cfDNA with methylation-sensitive restriction enzyme digestion (MSRE) on droplet digital PCR (ddPCR)

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Background & Objectives: Mounting evidence demonstrates the utility of analysing methylation status as an indicator of early-stage cancer development and as a method for monitoring tumour response to therapy. Detecting methylation changes in cfDNA is attractive given the noninvasive nature of blood draws. Unfortunately, sensitive, robust, and cost-effective methods to perform methylation analysis on cfDNA samples remain an unmet need. Here we demonstrate how Methylation-Sensitive Restriction Enzymes (MSRE) digestion combined with Droplet Digital PCR enhances analysis of precious samples.
Methods: This method mitigates the drawbacks of bisulfite conversion, such as extensive DNA degradation and high starting material input requirements. Since analysis is based on restriction enzyme cleavage, the amplicon sequence must include MSRE cleavage sites. To mitigate this potential limitation and provide high specificity, a range of different MSRE enzymes and cut sites are available that can be used in combination.
To reliably measure DNA methylation, we designed a range of assays for cancer relevant targets with at least two but not more than four restriction sites within the amplicon. To detect the methylation status at a specific locus, control samples were digested by a range of methylation-sensitive restriction enzymes and analysed with Droplet Digital PCR. When using probe-based detection methods, multiplexing several methylation sites or targets is possible.
Results: Our experiments were designed in a duplex reaction with a reference target (no restriction sites) such as RPP30. The reference assay is used to normalize and correct for small input differences between duplicate digested and undigested control reactions caused by pipetting. Percentage methylation status was calculated with high precision via Droplet Digital PCR by measuring DNA concentration in samples with (MSRE+) and without (MSRE-) enzyme.
Conclusion: With our method we have successfully demonstrated that methylation status can be determined with inputs as low as 1ng. Using this methodology we tested >50 most published oncology methylation targets.

PS-MD-01-002
Development and validation of the OncoCompass® Mate Assay for the detection of DNA and RNA variants in tumours

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Background & Objectives: NGS-based cancer diagnostics have proven effective for diverse genomic alterations. As new actionable targets emerge, the need for integrated DNA and RNA analysis is growing. To address this, we developed OncoCompass® Mate, a dual-calling assay for comprehensive genomic profiling in a single workflow.
Methods: OncoCompass® Mate is designed for comprehensive pan-cancer genomic profiling. It provides in-depth analysis of 520 genes for DNA variants, 115 genes for RNA fusions and splice variants, as well as key genomic signatures. It allows simultaneous DNA and RNA analysis from a single sample, with single-calling available.
Results: The analytical performance of OncoCompass® Mate has been validated using reference standards and clinical samples across multiple cancer types. Specifically, it was able to identify SNVs and Indels in DNA at an allele frequency as low as 2% and gene fusions and splice variants from RNA at a LOD of 3 transcript copies per nanogram. The assay was further evaluated on 123 FFPE samples from various cancer types, including lung, colon, liver, bile duct, endometrium, sarcoma, and pilocytic astrocytoma. Among these samples, 58 were also analysed using the TruSight Oncology 500 (Illumina) assay. The results showed a positive percent agreement (PPA) and negative percent agreement (NPA) of 100% (95% CI, 87.7-100%) and 100% (95% CI, 88.4-100%), respectively, indicating excellent concordance between the two assays. Notably, two samples containing the KIAA1549-BRAF fusion (K16:B9), which had been missed by the single-calling module, were successfully identified by the dual-calling algorithm and confirmed by fluorescence in situ hybridization. These results highlight the diagnostic benefits of integrating DNA and RNA profiling in clinical practice.
Conclusion: OncoCompass® Mate offers a comprehensive solution to enhance diagnostic accuracy and support therapeutic decisions across various cancer types. Leveraging an advanced automation and bioinformatics platform, the assay enables seamless integration into existing laboratory workflows.

PS-MD-01-003
Potential association of MYCN gain, segmental chromosomal aberrations and MDM2/CDK4 amplification with reclassification into high-risk neuroblastoma

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Background & Objectives: Patients initially diagnosed with non-high-risk neuroblastoma who later reclassify into high-risk have poor survival outcomes. Little research has focused on this subgroup. We aimed to identify molecular aberrations explaining why some non-high-risk neuroblastomas progress to high-risk.
Methods: Data were collected from non-high-risk neuroblastoma patients diagnosed at our centre over 7 years, yielding 89 patients, of whom 13 reclassified into high-risk. Fluorescent in situ hybridization (n=72), single nucleotide polymorphism array (n=48) and next generation sequencing (n=69) were used to detect MYCN gain (gene/centromere ratio 1.5-4.0), copy number variations, amplifications and mutations. Fisher's exact test was employed to assess the relationship between MYCN gain and reclassification. Log-rank tests were employed to compare overall survival (OS) and event-free survival (EFS) since diagnosis for MYCN gain and segmental chromosomal aberration (SCA) profile. A univariate logistic regression model was estimated to assess the effect of SCA count on reclassification. Multiple imputation was used to impute missing SCA counts. Pooled odds ratio (OR) and 95% confidence interval (CI) were computed with Rubin's rule.

Results: MYCN gain was not significantly associated with reclassification (11/13 vs. 56/57, p=0.086). Patients with MYCN gain showed poor 5-year OS (67% S.E. 0.272 vs. 91% S.E. 0.035, p=0.193) and EFS (37% S.E. 0.272 vs. 75% S.E. 0.055, p=0.185). All reclassified neuroblastomas showed SCA profile (9/9) whereas 9/39 non-reclassified cases had no SCA profile. Five-year OS for patients with SCAs was 90% (S.E. 0.0049), no other patients died. Patients with SCA profile had poor EFS (74% S.E. 0.074 vs. 89% S.E. 0.105, p=0.370). After imputation, SCA count was associated with reclassification (pooled OR 1.256 with 95% CI 1.006-1.568, p=0.044). Two patients, both reclassified, exhibited MDM2/CDK4 amplification.
Conclusion: MYCN gain, SCA profile, SCA count, and MDM2/CDK4 amplification may be associated with reclassification into high-risk neuroblastoma. Larger studies are needed to draw firm conclusions.

E-Posters

E-PS-01 E-Posters Autopsy Pathology

E-PS-01-001
Urorectal septum malformation sequence - a post-mortem diagnosis

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Background & Objectives: The urorectal septum malformation (URSM) sequence is an extremely rare anomaly that consists of an association of absent perineal and anal openings with ambiguous genitalia and urogenital, colonic and lumbosacral anomalies. In the presence of a single perineal and anal opening draining a common cloaca the findings are better described as a partial URSM, which is compatible with life but with notable comorbidity.
Methods: We present a case of a 20 year old pregnant woman at 30 gestational weeks, with no previous follow-up on our hospital, whose ecographic findings revealed: dilation of colon, bilateral hydronephrosis with loss of corticomedular differentiation, disproportionate thoracic and abdominal perimeters, associated with a pelvic cystic cavity interpreted as a urethral obstacle with bladder distension. Sacrum was also described as disproportionately short, raising the differential diagnosis of caudal regression syndrome. Due to multiple malformations a medical termination of pregnancy was performed.
Results: Autopsy findings include association of imperforated anus, ambiguous external genitalia and markedly distended pelvic organs: megabladder with 5,5x4,5x2,5 cm; hydrocolpus with 5,5x3x3,5 cm and colon with 2,5 cm of maximum perimeter. The urethra and rectum had stenosis and both communicated with the vagina through fistulas. The kidneys had increased weight and pyelocalicial dilation, without evidence of dysplasia. Additional findings include double uterus, lumbar hemi-vertebra and fusion of the last two sacral vertebrae. The placental evaluation revealed a single umbilical artery. The diagnosis was consistent with URSM sequence.
Conclusion: URSM sequence is a severe congenital anomaly of unknown aetiology, involving multiple organ systems, associated with cloacal malformations. The findings of ambiguous genitalia and dilated colon can raise the suspicion of this diagnosis during the pre-natal ecographic screening and prompt medical termination of pregnancy. Careful pathological examination is important to identify this complex malformation sequence and allow correct follow-up and further investigation.

E-PS-01-002
Fatal outcome of a perilaryngeal cavernous haemangioma with laryngeal extension: a case report

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Background & Objectives: Cavernous haemangiomas are benign vascular malformations that can present in various organs, most frequently in the skin and liver. Involvement of the larynx and perilaryngeal tissues is rare but may lead to life-threatening complications. This report presents an interesting case of multifocal cavernous hemangiomatosis with fatal outcome due to airway obstruction, aiming to highlight the potential severity of these lesions and the importance of long-term follow-up.
Methods: A postmortem examination was performed on a 77-year-old female with a known history of cavernous haemangiomas of the skin and a previously resected laryngeal haemangioma. Clinical history, gross and histopathological findings were correlated to determine the cause of death.
Results: The autopsy revealed a large cavernous haemangioma located in the perilaryngeal soft tissue with direct extension into the laryngeal structures. The lesion caused marked glottic oedema and extensive haemorrhagic suffusions within the laryngeal mucosa. These findings resulted in critical upper airway obstruction and subsequent acute respiratory failure. Multiple cutaneous cavernous haemangiomas were observed on the laterocervical region, along with hepatic hemangiomatosis. Histopathological examination of the pancreas revealed incidental findings of low-grade pancreatic intraepithelial neoplasia (PanIN-1), without evidence of invasive carcinoma.
Conclusion: This case illustrates a rare but severe presentation of cavernous haemangioma involving the perilaryngeal and laryngeal structures, leading to fatal airway compromise. It underscores the importance of considering recurrent or progressive vascular malformations in patients with a history of multiple haemangiomas, even after long periods of clinical stability. Early recognition and long-term monitoring of such lesions are essential to prevent potentially life-threatening outcomes.

E-PS-01-003
Idiopathic giant cell myocarditis: an autopsy case report

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Background & Objectives: Idiopathic giant cell myocarditis is a rare condition, with immune-mediated pathogenesis, that mainly affects young to middle-aged patients, and may rapidly progress to arrhythmias and heart failure. We present an autopsy case of fatal idiopathic giant cell myocarditis in a 40-year-old female patient, with previous history of thymoma and doxorubicin treatment.
Methods: An autopsy was performed and relevant tissue samples were collected for microscopic evaluation on haematoxylin-eosin stain. Special stains and immunohistochemistry assessments were also conducted.
Results: The heart exhibited pressure-overload hypertrophy. In the superior mediastinum, an encapsulated tumour was identified, measuring 7.5/4.3 cm, adherent to the visceral and parietal pleura

of the left lung. In the left paravertebral, supradiaphragmatic region, another nodular tumour was observed, with a similar aspect, measuring 8.5/5.5 cm. The microscopic examination of the myocardium revealed a marked inflammatory infiltrate, with neutrophils, eosinophils, lymphocytes, macrophages, and multinucleated giant cells, with foci of cardiomyocyte necrosis. No well-formed granulomas were observed. The special stains performed were negative for the presence of infectious agents. The sections examined from the two tumours were compatible with thymic carcinoma.
Conclusion: This case illustrates a rare case of idiopathic giant cell myocarditis that occurred in a patient with at least two risk factors (thymoma/thymic carcinoma and previous chemotherapy), with fulminant and fatal evolution. The marked left ventricular hypertrophy without gross evident signs of myocarditis is another particular aspect of this case, emphasizing the importance of correlation with clinical and microscopic findings.

E-PS-01-004
Case report of a foetal GLI3-related Pallister-Hall syndrome and literature review
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Background & Objectives: GLI3-related Pallister-Hall syndrome (PHS) is an autosomal dominant disorder causing a wide range of abnormalities, including mesoaxial or postaxial polydactyly, hypothalamic hamartoma, bifid epiglottis, and other malformations affecting the limbs, genitourinary system and midline. Around 25% of cases result from de novo mutations.
Methods: Our findings have been obtained from a necropsy of a 22+3 weeks of gestation foetus. Interruption of the pregnancy was performed due to foetal malformations, with right renal agenesis and an presumptive ecographic diagnosis of arthrogryposis due to lower limb hyperextension and upper limb hyperflexion diagnosed at 21 weeks of gestation. We also performed a radiological study and a study of the placenta.
Results: The necropsy revealed bilateral renal hypoplasia, with a remnant of the right kidney measuring 5 mm showing dysplasia and left kidney pelvicalyceal dilation, imperforate anus, bilobed right lung, septate uterus, and empty sella. Radiological findings included postaxial polydactyly in the right hand, oligodactyly in the left hand, postaxial polydactyly with syndactyly in the left foot and delayed ossification. Placental histology showed dysmorphic villi with trophoblastic pseudoinclusions. Exome sequencing in amniotic fluid identified a de novo GLI3 mutation, confirming Pallister-Hall syndrome.
Conclusion: The present report highlights a rare case of PHS syndrome. Although some of the characteristic features were not confirmed in this case (bifid epiglottis, hypothalamic hamartoma), many findings were concordant with it, including oligodactyly, polydactyly and renal and uterus malformations. Absent or small pituitary gland has been described in some case reports, although is not a classical sign.

E-PS-01-005
A rare case of atelosteogenesis type II in the diastrophic dysplasia sulfate transporter spectrum: foetal autopsy findings and pathological features
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Background & Objectives: Mutations in the Diastrophic Dysplasia Sulfate Transporter (DTSDT, gene *SLC26A2*) cause a spectrum of skeletal dysplasias, ranging from lethal to non-lethal forms. These include Achondrogenesis Type 1B (ACG-IB), Atelosteogenesis Type II (AO2), Diastrophic Dysplasia (DTD), and recessive Multiple Epiphyseal Dysplasia (rMED). The sulfate transporter is essential for sulfate ion uptake, which is crucial for cartilage matrix integrity. Impaired cartilage sulfation in AO2 leads to abnormal endochondral ossification and severe skeletal deformities.
Methods: We report a case of an a 19-week foetus presenting with large cystic hygroma, short limbs, and persistent fixed limb hypokinesia on ultrasound, raising suspicion of severe skeletal dysplasia. Due to the poor prognosis, the pregnancy was medically terminated, and a postmortem examination was performed. Amniocentesis showed a normal karyotype and no abnormalities on array CGH.
Results: Radiographic findings revealed billateral trident acetabula and shortening of the long bones in both upper and lower limbs, consistent with a rhizomelic pattern. Autopsy showed facial dysmorphism and skeletal abnormalities, with most pronounced changes in the appendicular skeleton. These included macrocephaly, microretrognathia, shortened limbs with angulation, hitchhiker thumbs and halluces, brachydactyly, syndactyly, bilateral clubfoot, and a bell-shaped thorax. Histologically, there were signs of foetal hypoxia, with irregular and intramembranous ossification in long bones. Additionally, cystic/myxoid degeneration of resting cartilage pointed to abnormal skeletal development. Molecular analysis identified the pathogenic variants *c.532C>T p.(Arg178*) and c.835C>T p.(Arg279Trp),* in compound heterozygosity, seen in both AO2 and DTD.
Conclusion: The overlap in radiological, pathological, and genotypic findings between AO2 and DTD complicates diagnosis, requiring a multidisciplinary approach. AO2 was favoured due to its severe presentation and poor prognosis, with most affected infants not surviving beyond the neonatal period. In contrast, DTD is typically diagnosed later, presents with a milder phenotype, often manageable with appropriate treatment, and can allow for a significantly longer life expectancy, even a normal lifespan.

E-PS-01-006
Filamin A mutation associated malformations: a necropsy report
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Background & Objectives: Filamin A (FLNA) stabilizes actin networks, aiding cell motility. FLNA mutations cause developmental cardiovascular, skeletal malformations, periventricular nodular heterotopia and otopalatodigital spectrum disorders, exhibiting genotype-phenotype correlation and likely gain of function effects.
Methods: Our findings have been obtained from a complete necropsy of a 31 weeks old male foetus with postmortem radiology, placenta analysis, and genetic studies of the amniotic fluid. The studies were initiated following an ultrasound detecting cardiac and brain abnormalities later confirmed by foetal brain magnetic resonance imaging (MRI). Pregnancy was terminated due to severe malformations.
Results: The 31+6 weeks stillborn (1560 g, p50-75) presented microretrognathia, low-set ears, and hypertelorism. Radiology showed short, symmetric first fingers with clinodactyly, delta-shaped proximal phalanges, broad distal phalanges, and a small distal notch in the left hand. The feet had short proximal first-toe phalanges. Long bones were slightly thin, ribs were short and bell-shaped, with six lumbar vertebrae and asymmetric sacroiliac ossification. Brain histological anomalies included dentate nucleus and bulbar olive dysplasia. During foetal life, genetic analysis detected a hemizygous variant in the

FLNA gene. Prenatal imaging revealed vascular ring, right aortic arch with aberrant left subclavian, and left isomerism. Foetal brain MRI showed cerebellar vermis hypoplasia and corpus callosum dysgenesis. The placenta showed a dysmorphic and hypoplasic villous.
Conclusion: This case reinforces the crucial role of FLNA in organogenesis, demonstrating its involvement in multiple developmental pathways. The genotype-phenotype correlation observed in this case highlights the complexity of FLNA mutations and their variable expressivity. The combination of phenotype, radiological, histological, and genetic analyses provides a comprehensive understanding of the syndrome's manifestations. Further research on filamin A function will improve diagnostic approaches and potential therapeutic strategies for related disorders.

E-PS-01-007
Myocarditis at autopsy: review of 3 cases with different aetiological factors
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Background & Objectives: The diagnosis of myocarditis may remain challenging during life. At autopsy the macroscopic findings may be subtle and inconclusive. However on microscopy the striking findings within the myocardium can help render the diagnosis. In this series I would like to present three cases with different aetiological factors.
Methods: Case 1: A 36-year-old man presented with history of fever and feeling unwell. Investigations showed left ventricular impairment and raised troponin and he died before a conclusive diagnosis. The clinical differential diagnoses included an unusual infection, myocarditis, systemic inflammatory condition or a pulmonary embolism.
Case 2: A 62-year-old male was admitted with one day history of fever. He had a background history of allogeneic peripheral blood stem cell transplant for myelodysplastic syndrome. Investigations showed evidence of neutropenic sepsis and it was suspected that he had an infective source in the central nervous system. He had a VT arrest and it was suspected that this could be drug induced Brugada syndrome.
Case 3: A 51-year-old male became unresponsive in a car park and an echocardiogram performed at emergency department showed a standstill heart. He had a background history alcohol misuse, drug overdose and mental illness for which he was receiving olanzapine.
Results: All 3 cases showed evidence of myocarditis
Case 1: Florid lymphocytic myocarditis, further investigations revealed very high SARS-Cov-2 antibodies. This was concluded as a case of multisystem inflammatory syndrome-adults (MIS-A, post COVID-19).
Case 2: Florid lymphocytic myocarditis and occasional toxoplasma cysts identified, consistent with toxoplasma myocarditis.
Case 3: Eosinophilic myocarditis and taking into account the background history olanzapine induced eosinophils myocarditis was proposed as the most likely cause of death
Conclusion: These three cases exemplify the important role that histology plays in arriving at the correct diagnosis of myocarditis and offering an accurate cause of death.

E-PS-01-008
Short Rib Polydactyly syndrome in a Filipino infant: a case report
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Background & Objectives: Skeletal dysplasias (SD) are rare genetic disorders affecting bone and cartilage development, leading to abnormal growth. Prenatal ultrasound findings, such as short or dysmorphic long bones, often suggest SD, confirmed by postnatal X-rays and physical examination.
Methods: This autopsy involves a preterm infant born at 35 weeks AOG to a 35-year-old primigravid. Prenatal ultrasounds and postmortem X-rays suggest SD. Craniofacial abnormalities include a midline cleft lip and low-set, dysplastic ears. The thorax is narrow, and all extremities are short, with postaxial polydactyly and syndactyly of the right 4th and 5th fingers. The right lung is hypolobated, and the foetal lung weight to body weight ratio is <10th percentile. Microscopic lung examination shows a radial alveolar count of <4, indicating pulmonary hypoplasia. The kidneys are light, with multiple cysts, indistinct corticomedullary junctions, and poorly defined medullary pyramids. The cysts are lined by cuboidal epithelium, with immature stromal elements, primitive tubules, glomeruli, and cartilage islands, indicating multicystic dysplastic kidneys. The genitalia are ambiguous, but karyotyping confirms a 46, XY male.
Results: SDs occur in 1 in 4000 births, with 25% of affected infants stillborn. Short Rib Polydactyly Syndrome, characterized by a narrow thorax, short extremities, postaxial polydactyly, pulmonary hypoplasia, and craniofacial/genitourinary abnormalities, aligns with this case. Diagnosis is mainly clinical, radiologic, and pathologic, but genetic testing for the DYNC2H1 gene, which encodes motor proteins essential for ciliogenesis, offers a definitive diagnosis.
Conclusion: Limited access to genetic testing restricts the ability to definitively diagnose overlapping SDs. This case highlights the importance of a comprehensive autopsy, combined with prenatal and postmortem radiologic findings, in providing diagnostic clarity, aiding in parental counselling and prenatal care.

E-PS-01-009
The death of a 25-year-old male with sickle cell trait and lymphocytic myocarditis. Histopathological, molecular, and ultrastructural findings: an autopsy case report
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Background & Objectives: Sickle cell trait (SCT) is typically considered a benign and asymptomatic carrier state (Hb AS); however, recent studies have indicated it may increase the risk of sudden death under certain circumstances. Lymphocytic myocarditis (LM), characterized by lymphocyte-mediated myocardial inflammation is also recognized as a major cause of sudden unexpected death in young adults. This report aims to present and discuss the clinical, pathological, and molecular findings in a case of sudden death in a young patient with SCT and LM, highlighting potential clinical implications.
Methods: A comprehensive pathological examination was performed in a 25-year-old male patient who presented sudden cardiac arrest at home, preceded by bradycardia and unconsciousness. Methods included macroscopic and histological assessment of the heart and other organs, immunohistochemical staining for CD3-positive T lymphocytes, ultrastructural examination of erythrocytes within myocardial capillaries, molecular identification of the Hb S mutation through next-generation sequencing (Devyser Thalassemia panel), and PCR-based testing for viruses commonly associated with myocarditis (HHV8, Parvovirus B19, and adenovirus).
Results: Macroscopically, cardiomegaly (550 g) was observed with signs of systemic congestion, but no evidence of pulmonary or

coronary thrombi or emboli. Histological analysis revealed a lymphocytic inflammatory infiltrate (up to 21 cells/mm²), myocardial focal necrosis, and subendocardial hypereosinophilic areas. Ultrastructurally, abundant sickle-shaped erythrocytes were identified within myocardial capillaries, arranged as fiber bundles. Molecular testing confirmed the heterozygous c.20A>T (Hb S) mutation, consistent with sickle cell trait. Viral PCR results were all negative.
Conclusion: The sudden death of this young male patient with sickle cell trait and lymphocytic myocarditis remains unclear, as neither condition alone can be definitively established as the sole cause. The coexistence of myocardial inflammation, focal necrosis, and ultrastructural evidence of sickled erythrocytes within myocardial capillaries suggests a potential multifactorial scenario. Further research is needed to determine whether these conditions contributed independently or synergistically to the patient's death.

E-PS-01-010
Hypoxic-Ischemic injury and its relationship with placental lesions: a 20-year analysis of foetal, perinatal and infant autopsies
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Background & Objectives: Central nervous system (CNS) development depends on maternal health, placental function, and neonate´s cardiopulmonary system, influencing susceptibility to hypoxic-ischemic encephalopathy (HIE). Several studies suggest that placental abnormalities play a critical role in brain injury pathophysiology. This study aims to analyse the relationship between selective acute neuronal necrosis (SANN) and placental lesions, identifying the most vulnerable brain regions.
Methods: We reviewed foetal (from week 22), perinatal, and infant autopsy records from 2000 to 2019. Cases with selective acute neuronal necrosis (SANN) in more than one vascular territory were selected, and associated placental lesions were classified using the Amsterdam Consensus Criteria.
Results: Among 205 SANN, placental studies were available in 122 cases (122/205, 59.5%), with some type of lesion observed in 97 cases (97/122, 79.5%). The most frequent placental pattern was maternal vascular malperfusion (MVM), presented in 68 cases, either alone or combined with other lesions (55.7%). It was followed by foetal vascular malperfusion (FVM) in 47 cases (38.5%), chronic villitis in 38 cases (31.1%) and ascending intrauterine infection (AII) in 30 cases (24.6%). More than half (51.6%) presented extreme placental percentiles (<p10 and >p90).
Both MVM and FVM were significantly associated with greater damage to the pons (p=0.003). In cases of AII, there was a slight correlation with the pons, although it did not reach statistical significance (p=0.078). Additionally, MVM was linked to increased involvement of the dentate nucleus (p = 0.047). In contrast, chronic villitis was not significantly associated with any specific area.
Conclusion: Our findings demonstrate a clear association between placental lesions and hypoxic-ischemic injury. Moreover, they highlight the predictive value of these abnormalities, as specific placental lesions correlate with involvement in different brain areas. These results underscore the importance of placental examination in understanding neuropathological injury.

E-PS-01-011
Approaches to the pathoanatomical study of lymphatic vessels of the lower limb in conditions of military trauma
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Background & Objectives: The issue of limb amputation has become one of the most pressing problems of military surgery in the conditions of the Russian- Ukrainian war. The visualization of lymphatic vessels remains out of the attention of pathologists due to the complexity of their study.
This study aims to develop an accessible pathoanatomical method for examining the lymphatic vessels of the skin in amputated limbs.
Methods: The study was conducted on eight re-amputated stumps of male patients aged 25 to 40. The surgical material included stumps below the knee.
Results: A separated skin preparation with subcutaneous fat and superficial fascia, heated in warm water, was laid on a wooden surface with the epidermis facing up. The injection mass, which included 1 g of artistic oil paint "Perlin blue" and 20 mL of chloroform, was injected into the distal edge with a 1.0 mL insulin syringe at the exact site of the incision, under the epidermis. After each subsequent injection, the skin preparation was massaged with a glass cylinder toward the injection site. The successful injection procedure was indicated by the leakage of the injection mass from the proximal end of the preparation section. After that, the preparation was fixed in a 10% formalin solution. Then, fragments measuring 1.0 cm × 1.0 cm each, with an injected lymphatic vessel in the centre, were cut out for histological examination. During histological examination, lymphatic vessels were contrasted with blue, unlike arteries and veins. When using this technique, chloroform, which is diluted with oil paint, evaporates, leaving the paint in the lumen of the lymphatic vessel.
Conclusion: Studying the condition of the lymphatic vessels of limb stumps allows you to determine the pathomorphological changes occurring in them. This can improve patient treatment, preserving a larger portion of the lower limb for subsequent prosthetics.

E-PS-01-012
Prevalence of cardiac amyloidosis in forensic autopsies: a clinicopathological analysis (2023-2024)
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Background & Objectives: Amyloidosis is a heterogeneous disease characterized by extracellular deposition of misfolded proteins in organs and tissues. Cardiac involvement is associated with high morbidity and mortality. This study aims to analyse the epidemiological and clinicopathological characteristics of cardiac amyloidosis (CA) identified in forensic autopsies.
Methods: Retrospective study based on forensic autopsies conducted in a Southern European province between 2023 and 2024. Autopsies were performed according to the Association for European Cardiovascular Pathology guidelines, including histopathological analysis. All cases with histologically confirmed CA were included. The following variables were analysed: sex, age, cardiovascular risk factors, cardiac imaging findings, clinical manifestations associated with CA, and both macroscopic and microscopic autopsy findings. Results were statistically analysed using SPSS.
Results: A total of 36 cases (3%) of CA were identified among 1,251 autopsies performed during this period, with one previously diagnosed and one suspected during life. The mean age was 87.4 years (SD 8; range: 65–100). Prevalence was higher in individuals ≥75 years (33/364; 9%) and in males (81% vs. 19%) (p=0.01). 24

cases were violent deaths, and among the remaining natural deaths, 8 were of cardiac origin, including one due to CA. Cardiovascular risk factors were present in 31 cases and clinical features of CA in 29, mainly atrial fibrillation and bundle branch blocks. All cases showed increased heart weight at autopsy. Amyloid deposits in other organs (mainly lungs) were found in 15 subjects.
Conclusion: CA is a relatively common autopsy finding in elderly individuals, especially men over 75. In most cases, the disease had not been diagnosed during life. Although violent death was the most common cause, some cases suggested that CA may have contributed to mortality. Clinical findings such as atrial fibrillation, conduction abnormalities, and unexplained cardiac hypertrophy in elderly males should raise clinical suspicion to improve early diagnosis and potentially prevent fatal outcomes.

E-PS-01-013
Can structural changes in the parotid salivary glands serve as a compensatory mechanism in type 2 diabetes?
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Background & Objectives: In diabetes, hypertrophy of the salivary glands occurs as a compensatory mechanism: increased production of parotene and synthesis of insulin-like substances partially compensate for the deficiency of insulin in the pancreas. The aetiology of sialadenosis remains poorly understood, and the role of LV in compensating for insulin deficiency has been proven. The aim of the work was to identify the morphological features of changes in the parotid gland in diabetic sialodenosis.
Methods: 62 salivary glands taken from the deceased aged 45 to 56 years were examined. The first group included people with type 2 diabetes mellitus (N=36), and the second group included people without diabetes mellitus (N=26). Anatomical and histological structures of the salivary glands were studied, the severity of dyscirculatory disorders, dystrophic changes and compensatory adaptive reactions were determined.
Results: Patients with diabetic sialodenosis showed a significant increase in the mass (38.9±1.2 g) and volume (by 34%) of the parotid salivary glands compared with the control group. The area of terminal acinuses in group 1 exceeded the control values by 8.11±0.73 mm2 ($p<0.001$) due to hypertrophy of secretory cells with granular inclusions. The ratio of parenchyma to stroma is 69:31 in group 2, 47:53 in group 1, which is associated with fat replacement and stroma fibrosis. An increase in the area of the insertion ducts (38.19±4.74 mm2 versus 21.98±2.19 mm2) and the presence of eosinophilic secretions in 23% of cases indicate compensatory hyperfunction of the salivary glands. In group 1, the nuclei in the acinus cells were shifted to the apical part (72%), which correlated with an increase in the optical density of serocytes.
Conclusion: The revealed patterns indicate an active secretory function and reflect the compensatory role of these characteristics in case of insulin deficiency.

E-PS-01-014
Toothpaste tumour or caseous calcification of the mitral valve: a rare autopsy finding
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Background & Objectives: So-called "toothpaste tumours" of the heart, medically referred to as caseous calcification of the mitral valve (CCMV), are rare pathological findings. These lesions are predominantly reported in radiological and cardiological literature and are scarcely mentioned in standard pathology textbooks. Their rarity and imaging appearance can pose a diagnostic challenge, particularly in autopsy settings where the lesion may be misinterpreted. This case highlights the importance of pathologists being familiar with such entities.
Methods: During a standard clinical autopsy of a 77-year-old female patient with known secondary mitral valve insufficiency, type I diabetes mellitus, advanced arteriosclerosis, and a cardiac pacemaker implanted three years prior, the heart was examined macroscopically and photographed. Following formalin fixation, representative tissue samples were embedded in paraffin and analysed histologically using haematoxylin and eosin (H&E), alcian blue / PAS, Masson's trichrome, and Gram stains. Immunohistochemistry included CD45, CD3, CD20, CD163, CD68. All slides were digitized.
Results: The lesion was not identified in the emergency setting via transesophageal echocardiography. The cause of death was determined to be acute heart failure due to ischemic cardiomyopathy and chronic valvular disease. On gross examination, a homogeneous, beige, toothpaste-like mass was observed in the mitral annular region. The mitral valve exhibited nonbacterial thrombotic endocarditis with pronounced calcifications, alongside chronic occlusive coronary disease. Histology revealed amorphous, amphophilic, acellular material surrounded by macrophages, neutrophilic granulocytes, plasma cells, and predominantly CD3-positive T-lymphocytes. Adjacent myocardial tissue showed multifocal calcifications and areas of fibrosis. Histochemical stains for fungi and bacteria were negative.
Concl.usion: This rare autopsy finding of a toothpaste-like mass in the mitral annulus underscores the need for pathologists to be aware of caseous calcification of the mitral valve. Proper histological interpretation and clinical correlation are essential, as these lesions may be underrecognized. Collaborative discussion with cardiology is recommended to ensure accurate diagnosis and documentation of such unusual cases.

E-PS-01-015
Eosinophilic pulmonary vasculitis in Sjögren's syndrome: un unusual association
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Background & Objectives: Sjögren's syndrome (SS) is an autoimmune disorder primarily affecting the salivary and lacrimal glands, causing dry mouth and eyes. In 10-20% of cases, the lungs are involved, manifesting as interstitial lung disease (ILD). This report presents an unusual case of pulmonary eosinophilic vasculitis (PEV) in a patient with SS.
Methods: A 71-year-old woman with a medical history of SS, systemic hypertension, diverticular disease, asthmatic COPD, and allergy to NSADs was admitted for persistent nausea and vomiting for 10 days, along with a recent rectal bleeding. Blood tests showed hypereosinophilia and elevated inflammatory markers. Stool analysis for parasites and fungi yielded negative results. During hospitalization, she developed progressive dyspnea, prompting a CT scan that

revealed diffuse thickening of the bronchial walls and peribronchial tissue in the lungs, consistent with chronic bronchitis. On the day following admission, she was found deceased in her bed. Clinicians suspected cardiac arrest; however, autopsy was performed to rule out hypereosinophilic enteritis. Upon necropsy, the large intestine featured oedematous walls and numerous rectal ulcers, with no evidence of hypereosinophilic enteritis. Other organs exhibited pallor, attributed to chronic anaemia. Notably, the lungs appeared oedematous with reinforcement of perivascular and peribronchial tissues. Histological examination confirmed mucus plugs in the bronchial lumen, associated with smooth muscle hypertrophy and inflammatory infiltrate, supporting the asthma diagnosis. Unexpectedly, a dense eosinophilic infiltrate was observed in the perivascular space and within the walls of small- and medium-caliber lung vessels, sparing the interalveolar septa. No inflammatory vascular involvement was detected in other organs. Consequently, isolated PEV was diagnosed.
Results: In SS patients, ILD is often observed as a pulmonary condition. Although PEV alongside SS is infrequent, it is recognized as a potential scenario, with few documented cases.
Conclusion: This case highlights the importance of including PEV in the differential diagnosis for SS patients with blood hypereosinophilia.

E-PS-01-016
Advanced adrenocortical carcinoma with brain metastasis. A case report
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Background & Objectives: We report an autopsy case of advanced ACC with multiple liver, lung and brain metastasis.
An 82-year-old white male patient with a history of sudden and progressive deterioration of consciousness, vomiting, and left-sided hemiparesis was admitted to emergency department in the severe state. Non-contrast computed tomography (NCCT) and contrast-enhanced computed tomography (CECT) of the brain revealed hematoma in occipital lobe of the left hemisphere. He died in ten hours of multiple organ failure.
Methods: Autopsy. Histological examination of autopsy material using routine histological stains.
Results: The findings at autopsy were both right and left adrenal tumours with multiple metastasis involving liver, left lung, multiple lymph nodes and the occipital lobe of the left hemisphere of the brain with massive brain hematoma. Histological examination of primary adrenal tumours and metastatic tumour tissue from the brain revealed advanced adrenocortical carcinoma (oncocytic variant). The immediate cause of death was massive brain hematoma.
Conclusion: Adrenocortical carcinoma (ACC) is a rare aggressive malignancy with an annual incidence of 0.5–2 cases per 1 million population. Most cases of ACC are considered to be sporadic, but it can also present as part of hereditary syndromes such as Li–Fraumeni syndrome (LFS), Beckwith–Wiedemann syndrome, Carney complex and Multiple Endocrine Neoplasia (MEN)I. Up to 40% of patients already present with metastatic disease frequently involving liver, lung and bone at the time of diagnosis.

E-PS-01-017
Retrospective analysis of maternal mortality: obstetric direct and indirect causes in Kazakhstan in 2024
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Background & Objectives: An analysis of 24 cases of maternal mortality out of 37 cases of maternal mortality registered in the Republic of Kazakhstan in 2024 was conducted.
Methods: The Research Centre for Obstetrics, Gynaecology, and Perinatology, Department of Pathology conducted a thorough analysis of autopsy reports spanning from January 1st, 2024, to December 31st, 2024 from different regions of Kazakhstan. We divided all cases into direct (11) and indirect maternal deaths (10).
Results: The analysis of obstetric maternal mortality cases showed that there were 4 cases of severe preeclampsia and HELLP syndrome; 2 cases of obstetric (maternal) sepsis; 2 cases of amniotic fluid embolism; 2 cases of postpartum haemorrhage; 1 case of acute fatty liver of pregnancy. In the group of obstetric maternal mortality, iatrogenic pathology in the intensive care unit was detected: tracheal necrosis complicating endotracheal intubation and mechanical ventilation-associated purulent bronchopneumonia, osmotic nephrosis. We attributed a case of uterine suture failure after caesarean section, which caused post-caesarean severe sepsis and uterine wound disruption, as iatrogenic pathology. Analysis of 10 cases of indirect causes showed that infectious diseases were detected in 4 cases: 3 cases -community-acquired pneumonia; 1 case - acute intestinal infection with necrotizing colitis. In all cases of infectious diseases, there was late consultation. Non-infectious pathology included 2 cases of subarachnoid haemorrhage; 2 cases of hyperthyroidism and thyrotoxicosis and in one case death occurred as a result of thyroid storm; in 1 case - unilateral renal agenesis and chronic tubulointerstitial nephritis of the right kidney; in 1 case - acute generalized lymphedema complicated by pulmonary embolism.
Conclusion: The analysis showed that obstetric maternal mortality dominates over indirect maternal mortality. Most cases of obstetric maternal mortality can be classified as manageable, while all cases of indirect maternal mortality are manageable.

E-PS-01-018
Arteriovenous brain malformation findings in forensic pathology
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Background & Objectives: Arteriovenous brain malformations (AVMs) represent vascular system developmental anomalies, composed of tangles of abnormal blood vessels, with arteries directly connected to veins, without interposing capillaries. Our study aims to analyse the characteristics of brain AVMs (BAVMs) associated with brain bleeding, diagnosed during autopsy, in the last 10 years, in our institution.
Methods: Autopsy examination has been associated with collection of tissue specimens for microscopy. Routine haematoxylin-eosin, elastin staining, along with SMA immunohistochemistry have been performed.
Results: The review of our files identified nine cases, which were diagnosed in five women (55.55%) and four men (44.45%), with age range between 20 and 85 years old, 66,66% being registered in people $\geq$ 50 years. Brain gross examination showed variable areas of intraparenchymal and subarachnoid space haemorrhages. The microscopic examination of the BAVMs revealed, beside haemorrhagic areas, high vascular density, variable degrees of venous enlargement, intimal hyperplasia, abnormal muscular layers, intra-luminal fibrin, infiltration with inflammatory cells in the vascular walls and in the perivascular spaces, and variable areas of gliosis. BAVM was associated, in a case, with a cyst lined by meningothelial cells, with areas of fibrosis and calcifications, diagnosed as an arachnoid cyst. The differential diagnosis included

other vascular pathologies, such as aneurysm, thrombosis, dissection, and stroke.
Conclusion: BAVMs show a large age distribution, with a relatively higher incidence in people of 50 years or older and women. Their main complication is cerebral haemorrhage, which is involved in the mechanism of death. The microscopic examination may add valuable information for diagnosis in these cases, showing haemorrhages, vessels anomalies, along with variable inflammation and glial cells reaction. Although relatively rare, BAVMs diagnosis is important in forensic practice, considering their involvement in thanatogenesis.

E-PS-01-020
Multiple (plasma cell) myeloma and systemic amyloidosis: clinical and histological characteristics
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Background & Objectives: Multiple myeloma (MM) is one of the common underlying causes of systemic AL amyloidosis. The study objective is to describe histopathological features of amyloid deposits in different organs of the patients with MM and systemic AL amyloidosis.
Methods: The study included 23 autopsy cases (15 males and 8 females). Histological sections were stained with haematoxylin and eosin and Congo red. Immunohistochemistry with a broad panel of antibodies against various amyloid types was used. Myeloma cells were verified with Syndecan-1/CD138 antibody.
Results: Based on clinical data, 12 patients had MM with monoclonal IgG of lambda type associated with extensive bone destruction, Durie-Salmon stage II (n=5) and III (n=7). In 7 patients the diagnosis of MM with monoclonal IgG of kappa type, Durie-Salmon stage III, was established. And in 4 cases a non-secretory MM, Durie-Salmon stage II and III, was found. Amyloidosis was diagnosed in 14 of 23 patients before death.
Microscopic postmortem examination revealed multiple amyloid deposits in the myocardial stroma, blood vessel walls. Findings in the liver included multiple sites of infiltration with atypical plasma cells with amyloid deposits in the spaces between hepatic plates and vascular walls. Diffuse amyloid deposits were detected in kidneys.The microscopy of vertebral bodies revealed accumulations of atypical polymorphic multinucleated plasma cells of various stages of maturity, plasmablasts and proplasma cells. Presence of immunoreactivity was proven in myeloma cells by using CD138 immunohistochemical staining. Based on IHC typing, AL lambda amyloidosis was determined in 16 cases (70%) and AL kappa – in 7 (30%).
Conclusion: The study demonstrated that patients with MM and co-occurring systemic AL amyloidosis had extensive amyloid deposits in organs leading to a rapid development of multiple organ failure.
Patients with MM should be investigated for coexisting systemic amyloidosis, which is an independent poor prognostic factor for MM.

Funding: This work was supported by the Russian Science Foundation, grant No 23-15-00138

E-PS-01-021
Histomorphological profile of postmortem inflammatory lung lesions
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Background & Objectives: **Background:** The lung is a major organ involved in almost all fatal events. The lungs develop inflammatory lesions in the context of infectious and occupational diseases and, quite frequently, neoplasms. Postmortem examination provides unbiased, objective and useful information to understand the peculiarities of each individual's response to a given pathogen in relation to sex, age and comorbidities present.
Aims: To study the postmortem histopathological pattern of lung lesions in 26 cases.
Methods: We performed an observational study on 26 postmortem lung specimens collected at the Pathology Department of the Infectious Diseases Hospital "St. Parascheva", Iasi, over a period of 1 year from August 2023. The lung specimens were examined macroscopically and sections were taken from the most representative areas. These sections were processed for paraffin blocks; slides were prepared and stained with routine haematoxylin and eosin. The slides were examined microscopically and the results were recorded.
Results: Of the 26 cases, 15 cases showed changes of bronchopneumonia, 7 cases of pneumonia; 1 case of granulomatous pathology, 2 cases of chronic venous congestion and 1 case of non-specific terminal lesions.
Conclusion: The most common inflammatory lung disease leading to death is bronchopneumonia, which is usually complicated by sepsis. Lesions of the pneumonic type are less common, usually diagnosed in young patients, followed by tuberculosis. Efforts should therefore be made to prevent these infectious diseases.

E-PS-01-022
Autopsies and their significance: a survey of knowledge, attitudes, and practices among non-pathology residents at Korle Bu Teaching Hospital, Ghana
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Background & Objectives: Autopsy rates have experienced a decline in Ghana and globally. In anatomic pathology residency, residents to gain experience through hospital autopsies, both for educational purposes and to provide diagnostic services to clinicians. Autopsies offer insights into various medical conditions and even treatment modalities which may not be evident outside post-mortem examination. However, there have been alarming barriers to conducting hospital autopsies including a lack of clinician interest, family reluctance to consent to autopsies, and the increasing workload on pathologists, who are responsible for both coroners' and hospital autopsies in Ghana.
Methods: A survey was developed and distributed to non-pathology residents at Korle Bu Teaching Hospital. Responses were collected anonymously using Google Forms. Of the 42 residents invited, 30 participated, yielding a 71% response rate. The survey employed a 3-point Likert scale to assess residents' perceptions of the importance of autopsies, their knowledge of autopsy request procedures, interactions with pathologists, and perceived barriers to requesting autopsies.
Results: Respondents were from various specialties and exposure to autopsies varied, with 77% having observed an autopsy during their training, while 23% had no exposure to autopsy procedures. None of the respondents had assisted in or independently performed an autopsy. There was strong consensus regarding the value of autopsies. Regarding interactions with pathologists, only 10% of respondents felt that pathologists were easily accessible for discussing autopsy cases.The data suggested that clinicians highly value collaboration with pathologists with 96.67% of respondents reporting that they value educational discussions with pathologists after an autopsy. Perceived barriers to autopsy requests were significant: 76.7% believed autopsies were unnecessary when the cause of death

seemed obvious, 66% hesitated to request autopsies due to families being too distressed.
Conclusion: The survey shows that non-pathology residents value autopsies, but improving pathologists' accessibility and resident education on autopsy procedures will be important in improving hospital autopsy requests.

E-PS-01-023
Undiagnosed congenital heart defect in children under 5 years of age. Autopsy study from two pathology centres in South Africa
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Background & Objectives: Congenital heart defect is a hereditary abnormality of the heart structure arising from improper embryogenesis; it is the commonest birth defect that affects 1% to 2% of all live births across the world. The prevalence of congenital heart disease may be under-reported in Africa due to limited resources.
The objectives of this study was to report on the prevalence and subtypes of undiagnosed congenital heart defects at the two pathology centres in South Africa.
Methods: This was a retrospective, descriptive study of autopsies performed on children under 5 years at two pathology centres in Ga-Rankuwa, South Africa, between 01 January 2012 and 31 December 2020. The clinicopathological data concerning both the mother and baby were retrieved from the National Health Laboratory Service's laboratory information system and Forensic Pathology Services death registers. Data was analysed using a statistical software package.
Results: Within the study period, a total of 472 autopsies were performed on children aged 0 – 5 years at the two pathology centres. Of these, only 25 met the inclusion criteria and formed the study cohort, thus having a prevalence of 5.3%. The most frequent congenital heart disease diagnoses were atrial septal defect (8), ventricular septal defect (6), Tetralogy of Fallot (4), transposition of great vessels (4), atrioventricular septal defects (2) and patent ductus arteriosus (1). Associated lesions of the congenital heart disease comprised patent ductus arteriosus (6), atrial septal defect (2), hypertrophic right ventricle (2), and single atrium (1). Down syndrome was noted in 2 cases, while Treacher-Collins Syndrome was noted in 1 case.
Conclusion: The study highlights the complexity of undiagnosed CHD in infants, suggesting that academic entities in various fields should continue seeking state assistance to reduce healthcare delivery backlogs and invest in human resources through collaborative and financial efforts.

E-PS-01-024
Keratinizing squamous cell carcinoma of the cervix presenting with sister Mary Joseph nodule – a rare autopsy case report and a review of literature
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Background & Objectives: A 50-year-old female presented with a year-long history of postmenopausal bleeding, severe anaemia, and weight loss. Clinical signs included a cervical mass and a Sister Mary Joseph nodule at the umbilicus, a rare indicator of metastatic malignancy. Differential diagnoses included ovarian, endometrial, and cervical cancer. However, the patient declined to biopsy.
Methods: This case is a retrospective review of an autopsy following the patient's death. Clinical investigations indicated advanced malignancy, with signs of uremia from obstructive uropathy and distant metastases. The autopsy aimed to confirm the diagnosis and explore the malignancy's spread, including the possibility of spread to the umbilicus.
Results: Autopsy revealed a large, fungating cervical tumour extending to the uterus and bladder, causing bilateral hydronephrosis. The Sister Mary Joseph nodule was ulcerated with a necrotic core. Distant metastases were observed in the liver, spleen, and diaphragm. Histopathology confirmed keratinizing squamous cell carcinoma with keratin pearl formation and lymphovascular invasion. Tumour deposits were found in the umbilical nodule, bladder, liver, and spleen. These findings align with the aggressive metastatic behaviour of cervical cancer, emphasizing its capacity for early and widespread dissemination, often overlooked in traditional diagnostic frameworks. Advanced imaging and molecular profiling have revealed a growing understanding of the rapid spread of such cancers, especially through epithelial-mesenchymal transition (EMT), underscoring the importance of a comprehensive diagnostic approach.
Conclusion: This rare case highlights the unusual presentation of cervical squamous cell carcinoma with a Sister Mary Joseph nodule. It emphasizes the need for heightened awareness in postmenopausal bleeding cases, especially when metastatic signs are present. Early detection and intervention are critical, as this case illustrates the aggressive nature of cervical cancer, which, once metastasized, leads to a poor prognosis.

E-PS-01-025
Case report of Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS) syndrome and literature review
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Background & Objectives: MELAS is a mitochondrial syndrome characterized by stroke-like episodes, lactic acidosis, ragged-red fibres, and encephalopathy. Neuropathological findings include necrotic foci in the cortex, especially the occipital and temporal lobes, perivascular calcifications in the basal ganglia and sparing of the white matter.
Methods: A complete autopsy was performed on a 65-year-old female diagnosed with MELAS syndrome with genetic confirmation of m.3243A>G mutation. Additionally, a literature review was conducted.
Results: After reviewing the clinical history, the patient exhibited symptoms consistent with MELAS syndrome, including recurrent migraines, sensorineural hearing loss, hypertrophic cardiomyopathy, and type 2 diabetes. She presented to the ER with a refractory status epilepticus affecting the bilateral temporo-parietal region, compatible with a stroke-like episode. She died a month later due to ventilator associated pneumonia. CNS findings revealed diffuse brain atrophy, cortical laminar necrosis in the right temporal gyrus, arteriosclerosis, and signs of subarachnoid haemorrhage. Cardiopulmonary findings included slightly asymmetric hypertrophic cardiomyopathy, pulmonary hypertension and bronchopneumonia. Postmortem muscle biopsy showed a mild increase in lipid content with Oil Red O stain.

Conclusion: The findings in this case align with previous MELAS reports, including cardiomyopathy, white matter involvement with gyral predilection sparing sulci and gray matter, and diffuse brain atrophy. However, the typical perivascular calcifications in the basal ganglia were absent. While pulmonary hypertension is not a classic feature of MELAS, it has been reported in other autopsy cases. These findings highlight the variability in MELAS presentations and the importance of thorough neuropathological evaluation.

E-PS-01-026

Can AI replace the pathologist? Insights from 10 cases of indirect maternal mortality

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Background & Objectives: An analysis of 10 cases of indirect maternal mortality was conducted using AI (ChatGPT Plus). The main goal of the study was to evaluate the accuracy and reliability of artificial intelligence in analysing autopsy data related to indirect maternal deaths, with and without expert input.
Methods: The Research Centre for Obstetrics, Gynaecology, and Perinatology, Department of Pathology, conducted a thorough analysis of autopsy reports spanning from January 1st, 2024, to December 31st, 2024, from various regions of Kazakhstan. We analysed all cases of indirect maternal deaths (10 cases).
The analysis of maternal mortality cases using artificial intelligence involved two approaches.
In four cases, the AI system was provided with complete expert-reviewed medical documents, including autopsy report with the final version of the diagnosis formulated by pathologist.
In six cases, all expert comments and remarks, as well as the expert's diagnosis, were removed. The AI was asked to create the final diagnosis in all cases.
Results: In both groups, there was a tendency for simplified interpretation of the final diagnosis. For example, in a case of rupture of a saccular basilar artery aneurysm, signs of obstetric sepsis such as purulent thromboendometritis were not considered, even as a underlying condition. There were also excessive diagnoses within the structure of conclusions, such as sepsis, which lacked morphological confirmation. In almost all cases, the cause of death was simplified to acute heart failure. In one case, the diagnosis of "alcoholic cardiomyopathy" was proposed, despite the absence of any history of alcohol use.
Conclusion: The use of AI in analysing cases of indirect maternal mortality revealed notable limitations in diagnostic accuracy. It is difficult to imagine AI even as a supportive tool, because it lacks the understanding of the context of the pathological process development. Attention to detail and nuanced interpretation remain a key advantage of an expert.

E-PS-01-027

Autopsy as a definitive diagnostic tool: a case of an occult primary collecting duct carcinoma

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Background & Objectives: Despite significant advances in imaging and molecular studies over the past decade, post-mortem examination remains an important tool for confirming diagnoses, identifying rare diseases and resolving clinical uncertainties. Besides providing clarity in individual cases, it continues to play a crucial role in medical education and quality improvement.
Methods: We present the case of a male patient in his 70s who developed sudden, intense lower back pain. Imaging studies revealed lytic lesions on the L3-vertebra and the left iliac bone, the latter involving the surrounding soft tissues. A biopsy of the iliac lesion showed an epithelial malignant neoplasia with an immunohistochemical profile suggesting a primary renal origin, though other sites could not be definitively excluded. Subsequent imaging studies and renal biopsy failed to identify the primary tumour, while revealing an increase in the iliac lesion size and multiple other skeletal metastasis. The patient died 4 months after symptom onset.
Results: Besides confirming the presence of multiple osteolytic masses, autopsy revealed an ill-defined perihilar mass in the right kidney, measuring 2.9cm. Histologically, the tumour displayed a tubular, vaguely papillary architecture, with cuboidal, focally fusiform, and even hobnail neoplastic cells. Mitotic activity was remarkable. The iliac mass, measuring 12cm, was histologically similar to the renal tumour. The immunohistochemical profile of both iliac and renal lesions was diagnostic of Collecting Duct Carcinoma (CDC). Molecular studies performed on the initial iliac biopsy showed *NF2* and *SETD2* mutations, both described in CDC, reinforcing our diagnostic certainty.
Conclusion: CDC is a rare and aggressive renal cell carcinoma, often arising in the renal medulla and frequently metastatic at diagnosis. Its diagnosis requires the exclusion of other renal malignancies. Due to its aggressiveness and usual location, an accurate, in vivo diagnosis can be challenging—as in our case—reminding us that autopsy can provide the final answer to clinical uncertainty.

E-PS-01-028

Autopsy-revealed miliary tuberculosis: a diagnostic challenge in sudden death cases

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Background & Objectives: Miliary tuberculosis (MT) is a severe, disseminated form of *Mycobacterium tuberculosis* infection, often presenting with non-specific clinical signs, leading to diagnostic challenges. Despite global efforts in tuberculosis control, MT remains a significant cause of mortality, especially in vulnerable populations. Autopsy plays a crucial role in identifying undiagnosed cases and understanding disease patterns.
Methods: We report three cases of autopsy-confirmed miliary tuberculosis, all discovered postmortem due to sudden and unexplained death. Complete gross and histopathological examinations were performed to confirm tuberculous aetiology.
Results: •**Case 1**: A young incarcerated male with no prior medical history was found dead in his cell. Pulmonary and hepatic granulomas with caseous necrosis confirmed MT.

- **Case 2**: A young female presenting with prolonged fever and neurological deterioration prior to death. Autopsy revealed meningeal, pulmonary, and hepatosplenic tuberculosis.
- **Case 3**: A Somali refugee found dead in a hotel after reporting abdominal pain. Autopsy demonstrated a multi-visceral tuberculous involvement with a pseudo-tumoral bronchial aspect, affecting the liver, spleen, lymph nodes, and peritoneum.

Conclusion: Miliary tuberculosis remains an elusive diagnosis, often missed ante-mortem due to its protean manifestations. These cases underscore the crucial role of autopsy in detecting undiagnosed tuberculosis. Postmortem identification is essential not only for determining the cause of death but also for preventing contagion by enabling contact tracing and timely treatment of exposed individuals.

E-PS-01-029

The diagnostic value of autopsy in Potter syndrome: implications for genetic counselling

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Background & Objectives: Potter sequence is a fatal condition affecting 1 in 4,000–6,000 newborns. The associated oligohydramnios is caused either by renal agenesis, renal cystic disease (including autosomal dominant and recessive polycystic kidney disease), or premature rupture of membranes. All of these conditions lead to pulmonary hypoplasia, along with facial and lower limb deformities. In this study, we present a case of Potter syndrome due to polycystic kidney disease.
Methods: Data for this case study were obtained from the autopsy report and the clinical information of both the infant and the mother.
Results: A 16-year-old primigravida and primipara woman with an unsupervised pregnancy presented to the hospital with hypogastric pain. Ultrasonographic examination revealed a term pregnancy with oligohydramnios and a plurimalformed foetus, characterized by enlarged kidneys and pulmonary hypoplasia. A mature female infant weighing 2700 grams was delivered vaginally. She required resuscitation in the delivery room and was admitted to the Neonatal Intensive Care Unit, where she died four hours later.
Autopsy revealed classical Potter facies, including low-set ears, widely spaced eyes with epicanthal folds, a flattened nose, retrognathia, and bilateral clubfoot.
A thorough internal examination showed bilateral pulmonary hypoplasia (2 × 1.5 cm), hypoplasia of the urinary bladder, and bilaterally enlarged, spongy kidneys (10 × 4 cm) with uniformly distributed small cysts, absence of cortico-medullary differentiation, and fusiform dilatation of the collecting ducts. These findings were associated with bilateral ureteral atresia and hepatic fibrosis.
Histopathological findings were suggestive of autosomal recessive polycystic kidney disease. The histology of the placenta did not provide any additional insights.
Conclusion: The necropsy results in this case highlight the crucial role of postmortem examination in identifying conditions that warrant genetic counselling, thereby aiding in the management of future pregnancies.

E-PS-01-030
Clinical and morphological features of fatal hypothermia
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Background & Objectives: Post-mortem diagnosis of a fatal hypothermia remains relevant in modern forensic medicine due to the uncertainty and inconsistency of pathomorphological diagnostic criteria. The aim of this study was a clinical and morphological analysis of deaths from cold injury.
Methods: Seventy-six cases of standardized autopsies in cases of deaths related to fatal hypothermia were performed. The study group included 60 males' and 16 female's bodies. The investigation reviewed clinical data, autopsy protocols, postmortem toxicological analyses. Histological slides stained with haematoxylin and eosin were studied at magnifications x 5; x20; x40. The findings were analysed together with clinical data from the medical records.
Results: Present study has revealed that 79% were male and 21% of female patients included into the group. Most often, victims were within the following age groups: 45-59 years old - 37 people (28 men and 9 women); 60-74 years old - 29 people (24 men and 5 women); 25-44 years old – 7 people (all men); 75-89 years old – 3 people (1 man and 2 women). Cases of fatal cold injury in the specified years occurred mainly in the winter months. Post-mortem examination has shown foci of pulmonary emphysematous lesions (90% of cases), mucostasis in goblet cells of bronchial epithelium (37%), oedema of cardiomyocytes (85%), decreased content of glycogen granules in the cytoplasm of chest muscle fibres or liver parenchyma (100%), increased proliferation of spermatogenic epithelium of convoluted seminiferous tubules of testicles (85%), tightening of testicles to entrances to inguinal canals (88%), "goose bumps" in the thigh area (66%), haemorrhages under the mucous membrane of the renal pelvis (40%), presence of vitreous mucus in the lumen of the stomach (96%), Wischnewski spots under the mucous membrane of the stomach (98%).
Conclusion: Correlation of clinical, pathomorphological data with the results of toxicological, biochemical analysis will improve the accuracy of diagnosing fatal hypothermia.

E-PS-01-031
Correlation of autopsy findings with premortem diagnostics for invasive pulmonary aspergillosis in critically ill cirrhosis patients
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Background & Objectives: Critically ill patients with cirrhosis are at increased risk of invasive pulmonary aspergillosis (IPA). This study investigates the correlation between pre-mortem diagnostics and post-mortem pathological findings.
Methods: This monocentric retrospective study included cirrhosis patients with a fatal intensive care unit (ICU) stay between 2007 and 2020. Autopsy with systematic sampling of each lung lobe was performed as part of routine care after death at our ICU. Premortem IPA diagnosis was made according to an adapted version of the ECMM/ISHAM criteria including cirrhosis as a host factor. Premortem clinical findings were compared to autopsy results.
Results: This study included 79 patients with sufficient pre-mortem diagnostic data to classify patients as probable IPA or not. Median duration of antifungal therapy was 3 days (IQR 1-11). Probable IPA was diagnosed pre-mortem in 22 patients (27%). On autopsy, invasive hyphal growth was identified in 10 out of 22 patients with a pre-mortem probable IPA diagnosis. Autopsy identified 4 additional cases of proven IPA that were missed pre-mortem. Galactomannan (GM) on bronchoalveolar lavage had a sensitivity and specificity of 73% and 76% respectively for proven IPA. GM on serum had a sensitivity and specificity of 62% and 91% respectively for proven IPA. The positive predictive value of tracheobronchitis on bronchoscopy was 67% for proven IPA on autopsy. The adapted diagnostic criteria showed a sensitivity and specificity of 71% and 81% respectively for proven IPA. When only considering patients with less than 3 days of antifungal therapy, specificity of probable IPA increased to 94% for proven IPA.
Conclusion: Proven IPA is found regularly in deceased ICU patients with cirrhosis, highlighting the importance of IPA awareness in this population. Current diagnostic methods correlate only modestly with postmortem findings. However, true rates of proven IPA might be underestimated due to sampling bias at autopsy and prior antifungal therapy.

E-PS-01-032
An autopsy case report: cystic tumour of the atrioventricular (AV) node – a rare neoplasm with fatal outcome
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Background & Objectives: The cystic tumour of the atrioventricular (AV) node is an extremely rare benign epithelial neoplasm. Despite its non-aggressive histological appearance, its location within the cardiac conduction system can lead to fatal arrhythmias and sudden death.

Methods: An 80-year-old male patient died suddenly while having dinner. An autopsy was performed at the Institute of Pathology, Faculty of Medicine, University of Belgrade.
Results: In addition to chronic findings including liver cirrhosis and nephrosclerosis, microscopic analysis of the heart revealed myocyte hypertrophy and attenuation in several regions. Notably, a well-demarcated but non-encapsulated lesion was identified in the proximal interventricular septum near the right ventricle. The lesion consisted of compressed cystic and duct-like structures, occasionally filled with luminal debris, with sparse solid epithelial nests. The cystic areas were lined by non-ciliated, flat to cuboidal epithelial-like cells lacking cytological or nuclear atypia. Immunohistochemistry demonstrated epithelial differentiation (diffusely positive for EMA, focally for pCEA and CA19-9), while mesothelial and vascular markers (Calretinin, WT1, CD31, D2-40, GLUT-1, ERG, CD34) were negative. The stroma consisted of dense fibrous collagenous tissue infiltrated with inflammatory cells.
Conclusion: The morphological and immunophenotypic features are consistent with a cystic tumour of the atrioventricular node. Although histologically benign, such tumours can compromise the cardiac conduction system and may be a cause of sudden unexpected death. This case highlights the crucial role of autopsy in identifying rare cardiac lesions with potentially fatal outcomes.

E-PS-01-033
The development of septic shock associated with DIC (Disseminated Intravascular Coagulation) resulting from salpingitis: a case report
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Background & Objectives: Pelvic Inflammatory Disease (PID) can progress to tubo-ovarian abscess (TOA), which leads to septic shock. This condition induces coagulation dysregulation and organ dysfunction. Early salpingitis diagnosis is indispensable to prevent fatal outcomes. This study highlights the impacts of untreated salpingitis.
Methods: This case study examines a 17-year-old patient analysed post-mortem through medical records, examinations, and death certificate review. Initially treated for UTI due to hypogastric pain. However, two days later, symptoms progressed to purpura, nausea, anorexia, and febrile sensation. After one week, on the day of her death, the patient experienced hematemesis and subsequently passed away.
Results: The histopathological analysis showed haemorrhage in the lungs, heart, liver, spleen and fallopian tubes; congestion in the liver and spleen; pulmonary oedema; and serosanguinous substrate with narrowing of the lumen.On macroscopic examination, the fallopian tubes were expanded, which were both 1,5cm in diameter, and with inflammatory characteristics and petechiae were observed on various serous membranes, such as the heart and lungs. Thrombi were also identified in medium-caliber pulmonary vessels and in the left lobe of the cerebellum. Necrosis was also identified in segments of the small intestine loops and the cecal region.
Conclusion: It is evident that the consequences of an improperly treated inflammation – as PID – can lead to a severe septic shock, culminating in DIC (Disseminated Intravascular Coagulation) and death. This case highlights the importance of a meticulous inflammatory investigation, such as imaging methods, urinary exams and hemograms, which can help the detection of a salpingitis, as described before. Under those circumstances, this analysis enables early diagnosis and treatment, preventing fatal outcomes even in young individuals.

E-PS-01-034
Undiagnosed rheumatic fever: autopsy report
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Background & Objectives: Rheumatic fever (RF), prevalent in developing countries, is a systemic autoimmune disease commonly resulting from streptococcal pharyngotonsillitis caused by group A beta-haemolytic Streptococcus pyogenes, with several complications such as arthritis, carditis, subcutaneous nodules, erythema marginatum and chorea.
Methods: A 27-year-old woman who, two hours before death, had a dyspnea and vomiting crisis and was taken to the hospital. The medical report describes severe respiratory syndrome refractory to the measures used, with hemodynamic instability.
Results: At autopsy, the brain showed no macroscopic changes, the lungs were enlarged due to oedema and marked congestion/haemorrhage. The heart showed dilation of the right atrium and severe stenosis of the mitral valve. Hepatic steatosis, intense renal congestion. The intestines showed no macroscopic changes, myomatous uterus, with 4 nodules. Histopathological analysis of the heart revealed congestion, intercellular oedema and cardiomyocyte hypertrophy, presence of Aschoff nodules and mitral valve fibrosis; congestion, inflammation and pneumonia in the lung; congestion and acute tubular necrosis in the kidney; congested sinusoids in the liver and congested spleen.
Conclusion: The anatomical and histological findings correlated with the patient's clinical history indicate rheumatic fever as the cause of the undiagnosed cardiac comorbidity that led to severe heart failure (severe mitral valve stenosis and enlargement of the right atrium), leading to the patient's death due to oedema and pulmonary congestion.

E-PS-02 E-Posters Breast Pathology

E-PS-02-001
A retrospective clinicopathological analysis of HER2-low breast cancer: experience from a tertiary care centre
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Background & Objectives: HER2-low breast cancer, defined by immunohistochemical expression of HER2 1+ or 2+/negative ISH, has emerged as a distinct category with potential therapeutic relevance. Accurate HER2 assessment is crucial for tumour classification and treatment decisions. This study aimed to describe the histopathological features of HER2-low breast carcinomas in a single-centre cohort, focusing on molecular subtypes and proliferative index.
Methods: A retrospective analysis was conducted on 171 patients diagnosed with invasive breast carcinomas at the Clinical County

Emergency Hospital "Sf. Ap. Andrei" Galați, Romania, over an 9-month period (April 2024 to December 2024), all of whom provided written informed consent. Variables collected included tumour type, TNM classification, Nottingham grade, lymphovascular invasion, perineural invasion, axillary nodal metastases, hormone receptor status, Ki-67 index, and molecular classification.
Results: Out of 171 invasive breast cancer cases, 27% were classified as HER2-low. The median age was 62 years, with 83% of patients being postmenopausal. Most tumours were diagnosed at stage T2, and the predominant histopathological type was invasive ductal carcinoma of no special type (78%), with Nottingham Grade 2. Lymphovascular invasion was present in 8% of cases, perineural invasion in 2% of cases, and axillary nodal metastases were identified in 10% of cases. Molecular subtypes were distributed as follows: Luminal B-57%, Luminal A-30% and triple negative breast cancer-13%. Ki-67 values were <14% in 26% of cases, between 14-20% in 28% of cases and >20% in 46% of cases. This distribution indicates increased proliferative activity, even in hormone receptor-positive tumours, in line with curent literature on HER2-low cancers.
Conclusion: In this cohort, HER2-low breast carcinomas showed hormone receptor positivity, but also high proliferative indices in nearly half of the cases, suggesting significant biological heterogenity. These findings highlight the importance of accurate and standardized pathological evaluation of HER2 status, with potential implication for therapeutic decision and further understanding of this tumour subgroup.

E-PS-02-002
Polymorphous adenocarcinoma: a rare entity of the breast
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Background & Objectives: Polymorphous adenocarcinoma of the breast, a rare malignancy, consists of monotonous neoplastic cells and shares histomorphological similarities with its salivary gland counterpart. Classified as a rare and salivary gland-like tumour by the WHO in 2022, this tumour remains poorly understood in terms of prognosis and treatment. The aim of this study is to present a case diagnosed with polymorphous adenocarcinoma of the breast and to contribute to the literature.
Methods: A 50-year-old female patient presented to our hospital for diagnostic confirmation. Imaging showed a 29x27 mm mass in the left breast. The patient was diagnosed with triple- negative invasive breast carcinoma. Following neoadjuvant chemotherapy, the patient underwent lumpectomy. The resected tumour measured 1.8 cm and consisted of monotonous cells with tubular structures. Immunohistochemical tests revealed negative staining for oestrogen receptor, progesterone receptor, human epidermal growth factor receptor 2, P63, and GATA3, but Bcl-2 was positive. The Ki67 proliferation index was 2%. Based on these findings, the diagnosis of polymorphous adenocarcinoma of the breast was confirmed. The patient received adjuvant chemoradiotherapy, and no recurrence was observed during 8 months of follow-up.
Results: Polymorphous adenocarcinoma of the breast is extremely rare, with only four reported cases in the literature. Three of these were presented by Asioli et al. in 2006, and a molecular analysis was conducted by Trihia et al. in 2019. The average age at diagnosis is 55.7 years, and the typical tumour size is about 2.5 cm. In our case, the tumour size after treatment was 1.8 cm. One case presented by Asioli showed widespread metastasis after 3 years, but no recurrence has been observed in our patient after 8 months.
Conclusion: Polymorphous adenocarcinoma of the breast is significant not only due to its rarity but also because of the lack of reliable prognostic markers and established treatment protocols.

E-PS-02-003
Comparison of histopathological characteristics of breast cancer between young and older women
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Background & Objectives: Breast cancer (BC) in young women is uncommon and tend to present with aggressive clinico-pathological characteristics. We aimed to compare the histopathological characteristics of BC between young women and older women.
Methods: We retrospectively reviewed all consecutive female BC cases diagnosed between January 2018 and December 2023 at our department over a period of 6 years. Histopathological characteristics were compared between young (≤ 40 years old) and older women (>40 years old).
Results: Of a total of 449 patients included in the analysis, 82 were younger than 40 years (18.26%) and 367 were older than 40 years (81.74%). Younger women had a greater tumour size (4cm vs 3cm, p<0.001), higher frequency in terms of high histological grade (54.9% vs 36.2 %, p=0.006), positive surgical margins (24.7 % vs 13.6 %, p=0.01), high pathological stage (pT3/pT4) (36.6% vs 20.4%, p=0.002), triple negative tumour (36.6 % vs 11.7 %, p<0.001) and diagnosed at an advanced stage disease (stage III/IV) (52.4 % vs 39.8 %, p= 0.036) compared to older women. No statistical difference was identified between the two-age group regarding bilateral tumour, histological subtype, lympho-vascular invasion, lymph node involvement, pathological nodal stage and Her2 status.
Conclusion: The incidence of BC among young women is widely heterogeneous worldwide. In our study, 18.26% of patients were aged less than 40 years; this fraction is relatively higher than that reported in western countries. Young women are felt to be diagnosed at an advanced stage and bear more aggressive BC, which could be explained by the fact that mammography screening is targeted to older women or related to the aggressive biological behaviour of BC in young women. Our study was consistent with most of the earlier research and proved that BC in young women needs more attention as the presentation has more aggressive behaviour at advanced stages.

E-PS-02-004
Tall cell carcinoma with reverse polarity: a case report
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Background & Objectives: Tall cell carcinoma with reverse polarity is a rare subtype of invasive breast carcinoma, which can grow in solid or papillary patterns, thus creating diagnostic difficulties, especially on small core biopsies. Therefore, its' distinguishing can be difficult for the general surgical pathologist therefore reporting and discussing such cases is of great importance.
Methods: The methods used are light microscopy, H-E staining, IHC testing. Genetic tests were not performed due to high monetary cost.
Results: A 68 -year old female patient with history of Multiple myeloma was sent for a CAT-CT scan by her haematologist, where a lump is discovered in the left breast- lower inner quadrant: 2.5x2 cm in size with one reactive axillary lymph node. The ultrasonograph score was BI-RADS 5. The patient underwent excision biopsy and the permanent section showed solid nests consisting of tall columnar cells with nuclei oriented away from the basal membrane. Some of the nests showed thin fibrovascular cores demonstrating solid papillary pattern. The neoplastic nests were surrounded by a thin rim of capillary vessels. Mitotic figures were scarce. IHC showed low expression of ER-10%, PR-5%, HER2- negative- HER2-0, Ki67-10% and E-cadherin- positive (+). Ck5/6 showed mosaic cytoplasmic

expression and Calretinin- positive, while p63 was negative in the invasive component of the tumour. Androgen receptor tested negative.
Conclusion: TCCRP as a rare entity can mimic both benign and malignant lesions and shows an interesting IHC profile, which poses a dilemma during the diagnostic process. This subtype of carcinoma with an indolent clinical course has much more favourable prognosis than other triple negative carcinomas, meaning that the treatment can vary drastically. Other malignant lesions like solid papillary carcinoma and metastatic thyroid carcinoma should be excluded before proceeding to it.

E-PS-02-005
Nipple adenoma in a young female: a case report
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Background & Objectives: Nipple adenoma is a rare, benign breast lesion arising from the glandular tissue of the nipple-areolar complex, primarily affecting women in their fifth decade. It presents the proliferation of lactiferous duct epithelial cells. Due to its rarity and resemblance to other breast lesions, misdiagnosis is common.
Methods: A 26-year-old female with a family history of breast cancer presented with a firm, palpable mass in her right nipple. Physical examination revealed a non-tender, mobile mass without skin changes or nipple discharge. Nipple adenoma typically appears as a solitary, well-defined, oval-shaped nodule, though imaging findings are often nonspecific. A punch biopsy indicated a benign lesion with proliferating ductal structures and usual ductal hyperplasia, consistent with nipple adenoma. Surgical excision was performed for definitive diagnosis, confirming nipple adenoma histopathologically.
Results: The Gross specimen examination revealed a grayish, solid tumour measuring 18 x 13 x 10 mm. Microscopically, the lesion displayed a well-circumscribed tumour with ductal hyperplasia and papillary proliferation of glandular stroma, characteristic of nipple adenoma. Histological findings showed glandular and tubular structures lined by an inner layer of epithelial cells and an outer layer of myoepithelial cells. Immunohistochemical staining revealed ductal epithelial cells positive for AE1/AE3 and CK5/6, while the myoepithelial layer showed p63 and Calponin expression, confirming the diagnosis.
Conclusion: Due to their rarity, nipple adenomas can be challenging to distinguish from other nipple and areolar masses, such as intraductal papillomas and breast carcinoma, without histopathological confirmation. Surgical excision is the treatment of choice, offering an excellent prognosis and low risk of recurrence. Early recognition, imaging, and histopathological evaluation are crucial for differentiation. A comprehensive understanding of the pathological and immunohistochemical features of nipple adenoma is essential for accurate diagnosis.

E-PS-02-006
Breast amyloid tumour and Sjogren syndrome: a rare association
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Background & Objectives: Systemic amyloidosis is a well-known condition characterized by abnormal amyloid deposits in multiple organs. Breast amyloidosis (BA) is a rare form of localized amyloidosis, involving amyloid protein accumulation exclusively in the breast tissue. Given the rarity of this condition, our aim is to shed light on this unique case, review the literature, emphasize the growing association between Sjögren syndrome (SS) and BA, and elucidate the importance of proper diagnosis to prevent unnecessary interventions.
Methods: A 74-year-old woman with a history of SS, hypertension and diabetes, came to our hospital for a breast outpatient clinic appointment, after noticing a few palpable nodules in her left breast. Mammographic examination showed nodular lesions with calcifications and suspicious signs of malignancy. A core needle biopsy was then performed.
Results: Histologic examination of the breast biopsy revealed a diffuse deposition of eosinophilic amorphous material throughout the breast parenchyma, and also surrounding blood vessels and lobulo-acinar structures. This material was Congo red-positive, with a characteristic apple-green birefringence under polarized light, thus confirming the diagnosis of amyloidosis. The nodular area was then rebiopsied and eventually surgically excised, confirming the diagnosis of BA. No neoplasia was found on any of the additional specimens. After clinical and laboratory investigation, no signs of systemic involvement were found, rendering the final diagnosis of localized BA. Our literature review suggests a possible increased association between BA and SS.
Conclusion: Though exceptionally rare, localized BA should be considered when evaluating breast nodules, especially in patients with autoimmune conditions like SS. Because these lesions can mimic malignancies, a thorough histopathological evaluation is crucial to ensure accurate diagnosis and avoid unnecessary surgical treatments. This case underscores the importance of clinical awareness and rigorous use of diagnostic techniques, to provide the best possible care for patients with this rare but significant condition.

E-PS-02-007
Clinicopathological features of breast carcinomas with group 4 HER2 FISH results
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Background & Objectives: The American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) defined the guidelines in 2018 to address issues arising from uncommon HER2 fluorescence *in situ* hybridization (FISH) results. We aimed to collect a series of invasive breast carcinomas with equivocal FISH results, focusing on group 4.
Methods: From 2019 to 2025, all breast carcinomas classified as group 4 (HER2/CEP17 Ratio<2.0; Average HER2 Signals/cell ≥4.0, and <6.0) by FISH were retrieved. By FISH, all cases were examined with PathVysion HER2 DNA Probe Kit (PathVysion Kit). By immunohistochemistry (IHC), slides were stained using an automatic immunostainer (Benchmark Ultra, Roche) with the following antibodies: oestrogen receptor (ER-SP1), progesterone receptor (PR-1E2), Ki67 (Mib-1), HER2 (4B5). Cases were defined as ER-positive and PR-positive when ≥10% and with high Ki67 when ≥20%. HER2 IHC was scored using ASCO/CAP guidelines. Cases classified as group 4 by FISH only in the biopsy and not confirmed in the subsequent surgical specimens were excluded.
Results: A total of 99 specimens from 88 patients were collected. Cases were predominantly composed of surgical specimens (82%), diagnosed as invasive carcinoma not otherwise specified (NST) (84%), followed by lobular carcinoma (11%). Tumours were

predominantly high-grade (57%) and frequently multifocal (34%). By FISH, ratio HER2/CEP17 varied from 1.4 to 1.5, mean 1.5±0.1; HER2 signal varied from 4.0 to 5.2; mean: 4.6±0.8. By IHC, all cases were scored as HER2 2+. Ki67 varied from 5% to 80%, mean: 27.3±13.8%; most cases (67%) showed high Ki67 values. Most cases were ER-positive (91%) and PR-positive (76%).
Conclusion: Breast invasive carcinomas with group 4 HER2 FISH results usually show high grade, high Ki67 expression, positivity for both ER and PR, and are frequently multifocal. The clinical correlations are ongoing.

E-PS-02-008
Breast adenoid cystic carcinoma: a retrospective study upon 2 decades
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Background & Objectives: Adenoid cystic carcinoma of the breast (BACC) is a rare tumour, accounting for < 0,1% of all breast cancers (BC). Although often classified as a triple-negative tumour, ACC typically has a favourable prognosis, with a low risk of metastasis and high survival rates. This study aimed to review the clinical and pathological characteristics of breast ACC.
Methods: This is a clinical and pathological retrospective analysis conducted at the pathology department of Farhat Hached university hospital, including all BACC that were diagnosed over a period of 23 years (2000-2023)
Results: Only 4 BACC were diagnosed representing 0.07% of all BC, The mean age for ACC patients was 66 years ± 5.47 years. Clinically, three patients presented with nodules, one had nipple discharge, and one experienced mastodynia. Histologically, preoperative and final diagnoses were consistent across all cases, showing epithelial and myoepithelial proliferation. Architecturally, all cases exhibited trabecular, cord-like and cribriform structures centreed by pale material. One case showed high grade features including high mitotic rate (without atypia), necrosis and solid structures covering 50% of the tumour area. No vascular emboli nor lymph node metastases were detected in any of the cases. All tumours were of triple negative phenotype with one case showing <1% of RE and RP expression limited to luminal cells. The Ki67 proliferation index ranged from 1% to 5% in three cases and was 20% in one case. After 10 years of follow-up, only one patient had died. This patient did not exhibit high-grade histological features.
Conclusion: This study highlights the distinctive clinicopathological features of BACC. They occur mainly in elderly women, and exhibit the same histological patterns as ACC of salivary glands. It is a triple negative BC with a favourable prognosis , though distant metastases are possible. Diagnosis must be held on core needle biopsies to avoid overtreatment.

E-PS-02-009
Epithelioid schwannoma of the breast
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Background & Objectives: Epithelioid schwannomas are an uncommon histologic variant of benign peripheral nerve sheath tumours. Due to their morphological overlap with other tumour forms, epithelioid schwannomas have a low prevalence and are frequently difficult to diagnose. Epithelioid schwannoma of the breast represents an unusual localization of this tumour.
Methods: A 45-year-old woman was admitted to our hospital with a history of hypoechogenic, well-circumscribed lesion between the upper lateral quadrant and upper medial quadrant of the right breast, which was diagnosed by ultrasound examination. The first ultrasound examination was performed in 2022, and the follow-up examination in 2024. The lesion remained the same size. Fine needle biopsy was done. Cytologic analysis showed epithelial atypia. A tumorectomy was performed, and a firm lesion measuring 2,5 x 2 x 1,3 cm was sent for histological examination.
Results: On gross examination, the lesion was yellowish. Nodularity was observed on the cut surface. Microscopic examination revealed a multilobular tumour composed of epithelioid cells with round nuclei and eosinophilic cytoplasm in a hyalinised, myxoid background. Some of the cells had prominent nucleoli. Immunohistochemically, epithelioid cells were positive for S100 and vimentin and negative for cytokeratin 8/18, cytokeratin AE3/AE5, actin, desmin, h-caldesmon, p63 and p40. CD34 (cluster of differentiation 34) immunostain was patchy. Estrogen, progesterone and androgen receptors were negative, and HER2 (human epidermal growth factor receptor 2) score was graded 0. Ki-67 proliferation index was 2-3%. A follow-up examination showed no recurrence.
Conclusion: Due to their enhanced cellularity and epithelioid morphology, epithelioid schwannomas can cause diagnostic challenges and result in diagnostic errors. Immunohistochemistry may be helpful, as schwannomas stain diffusely positive for S-100 and are negative for breast markers (oestrogen, progesterone and HER2).

E-PS-02-010
Adenoid cystic carcinoma of the breast: a case report and literature review
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Background & Objectives: Adenoid cystic carcinoma (ACC) of the breast is a rare subtype of breast carcinoma, accounting for 0.1% to 3.5% of all breast cancers. Although it has a triple-negative phenotype, ACC generally has a favourable prognosis. This work presents a case report followed by a literature review to better understand this pathological entity.
Methods: A 52-year-old nulligravid woman presented with a palpable right breast mass. Imaging revealed a lesion classified as ACR5. A fine-needle biopsy showed a poorly differentiated carcinoma, and the patient underwent a lumpectomy.
Results: Macroscopic examination identified a well-defined 5×5×3 cm tumour. Histological analysis revealed a dual epithelial and myoepithelial proliferation with a characteristic cribriform architecture. The tumour cells exhibited minimal to moderate nuclear atypia and a low mitotic index, with no vascular or lymphatic invasion. Immunohistochemistry confirmed a triple-negative phenotype, with positive expression of CD117 and p63. Axillary lymph node dissection retrieved 30 non-metastatic lymph nodes.
Breast ACC shares histological features with its salivary gland counterpart but generally has a less aggressive clinical course. It is characterized by an epithelial and myoepithelial cellular component arranged in tubular, cribriform, or solid structures. Immunohistochemical analysis typically reveals positivity for cytokeratins and myoepithelial markers. On a molecular level, MYB-NFIB fusion is frequently observed. The main treatment is breast-conserving surgery, with postoperative radiotherapy recommended in certain cases. Axillary lymph node dissection or sentinel lymph node biopsy may not always be necessary.
Conclusion: Breast ACC is a rare tumour with a favourable prognosis. A multidisciplinary approach, including precise histopathological evaluation and conservative surgical treatment, is essential for optimal

clinical outcomes. Further studies are needed to better understand its biology and identify potential prognostic biomarkers.

E-PS-02-011

Tall cell carcinoma with reversed polarity: report of two cases with clinical, histopathological and molecular insights

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Background & Objectives: Tall Cell Carcinoma with Reversed Polarity (TCCRP) is a rare type of breast carcinoma with fewer than 100 cases reported to date and first described by Eusebi *et al*. in 2003. It is histologically characterized by tall columnar cells with reverse polarity and most commonly associated with IDH2 mutations. Due to its rarity TCCRP can pose significant challenges in its diagnosis.
Methods: We present two cases involving 68 and 79-year-old females without significant medical history. They presented with 20mm and 19mm breast nodules, respectively, and underwent vacuum-assisted biopsy.
Results: In the first case, the biopsy revealed a papillary solid tumour composed of tall columnar cells with apical nuclei and eosinophilic cytoplasm, positive for CK5 and negative for p63, oestrogen, progesterone and androgen receptors and ERBB2. The proliferation index was low.
Regarding the second case, the biopsy revealed a mixed invasive lesion. The first component was similar to the reported in the first case. The second component was a well differentiated invasive carcinoma, with a basal phenotype, positive for CK5.
Both tumours were removed with clear margins and no lymph node metastasis. Histopathological and immunohistochemical analysis confirmed the diagnosis of TCCRP. Molecular testing for the IDH2 R172 (R120) mutation is currently ongoing. Follow-up has shown no recurrence in either case.
Conclusion: TCCRP must be distinguished from other triple-negative carcinomas associated with aggressive behaviour. Due to its similarity to other tumours, such as metastatic thyroid carcinoma an accurate diagnosis is essential.

E-PS-02-012

Atypical presentation of histiocytoid lobular carcinoma of the male breast

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Background & Objectives: The histiocytoid variant of invasive lobular breast carcinoma is a very rare presentation of breast cancer, usually affecting postmenopausal women, with only a few cases described in males. We report a case of an unusual and underrecognized manifestation of the disease, with a first presentation as skin involvement of the axilla in a male patient.
Methods: We present the case of a 39-year old male with an axillary nodule clinically diagnosed as a cyst with erythematous and thickened overlying skin, developed over the course of a few months. The surgically removed tissue was submitted for microscopic and immunohistochemical examination.
Results: Microscopic examination revealed a dermic and hypodermic invasive neoplastic proliferation, arranged in cords and isolated, discohesive cells, without tubular/gland formation, composed of bland epithelioid cells with abundant pale-eosinophilic cytoplasm and irregular, hyperchromatic or vesicular nuclei, some with prominent eosinophilic nucleoli, moderate nuclear pleomorphism and inconspicuous mitotic activity. Perineural invasion was observed. In immunohistochemical studies, neoplastic cells were positive for cytokeratins (AE1/AE3, CK7), breast tissue markers (GATA3, GCDFP-15, mammaglobin-focally), ER (Allred 4 score) and negative for PR and HER2 (1+), with a low ki-67 index (10%). Negative E-cadherin further supports the diagnosis of a lobular breast carcinoma. Imaging studies confirmed the presence of a breast mass.
Conclusion: Skin involvement of histiocytoid lobular carcinoma is a rare manifestation of invasive breast carcinoma, especially in the male population, with limited representation in literature which poses significant diagnostic challenges. Considering the similar morphologic features shared with other entities, such as xanthogranulomatous lesions or primary cutaneous histiocytoid carcinoma, the latter also sharing its immunohistochemical profile, clinical and imaging correlations are critical. Even though there is a predilection for women, it is still an important diagnosis to be taken into consideration in male patients.

E-PS-02-013

Fibromatosis-like metaplastic carcinoma: a case of a rare breast tumour

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Background & Objectives: Fibromatosis-like metaplastic carcinoma (FLMCa) is classified as a rare histologic subtype of metaplastic carcinoma in the last WHO Classification of Breast Tumours (2019). FLMCas are spindle cell lesions of the breast showing mild nuclear atypia. Morphologically, it can be difficult to diagnose FLMCas as carcinomas and differentiate from other bland spindle cell lesions. Here, we present a case of this rare entity.
Methods: A 63-year-old female patient admitted to hospital with an irregular mass in the upper outer quadrant of the right breast . A core needle biopsy was performed and revealed a spindle lesion and then lumpectomy was performed.
Results: On macroscopic examination, there was a white, firm lesion 2.5×1.8×1.5 cm in diameter with irregular borders. Microscopically, the tumour was predominantly composed of bland spindle cells with pale eosinophilic cytoplasm and mild nuclear atypia. These cells infiltrated the surrounding fat tissue and normal breast parenchyma. The trapped ducts were present within the spindle cell areas, along with keloid-like collagenized stroma. Additionally, a focal area of squamous metaplasia was identified in a few section.
Immunohistochemically, the spindle tumoral cells were diffusely positive for CK5/6 and negative for oestrogen receptor (ER), progesterone receptor (PR), and CerbB-2. Smooth muscle actin (SMA), smooth muscle myosin (SMM), p63, and p40 showed focal positive expression. The Ki-67 proliferation index was low, at approximately 8%. With this findings, a diagnosis of fibromatosis-like metaplastic carcinoma was reached.
Conclusion: Fibromatosis-like metaplastic carcinoma should be considered in the differential diagnosis of low-grade breast bland spindle cell lesions with collagenous stroma and infiltrative margins. This diagnosis should be confirmed by immunohistochemical analysis especially with keratins.

E-PS-02-016

The clinical and pathological evaluation of 34 cases of Phyllodes Tumours

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Background & Objectives: Phyllodes tumours (PT) are rare biphasic fibroepithelial neoplasms, accounting for 0.3% to 1% of breast

tumours, primarily in women aged 45-49. Classified by the WHO into benign, borderline, and malignant categories, these tumours exhibit varying degrees of stromal atypia, cellularity, and mitotic activity. Although most are benign (35%-64%), both stromal and epithelial components can become malignant, with recurrence rates of 10%-17%. Differentiating benign phyllodes tumours from cellular fibroadenomas remains a challenge. This study aims to evaluate the clinicopathological characteristics of phyllodes tumours.
Methods: PT cases diagnosed between 2010 and 2022 at SBÜ Izmir Medical Faculty Tepecik Training and Research Hospital were retrospectively reviewed, and all cases were re-evaluated. Tumours were classified as benign, borderline, or malignant based on tumour margins, stromal cellularity, stromal atypia, stromal overgrowth, mitotic activity, and the presence of malignant heterologous elements.
Results: A retrospective review of 34 PT cases in women (mean age 38.7 years) found 18 benign (53%), 11 borderline (32.4%), and 5 malignant (14.8%). Leaf-like patterns were observed in 13 cases, and heterologous elements in 1. Tumour sizes averaged 3.95 cm (benign), 5.7 cm (borderline), and 6.1 cm (malignant). Mitoses were 1.8 (benign), 8.7 (borderline), and 19 (malignant) per 10 HPF. Malignant tumours showed well-circumscribed (3) and infiltrative (1) patterns. Borderline tumours had a mix of circumscribed and infiltrative types. Stromal overgrowth was common in malignant and borderline cases.
Conclusion: PT often mistaken for benign lesions are challenging to differentiate from cellular juvenile fibroadenomas, especially in core biopsies. Key factors for diagnosis include stromal cellularity, mitotic count, nuclear pleomorphism, and atypia Stromal cellularity may upgrade after excision. Study showed four benign cases upgraded to borderline post-excision. Accurate preoperative diagnosis and management are vital due to their recurrence and malignant potential. Tumours with increased stromal cellularity or atypia in biopsies should be excised with a 1 cm surgical margin.

E-PS-02-018
Angiosarcoma following breast-conserving surgery without radiation therapy or axillary lymph node dissection: a case report
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Background & Objectives: Angiosarcoma is the most common mesenchymal tumour of the breast. Radiation therapy (RT) and lymphedema due to axillary lymph node dissection (ALD) are the most well-known risk factors of secondary angiosarcoma. We report a case of angiosarcoma following breast-conserving surgery without RT or ALD for encapsulated papillary carcinoma in an 88-year-old female.
Methods: The patient initially visited Chugbuk National University Hospital with a left breast mass at the age of 82. She underwent breast-conserving surgery and sentinel lymph node biopsy. RT was not performed due to her old age. She presented with a fast-growing mass at the previous surgery site 66 months after the initial surgery. Total mastectomy and sentinel lymph node biopsy for the second mass was performed. Pathological examinations including immunohistochemical (IHC) assays were performed for both breast lesions.
Results: The initial mass was a grossly well-demarcated whitish-gray mass, measuring 4 x 3 x 2.3 cm. Microscopically, the mass showed a proliferation of monotonous round cells with papillary architecture and was surrounded by thick fibrous capsule. IHC results were hormone receptor-positive and HER2-negative. The second mass was grossly ill-defined red mass with multifocal necrosis, measuring 9 x 6.5 x 3.3 cm. Microscopic examination showed that the tumour cells were a mixture of round and spindle cells without conspicuous epithelial features. Both tumour cells were positive for CD31 and negative for pan-cytokeratin, epithelial membrane antigen, and desmin. IHC results for CD34 and c-myc varied according to the cell types: round cells were positive for c-myc and negative for CD34, whereas spindle cells were CD34-positive and c-myc-negative.
Conclusion: The diagnosis of angiosarcoma should not be ignored in patients with breast cancer who have previously undergone breast-conserving surgery without RT or ALD.

E-PS-02-019
Clinicopathological features of encapsulated papillary carcinoma in a cohort of predominantly African-American/Black women
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Background & Objectives: Encapsulated papillary carcinoma (EPC) is an uncommon low-grade carcinoma that has morphologic and immunohistochemical overlap with other papillary lesions of the breast. The classification of EPC as an in situ or invasive lesion, its long-term behaviour, and its management remain a matter of debate. Here we examined the clinical course of EPC in an almost exclusively African-American/Black population.
Methods: We identified thirty-one resection specimens with EPC between 2013 and 2024 to determine the long-term behaviour of this carcinoma, primarily in African-American/Black women. Clinicopathologic and follow-up data from the electronic medical record was reviewed for all cases.
Results: Our study population was predominately African-American/Black women (94%; 29/31), with a median age of 71 (range: 41 – 88). Pure EPC comprised 26% (8/31) of cases, EPC with invasive carcinoma [with and without ductal carcinoma in situ (DCIS)] represented 55% (17/31) of cases, and EPC with DCIS formed the remainder (19%, 6/31). The majority of invasive carcinomas arising in association with EPC were ER+ and PR+ (88%, 15/17, for both), and HER2-ve (94%, 15/16). Pure EPC and EPC with DCIS were collectively ER+ (100%, 13/13), PR+ (92%, 11/12), and HER2-ve (100%, 5/5). Median time of follow-up after diagnosis was 3.6 years (range: 1 week – 11.6 years). No recurrences were seen in pure EPC while four cases of EPC with invasive carcinoma or DCIS recurred, which was found after a median of 2.2 months (range: 2.0 – 15.9 months) after diagnosis.
Conclusion: No study has yet investigated the clinical course of EPC in African-American/Black women. Our findings indicate that EPC often coexists with invasive carcinoma and/or DCIS. In pure EPC, the prognosis was excellent with no recurrences, and even in cases with associated invasive carcinoma, the clinical course was indolent.

E-PS-02-020
CD8+ and CD20+ TILs in residual triple-negative breast cancer: a novel prognostic indicator
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Background & Objectives: Tumour-infiltrating lymphocytes (TILs) have been positively correlated with longer disease-free survival (DFS) and improved overall survival (OS) in patients with triple-negative breast cancer (TNBC), particularly when assessed in pre-neoadjuvant chemotherapy (NAC) biopsies. However, studies evaluating TILs after NAC setting remain scarce. This study evaluates the prognostic significance of CD8+ and CD20+ lymphocyte infiltration in residual TNBC post-NAC.
Methods: We reviewed 398 cases of TNBC across two centres in a period of 5 years (January 2019-December 2023). Of these, only 48 cases met the eligibility criteria for our study. Immunohistochemical staining for CD8 and CD20 was evaluated following the hotspot

method. Statistical analysis was conducted using SPSS Statistics, with outcome correlation assessed via Kaplan-Meier survival analysis.
Results: Our study found that 47.9% of patients were staged as ypT2, highlighting TNBC's chemoresistance and the need for additional prognostic markers beyond tumour shrinkage.
In terms of survival outcomes, the 3-years DFS rate was 68.8%, while OS was 72.1% in 5 years.
Immunohistochemical analysis showed a predominance of CD8+ T-lymphocytes over CD20+ B-lymphocytes, with a CD8/CD20 ratio>1 in 91.7% of cases. This suggests that cytotoxic T-cell infiltration plays a dominant role in shaping the post-chemotherapy immune microenvironment in TNBC.
A higher CD8/CD20 ratio>1 was correlated with better survival outcomes than those with a ratio<1, with a significantly improved 3-year DFS (75.2% vs. 25%, p = 0.002) and 5-year OS (79% vs. 66.7%, p = 0.01), emphasizing the pivotal role of T-cell-mediated anti-tumour immunity while also highlighting the supportive function of B-lymphocytes in antigen presentation and immune modulation.
Conclusion: Despite its limitations, our study suggests that a high CD8/CD20 ratio in residual TNBC following NAC is a strong prognostic indicator, correlating with improved DFS and OS. These results underscore the potential of immune profiling in refining post-chemotherapy prognostic stratification and guiding future therapeutic strategies.

E-PS-02-023
Association of pretreatment neutrophil-to-lymphocyte ratio with clinicopathological parameters in breast cancer
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Background & Objectives: Inflammation and tumour microenvironment have an important role in the different stages of cancer development - initiation, promotion and metastasis. Infiltrating leukocytes secrete a wide variety of factors which promote tumour growth and suppress host's immune response. Neutrophil-to-lymphocyte ratio (NLR) is an easily measurable marker of subclinical inflammation. Recent literature has demonstrated use of these inflammation markers for prognostication in various solid cancer, including breast cancer (BC). Breast cancer is the leading cause of cancer and cancer mortality in India. This study, evaluated the association of preoperative NLR with clinicopathological parameters and molecular subtypes of BC in India.
Methods: A hospital-based cross-sectional prospective study was conducted over 18 months on 228 histologically proven cases of BC. Molecular classification into four subtypes was based on IHC expression of ER, PR, Her2, and Ki67. Pre-treatment complete blood count was performed on Sysmex XN1000. Cutoff value of NLR was calculated using receiver operator characteristic curve (ROC) by STATA software. Statistical analysis was performed using Jamovi 2.3.18.0.
Results: Most common histological type was invasive ductal carcinoma, NST (97.4%) and the commonest molecular subtype was Luminal B (37.7%). There was no statistical association of molecular subtype with clinicopathological parameters except clinical TNM stage (P=0.019). Cutoff value of NLR was 2.64. High NLR (≥2.64) was most common in triple-negative BC (70.6%) and least in Luminal A (20.8%) which was statistically significant (P<0.001). Advanced cTNM was also statistically associated with elevated NLR (P=0.022). Significant association of high NLR was observed with ER/PR negative status (P=0.005) and high Ki67 (P=0.006). No association of NLR was found with age, gender, histological type, tumour grade, nodal status, metastasis.
Conclusion: High NLR is associated with unfavourable factors in BC. Pretreatment NLR has potential application as a simple, reproducible and inexpensive biomarker for prognostication in BC. It may help in pretreatment risk stratification.

E-PS-02-024
A systematic approach to the diagnosis of rare and salivary gland tumours of the breast and literature review
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Background & Objectives: Rare and salivary gland tumours of the breast often present with a triple negative phenotype . However their biological behaviour is not the same as the more comman triple negative breast carcinomas of no special type. The 5th edition of WHO classification of breast tumours has placed these tumours as a separate class under the category of epithelial tumours . Experience with the diagnosis of these tumours in the breast is limited due to their rarity at this site . At the same time their recognition is crucial as they are treated differently from triple negative breast carcinomas of no special type which they mimic owing to their triple negative phenotype.
Methods: Cases of Tall cell carcinoma with reversed polarity, adenoid cystic carcinoma in breast , secretory carcinoma breast and breast microglandular adenosis along with literature review will be used to illustrate a systematic approach to recognise important clues on histology which will prompt the appropriate IHC panel to recognise these rare tumours. The differential diagnosis of breast mucoepidermoid carcinoma and breast polymorphous adenocarcinoma will also be covered in the discussion.
Results: The presentation will use some representative cases of this class of tumours ,which rarely present in the breast, and highlight important clues to differentiate them from their more comman breast tumour mimics.
Conclusion: Review of literature and a systematic approach to diagnose rare and salivary gland tumours in the breast as it has significant management implications.

E-PS-02-025
Breast cancer in young women: the experience of a portuguese tertiary centre
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Background & Objectives: Breast cancer is the most common malignancy in women worldwide and the leading cause of cancer-related death in women under 45 years old. Its incidence has been increasing in this age group. In December 2024, the Portuguese Direção-Geral da Saúde (DGS) extended the age range for population screening to women aged 45-74, aiming for earlier detection.
Methods: Between 2022 and 2023, our institution diagnosed and managed 84 cases of breast cancer in women ≤45 years of age. Clinical and histopathological variables were analysed, including morphological and immunohistochemical characteristics, as well as treatment regimens, presence of metastasis, and clinical outcomes.
Results: The majority of patients presented with grade III (49%) "no special type" (NST) invasive carcinoma (87%). Most tumours were hormone receptor-positive (68%) with a high percentage of triple-positive tumours (14%). The median tumour size at presentation was 27.8mm. 30% of patients had homolateral lymph node metastasis at presentation. 46% of patients received neoadjuvant chemotherapy, followed by breast-conserving surgery in 63%. A complete pathologic response was achieved in 25%. Only 10% had distant metastasis.

Most patients did not have a family history of breast cancer (55%), and genetic studies revealed no alterations (63%). Two patients died of the disease, six are alive with disease, undergoing palliative care, and 90% are alive without evidence of disease. We also analysed the correlation between the presence of necrosis and tumour infiltrating lymphocites (TILs) in the invasive carcinoma on biopsy and the response to chemotherapy.
Conclusion: Our results are consistent with published literature, indicating that breast cancer in young women tends to be more aggressive, with larger tumour sizes and higher grades at diagnosis, as well as higher incidences of HER2 and triple-negative disease. The rising incidence of breast cancer in young women requires further investigation into environmental and genetic factors contributing to its aggressive biology.

E-PS-02-026
Clinicopathological characteristics of male patients with breast cancer in our centre
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Background & Objectives: Male breast cancer, while considerably rarer than female breast cancer, has seen a rising incidence in recent years. The typical complaint is a palpable mass in the breast, with many symptoms being overlooked, leading to delays in diagnosis and treatment. Several etiological factors, including age, race, family history, obesity, genetic predispositions, gynecomastia, Klinefelter syndrome, liver diseases, and radiation exposure, play a role in the development of this disease. The most common histopathological type found in male breast cancer is invasive carcinoma of no special type (NST), which constitutes 80-90% of cases. Generally, oestrogen receptor (ER) positivity is reported in 65-97% of cases, progesterone receptor (PR) positivity in 60-85%, and HER2 positivity varies from 3-28%. Secondary malignancies are observed in 5-33% of male breast cancer patients. This study evaluates the clinicopathological characteristics of male patients diagnosed with primary breast cancer in our centre.
Methods: A retrospective review was performed on the pathology archives from 2009 to 2023, focusing on 26 male patients diagnosed with primary breast cancer. Clinical data were obtained from our hospital's automation system, assessing age, tumour size, histological type, grade, biomarker status, and survival.
Results: Patients' ages ranged from 38 to 87 (mean age: 70.6 years). Involvement was predominantly unilateral, with 34.6% on the left and 61.5% on the right. Tumour sizes varied between 3 mm and 36 mm (mean size: 22.6 mm). All patients were alive. Of the cohort, 62% presented with breast swelling. All were diagnosed with invasive carcinoma-NST. Notable findings included axillary involvement in 15.4% and ER positivity in 92.3% of patients, while two cases of prostate cancer were recorded as secondary malignancies.
Conclusion: Male breast cancer, though rare, is on the rise. Delayed diagnoses often lead to advanced stages, underscoring the importance of early detection for successful treatment outcomes.

E-PS-02-027
A rare case of metastatic metaplastic breast carcinoma in the anal canal
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Background & Objectives: A 58-year-old woman with a known history of breast adenocarcinoma 18 years ago and metastatic breast adenocarcinoma involving the ovaries and uterine corpus 3 years prior, presented with a newly detected anal canal mass.
Methods: Following surgical excision, the specimen was sent to the pathology department for further examination. Macroscopically, the tumour appeared as a well-circumcised, multilobulated neoplastic mass, measuring 6 cm in diameter, with white-to-greyish cut surface. Microscopic examination and extensive immunohistochemical analysis were required to determine the diagnosis.
Results: Histopathological examination revealed a biphasic malignancy with an epithelial neoplastic component that abruptly transitioned to a mesenchymal component of chondroid differentiation. Immunohistochemical analysis revealed expression of CK7, EMA and GATA-3 in the epithelial component, while the mesenchymal component showed expression for S100 and SATB-2.
Conclusion: The morphological and immunohistochemical findings, in correlation with the patient's medical history, confirmed the diagnosis of metastatic metaplastic breast carcinoma with heterologous mesenchymal differentiation, also referred to as "matrix-producing carcinoma". This case not only highlights a rare metastatic site for metaplastic breast carcinoma, but also emphasizes the role of intratumoral heterogeneity in the tumour's metastatic propensity and immune evasion. Notably, while the vast majority of metaplastic carcinomas are categorized as triple-negative, in this case the tumour exhibited expression of HER2 [SCORE (2+)].

E-PS-02-029
Myoid hamartoma of the breast: an extremely rare diagnostic challenge
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Background & Objectives: Myoid hamartoma of the breast is an extremely rare entity, first described by Davies and Riddell in 1973, with only a few cases reported in the literature. It represents a unique variant of mammary hamartomas, characterized by a variable composition of glandular, fibrous, and adipose tissue, with a prominent smooth muscle component. The rarity of this lesion, combined with its histological complexity, makes its diagnosis particularly challenging.
Methods: A 48-year-old female patient, with no medical or surgical history, presented with a right breast nodule. Ultrasound examination revealed a solid, hypoechoic nodule in the upper outer quadrant of the right breast, initially suggestive of a fibroadenoma and classified as BI-RADS3.
A wide excision of the lesion with histological verification was performed.
Results: Macroscopically, the specimen was a well-circumscribed 3 × 2 cm nodule with a smooth surface and firm consistency. On sectioning, the cut surface appeared fleshy and whitish-gray.
Histologically, the breast parenchyma consisted of atrophic lobules within an abundant fibrous stroma, interspersed with numerous adipocytes and congested blood vessels. Rare peripheral ducts displayed a regular dual-layered epithelium without atypia. A predominant component of fascicles of spindle cells with regular nuclei was observed.
Immunohistochemical analysis confirmed the smooth muscle nature of the spindle cells, showing strong and diffuse positivity for smooth muscle actin and H-caldesmon. p63 was negative in the spindle cells and marked only the myoepithelial cells of the ducts. CD34 and S100 were negative.
Conclusion: Breast hamartoma is an uncommon and often underrecognized benign lesion. When it exhibits a predominant smooth muscle component, it is classified as myoid hamartoma, an even rarer entity. Its diagnosis can be challenging due to multiple differential diagnoses,

necessitating careful histopathological assessment. Immunohistochemical studies play a crucial role in confirmation.
Given its rarity and complexity, awareness of this lesion is essential to prevent diagnostic errors and potential mismanagement.

E-PS-02-032
Pleomorphic adenoma of the breast: report of two cases, one with malignant transformation
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Background & Objectives: Pleomorphic adenoma of the breast (PAB) is a rare benign mixed epithelial-myoepithelial neoplasm that morphologically resembles its salivary gland and skin counterparts.
Since its first description in 1906, only isolated cases of these lesions have been described in the breast (less than 100 cases).
Correct diagnosis is often difficult by core needle biopsy. Malignant transformation of BAPs is an extremely rare complication that has only been reported on three occasions. We present two new cases, one of which masked an invasive epithelial component (pleomorphic exadenoma carcinoma).
Methods: The two women were aged 67 and 57 years respectively. They presented with a new retroareolar mass of 10 and 13 mm in the left and right breast, from which an excisional biopsy was taken in both patients.
Results: The neoplasm consisted of two components. The epithelial component had a glandular or nest cell pattern. The mesenchymal myoepithelial component contained myxoid and chondroid areas. By immunohistochemistry, the glandular epithelial cells expressed CKAE1/AE3, CK 18, CK7. Myoepithelial cells expressed smooth muscle actin, p63 and CK5/6. Cartilaginous stromal cells expressed S-100. In the second case, an infiltrative epithelial growth, corresponding to an invasive carcinoma, is observed at the periphery of the BAP.
Conclusion: Pleomorphic adenoma is a mixed benign (epithelial-myoepithelial) and is one of the so-called salivary gland type mammary tumours. This tumour commonly occurs in the salivary gland, and rarely originates in the breast.
The tumour consists of epithelial, myoepithelial and stromal components, characteristically consisting of bone and/or cartilage. Differential diagnoses in the breast include fibroadenoma, phyllodes tumour, metaplastic carcinoma and mucinous carcinoma.
Pleomorphic adenomas on core needle biopsy may be misdiagnosed as a primary sarcoma or metaplastic breast carcinoma. Malignant transformation is extremely rare, having been described only three times before we presented our case.

E-PS-02-033
Expression of LEF- 1, β- catenin and Ki -67 labelling index in fibroepithelial neoplasms of breast
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Background & Objectives: Diagnostic challenges exist in distinguishing Phyllodes Tumour (PT) from Fibroadenomas (FA) and accurately grading them, especially in core needle biopsy (CNB) specimens. Lymphoid Enhancer Binding Factor 1 (LEF-1) is an important component of the Wnt/β-catenin signalling pathway. This study was undertaken to assess expression of LEF-1, β-catenin and Ki-67 labelling index in fibroepithelial neoplasms of the breast and assessing their utility as potential markers for differentiating between FAs, benign PTs, borderline PTs, and malignant PTs.
Methods: Expression of LEF-1, β-catenin, and Ki-67 labelling index was assessed by immunohistochemistry (IHC) on 100 cases of fibroepithelial neoplasms (study period January 2019 to 2023), of which 67 were resection specimens (30 FA and 37 PT). IHC was also put up on 21 CNBs for which subsequent resection specimen was available for comparison of IHC expression between CNBs and the corresponding resection specimens.
Results: Among PTs, 61.4% were benign tumours, 25% were borderline tumours, and 13.6% were malignant PTs. PTs were more commonly observed in older individuals, with a mean age of 42.10 years compared to FA patients with a mean age of 25.43 years. The size of PTs was significantly larger than FAs, with a mean size of 8.42 cm compared to 3.89 cm, respectively. Except for mitotic count, there were no statistically significant differences observed in terms of cellularity, atypia, stromal overgrowth, and heterologous elements between core needle biopsies and their corresponding resection specimens. Immunohistochemical analysis revealed increased expression of LEF-1, beta-catenin, and Ki-67 labelling index in the stroma of PTs compared to FAs. Also, the immunohistochemical expression of LEF-1 and beta catenin in CNBs corresponded to that in the subsequent resection specimens. Ki-67 labelling index in CNBs did not correspond with that in the subsequent resection specimens.
Conclusion: LEF1 and beta catenin can be useful in CNBs for refining diagnosis of fibroepithelial neoplasms

E-PS-02-034
A pitfall to avoid: Langerhans dendritic cells in lymph nodes may mimic metastases from breast cancer
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Background & Objectives: Langerhans dendritic cells (DCs) present tumour-derived antigens to T cells, facilitating anti-tumour response, and their presence in axillary lymph nodes has been linked with breast cancer prognosis. Here, we address a possible pitfall in diagnosis stemming from this connection by presenting a rare case of occult metastatic invasive lobular carcinoma (ILC) in a lymph node (LN).
Methods: The medical records and pathological findings of a 68-year-old patient who went through right breast mastectomy due to metastatic infiltrating duct carcinoma (IDC) are presented. Her medical background included lung lepidic adenocarcinoma treated by left upper lobectomy (7 years prior) and metastatic ILC of the left breast (10 years before) treated by lumpectomy and combination hormonal-targeted drug therapy. The patient showed a complete response.
Results: The right breast showed IDC, grade 2, with micropapillary features and extensive lymphovascular invasion. Three right axillary sentinel LNs showed metastases of IDC and extensive fibrosis. Surprisingly, AE1/AE3 immunostaining of the LN metastases demonstrated two staining patterns: strong membranous staining of the IDC with micropapillary features and an additional moderate cytoplasmic

staining of single spreading cells that were also positive for GATA3 and oestrogen (ER) and negative for TTF1 and progesterone (PR). Similarly, the stain for E-cadherin showed two patterns of staining: strong membranous staining of the IDC and an additional moderate cytoplasmic staining in a non-aggregated pattern of cells that were also positive for CD1a, S100, and langerin (CD207) and constituted Langerhans DCs. Indeed, the cytokeratin-positive single spreading cells located between the DCs were negative for E-cadherin and represented occult metastatic ILC.
Conclusion: This unusual case of dual metastatic ILC-IDC breast carcinoma brings to attention the intriguing contribution of Langerhans dendritic cells to immunity and their intimate association with tumour cells. It also highlights the pivotal role of careful and diligent pathological evaluation in reaching an accurate interpretation and diagnosis.

E-PS-02-035
Breast biomarker dynamics in primary and metastatic settings: insights from a tertiary cancer centre in India highlighting changes of expression pattern and its clinical impact
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Background & Objectives: Breast cancer (BC) is the second most common cancer globally and the leading cause of cancer mortality in women. Immunophenotypic discordance between primary and metastatic sites can impact treatment outcomes. While international guidelines suggest rebiopsy of metastatic lesions to reassess tissue biomarkers, studies focusing on Indian BC cohorts are limited.
Objective: To analyse the dynamics of BC biomarkers in primary versus metastatic sites and its impact on prognosis and survival.
Methods: This retrospective study, conducted at a tertiary cancer centre over a 5-year period, included BC cases with metastasis at presentation or during the disease course, with available biopsy samples from both primary and metastatic sites. Clinical metrics and immunohistochemical expression of oestrogen receptor (ER), progesterone receptor (PR), and HER2/neu were analysed.
Results: Out of a total of 113 cases, the commonest histological subtype was invasive breast carcinoma (no special type). 6 cases presented with metastasis at diagnosis, while 107 developed metastasis during follow-up. Common metastatic sites were lung, liver, bone, and brain. The majority of the cases were Type 1 [ER+PR+/-HER2-] (42 cases; 37.2%) followed by Type 4 [ER-PR-HER2-] (28 cases; 24.8%), Type 2 [ER+PR+/-HER2+] (24, 21.2%) and Type 3 [ER-PR-HER2+] (19, 16.8%). ER conversion was recorded in 24.8%, PR conversion in 39.8%, and HER2 conversion in 14.2% of cases. Conversion was predominantly from positive to negative in all three biomarkers. ER, PR conversion mainly occurred in Type 2, with HER2 conversion predominantly in Type 1 cases. Lung was the commonest site of conversion for all biomarkers. In 25% of ER conversion cases, disease progression occurred, while 22.2% of PR conversion cases and 18.75% of HER2 conversion cases experienced progression.
Conclusion: Biomarker status does change during metastatic progression in BC. Rebiopsy of metastatic sites with re-appraisal of breast biomarkers is essential for treatment re-stratification, allowing for tailored and specific therapy.

E-PS-02-036
Two rare cases of tuberculous mastitis mimicking breast carcinoma
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Background & Objectives: The breast is particulary resistant to tuberculosis invasion. Tuberculous mastitis (TBM) is a rare, often misdiagnosed condition, affecting <0.1% of breast specimens in the USA, altough, the only estimates date back to 1985, when only 500 cases were reported world-wide.
Methods: We report the only two cases of TBM extracted from the 2000-2025 digital archive of *Marius Nasta Institute of Pneumophitsiology*, Romania. The patients initially exhibited clinical and radiological features suggestive of malignancy or breast abscesses, prompting further histopathological and microbiological investigations. Based on the clinical and pathological presentation, the most likely routs of breast invasion are discussed.
Results: ***Case1*:** A 73-year-old woman presented with extreme weight loss (BMI=15, W=37kg), a firm breast mass, and bilateral axillary lymphadenopathy. CT scan showed diffuse pulmonary consolidations and mediastinal lymphadenopathy. Core breast biopsy revealed multiple clasical caseating granulomas with acid-fast bacilli on Ziehl-Neelsen staining.
***Case2*:** A 21-year-old woman presented with a breast lump consisting of multiple, non-caseating granulomas, initially diagnosed as granulomatous mastitis. Tuberculous aetiology was confirmed by Ziehl-Neelsen stain.
Both patients were diagnosed with nodular secondary TBM and had poor initial response to antibiotics. Clasically, TBM is considered to affect young, lactating women from the indian subcontinent. These cases highlight the diverse epidemiology of the disease, beyond clasical risk groups.
Conclusion: Given its rarity, TBM poses a significant diagnostic challenge and should be considered in the differential diagnosis of any granulomatous breast lesion. There are no specific standardized treatment protocols and initial treatment often fails, requiering a second, more aggressive antibiotic regiment or surgical intervention. Although tuberculosis is regarded as a disease of the past, the rise of extreme- or multidrug-resistant strains highlights the critical need for accurate diagnosis and tailored treatment strategies.

E-PS-02-037
Two cases of low-grade triple-negative breast carcinomas: is it enough to assign them as such?
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Background & Objectives: Triple-negative-breast-carcinomas (TNBC) are defined by the lack of expression of hormone and HER2 receptors and comprise a heterogenous group of invasive carcinomas with significant molecular, morphological and clinical heterogeneity. Although the majority are high-grade tumours, low-grade TNBC (LGTNBC) do occur and demonstrate characteristic

morphological and immunohistochemical profiles as well as indolent behaviours.
In this study, we illustrate histological and immunohistochemical features of two cases of LGTNBC (secretory carcinoma (SC) and adenoid cystic carcinoma (ACC)), highlighting the need for suggesting or diagnosing a specific histological-subtype, ideally as-soon-as the biopsy is analysed.
Methods: We report 2 cases of LGTNBC in two women aged 57 and 64 years-old respectively. Both patients were diagnosed as such on a preoperative-core-needle-biopsy and subsequently on the corresponding breast-surgical-specimen.
Results: On histologic sections, the first tumour was predominantly composed of tubules and cribriform structures with low-grade cytological features. Immunohistochemical analysis demonstrated a characteristic dual-cell population of luminal (CK7+, CD117+) and myoepithelial-basal cells (CK5/6+, p40+), as well as a basal-like phenotype (ER-, PR- and HER2-) and a low-proliferative-index. These findings were consistent with a LGTNBC further categorized as a classic-ACC. The second tumour was composed of tumour cells with low-grade cytological atypia arranged in microcystic/honeycomb, and tubulo-papillary growth pattern. Additionally, eosinophilic intracellular and extracellular secretions were evidenced and stained positively with PAS and Alcian blue. Tumour cells were of basal-like phenotype and S100-positive. Proliferative-index was low. Given these findings, we concluded to a LGTNBC, suggesting a SC. Nevertheless, ETV6-NTRK3 fusion could not be demonstrated given the non-availability of appropriate molecular tests in our pathology department.
Conclusion: LGTNBC is a descriptive term that could be used as a provisional diagnosis if a specific subtype could not be established, mainly in core-needle-biopsies. Indeed, accurate histological subtyping is crucial as prognoses and therapeutic strategies may differ among entities.

E-PS-02-038

MUC2 is a useful diagnostic marker for distinguishing primary mucinous cystadenocarcinoma and mucinous carcinomas of the breast: report of a case and comparative study

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Background & Objectives: Primary mucinous cystadenocarcinoma of the breast (MCA) represents an exceedingly rare neoplasm, with 45 cases described so far, distinct from mucinous carcinoma (MC).
Especially in small biopsies, the differential diagnosis with mucinous carcinomas (MC) can be challenging.
Mucin expression is occasionally and often only partially studied in MCA, with only 7 other cases reported in literature, all negative for MUC2.
We investigated mucin expression in one case of MCA and in a pool of 35 MC cases to evaluate differences and compare our results with literature.
Methods: Immunoistochemical data of MUC1, MUC2, MUC4, MUC5AC and MUC6 were evaluated using a semi-quantitative score. In all cases, a complete immunoprofile of molecular subtype for breast carcinoma was also performed.
Results: MCA showed a triple negative molecular subtype, expressed CK7 and was negative for CDX2 and CK20.
Out of 35 MC, 33 were luminal and 2 had a HER2 enriched immunoprofile.
The MCA case expressed MUC1 and focally MUC5ac, while MUC2, MUC4 and MUC6 showed negative stains.
All MC cases (35, 100%) expressed MUC1, 29/35 (82,8%) showed positive stain for MUC2, 2 cases (5,71%) were positive for MUC4, 18 (51,4%) demonstrated MUC5 expression and 22 (62,14%) were positive for MUC6.
In relation to clinicopathological features, MUC1 expression was significantly related to Nottingham score (p=0.0310), MUC1 and MUC5 score with vascular invasion (p=0.0268 and p=0.0204, respectively) and MUC5 with nodal status (p=0.0485).
Conclusion: The results of our study show that MUC2 could be a useful marker in the differential diagnosis between MCA and MC, particularly on limited biopsy material and especially in hypocellular or micropapillary MC cases.
The case herein reported increased the number of MCA cases with mucin immunoprofile.
Moreover, MUC1 and MUC5 expression in MC cases can have prognostic value.

E-PS-02-039

Upgrade rate and predictive factors for phyllodes tumour in fibroepithelial lesions of the breast in patients aged over 50 years

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Background & Objectives: Fibroepithelial lesions (FELs) of the breast are heterogeneous neoplasms that can present diagnostic challenges, especially in core needle biopsy (CNB). The aim of this study was to determine the upgrade rate of FEL core biopsies to phyllodes tumour (PT) and identify associated predictive factors in women over the age of 50.
Methods: This is a retrospective, population-based study of fibroadenomas (FELs) of the breast, including fibroadenoma (FA), FEL-indeterminate, and phyllodes tumour (PT) diagnoses, based on core biopsies conducted over a three-year period (2017-2019) in Vancouver, BC, Canada. Core biopsy diagnoses were compared with surgical pathology resection findings, and clinical and radiologic factors were analysed to identify features associated with PT.
Results: Of 104 core biopsies of fibroadenomas (FELs), including 90 diagnosed as fibroadenoma (FA), 3 as phyllodes tumour (PT), and 11 as FEL-indeterminate, 23 proceeded to excisional biopsy, with a 39.1% upgrade rate to PT. Of the 10 core biopsies initially diagnosed as FA, 1 was upgraded to PT on excisional biopsy, yielding a negative predictive value (NPV) of 90%. Among the 3 core biopsies diagnosed as PT, all were confirmed as PT on excisional biopsy, resulting in a positive predictive value (PPV) of 100%. The mean mass size was significantly larger in the PT group (3.3 cm) compared to the FA group (1.1 cm) (p<0.0001). A logistic regression model identified tumour size as a strong predictor of PT. Factors such as BIRAD score, needle gauge, clinical presentation, and a history of breast cancer were not associated with an upgrade to PT.
Conclusion: Core biopsy demonstrates high sensitivity and specificity in the stratification of FELs of the breast. In cases of indeterminate core biopsies, relevant clinical factors, such as tumour size, may assist

in making informed decisions. Core biopsy is essential in preventing unnecessary surgical procedures for FELs.

E-PS-02-040

Assessment of tumour microenvironment in malignant phyllodes tumour by immunohistochemistry and the clinical pathological parameters association

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Background & Objectives: Phyllodes tumour (PT), a biphasic tumour with epithelial and stromal components, account for <1% of all breast neoplasms. A combination of histological features of the stromal component such as cellularity, overgrowth, mitoses, atypia & tumour borders determine the benign, borderline and malignant classification. These histological features do not always accurately predict tumour behaviour, affecting clinical management.
We studied the tumour microenvironment (TME) in malignant phyllodes tumour (MPTs) in relation to various clinicopathological parameters.
Methods: Immunohistochemistry was performed on tissue microarrays from 30 MPTs with CD3, CD20, CD4, CD8, CD138, CD163 and PD-L1(SP263), and numerical immune cell scores assigned accordingly for each category. Immune cell scores were compared to clinicopathological parameters, disease free survival (DFS), overall survival (OS) outcomes.
Results: Macrophage scores were significantly higher in MPT than in benign breast tissue ($p<0.001$). Higher macrophage scores correlated with increased stromal cellularity ($p=0.025$).
Patient age ranged from 15 to 79 years (median 43 years). CD3 and CD8 scores were significantly correlated with increased age ($p=0.035$ & $p=0.023$), while CD8 scores also correlated with presence of stromal heterologous elements ($p=0.046$). No significant correlation was found between immune cell scores and survival outcomes. There was no expression of PD-L1 in MPTs.
Conclusion: Tumour-associated macrophages (TAMs) are a heterogeneous group of macrophages with varied functions, and can facilitate tumour growth by immunosuppression, invasion & metastasis. The diversity of phenotypes is a critical factor in development of therapeutic resistance. The significant presence of TAMs in MPTs in our study may provide new avenues in the diagnosis and development of therapeutics in this challenging field.

E-PS-02-041

To assess the concordance of breast lesion size of patients in radiology ultrasound and breast mammograms with breast pathology specimens

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Background & Objectives: To ensure high level of concordance between the pathology breast specimen and imaging.
Methods: Data was collected from Shrewsbury and Telford NHS trust hospitals clinical portal system in the United Kingdom. The data that was reviewed included patient mammogram and radiology ultrasound breast lesion sizes. An individual patient's radiology index data was collected; this included a score from R1 to R5 as well as ultrasound score from U1 to U5. The size of the breast lesion was documented from both the ultrasound and mammogram data from clinical portal data system on an excel spreadsheet. Breast tumour lesion sizes were also obtained from the pathology reports (both microscopic and macroscopic) and were documented also on an excel spreadsheet.
Results: 76% of the datasets between radiology ultrasound and mammogram to the pathology analysis were concordant. Concordancy was assessed in relation to TNM staging. Of the 59 datasets collected, 14 patients had discordancy between radiology and pathology tumour sizes. Of these 14 patients that had discordant results, eight patients had lobular and multifocal carcinomas in the pathology samples. Three of the 14 patients had started neoadjuvant therapy and the remaining three patients had high grade ductal carcinoma. In the discordant data, 50% of patients that had multifocal, lobular cancers also had additional tumours that were detected in the pathology review. The time taken from imaging to surgery with the 14 patients that have discordant results was on average 1.5 months. All discordant data patients did not require further surgery- they were all followed up with chemotherapy or radiotherapy and hormonal based treatments.

Conclusion: This project will help to improve collaboration between pathology and radiology teams by ongoing multidisciplinary discussions for best patient care. The next steps are for pathologists to re-familiarise with the breast cancer dataset on measuring tumour sizes.

E-PS-02-043

Sarcomatoid metaplastic carcinoma or sarcoma: immunohistochemical analysis of CK-negative or -minimal positive sarcomatoid breast tumours

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Background & Objectives: Distinguishing sarcomatoid metaplastic breast carcinoma (MBC) from breast sarcoma is challenging, particularly when the tumour lacks evidence of epithelial differentiation. In this study, we investigated if the commonly used breast epithelial markers — GATA3, SOX10, and TRPS1 — could help resolve this diagnostic dilemma.
Methods: This study included 48 malignant sarcomatoid breast tumours with high-grade spindle or pleomorphic cells and no or minimal (<5%) expression of multiple cytokeratins (CKs). These tumours were divided into two groups. Group 1 included 19 cases with biphasic morphology, featuring both sarcomatoid and epithelial (IDC and/or DCIS) components. Group 2 included 29 cases without epithelial components, of which 14 had a history of invasive breast carcinoma (IBC) and radiation therapy, 15 had no IBC history. Immunohistochemical stains for GATA3 (Cell Marque, L50-823), SOX10 (Leica, clone 991), and TRPS1 (Zeta, ZR380) were performed, and staining intensity and percentage in sarcomatoid elements were assessed.
Results: In Group 1, all cases showed intermediate to high TRPS1 positivity. TRPS1 with GATA3 and/or SOX10 was observed in 10 cases. In Group 2, among the 14 cases with IBC and radiation history, 1 case was negative for the 3 markers. TRPS1 with GATA3 or SOX10 was observed in 9 cases, and TRPS1 alone was positive in 4 cases. Among the 15 cases without IBC history, 5 cases were negative for the 3 markers. TRPS1 along with GATA3 or SOX10 was observed in 5 cases, and TRPS1 alone was positive in 5 cases.
Conclusion: Our study found that while sarcomatoid MBC may lose common epithelial markers, TRPS1 expression is consistently retained in these tumours (Group 1). The absence of CK, TRPS1, GATA3, and SOX10 may suggest primary sarcoma or terminal sarcomatoid differentiation of MBC, while the presence of TRPS1 with GATA3 and/or SOX10 supports an epithelial origin, such as MBC, potentially even in radiation-induced cases.

E-PS-02-045

Fibromatosis of the breast: a 20-year institutional experience

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Background & Objectives: Fibromatosis of the breast represents a rare type of desmoid tumour and is characterised by a clonal fibroblast proliferation with an unpredictable clinical course. It represents only 0.2% of all breast tumours. It is a nonmalignant tumour that often resembles cancer in both its clinical presentation and radiologic imaging characteristics, posing unique diagnostic and management challenges. The aim was to review our institutional experience of breast fibromatosis, in the last 20 years.
Methods: A search of pathological databases within a tertiary institution for all patients diagnosed with fibromatosis of the breast over a 20-year period (2005–2025) was performed.
Results: Twelve patients were identified. Median age at diagnosis was 55 (range 24–74). There are 11 females and 1 male. The mean lesion size was 17.2 mm (between 50 and 5 mm). Radiologically they were considered BIRAD 4 lesions. In 10 cases the diagnosis was made by core needle biopsy. In two cases surgery was performed directly. The diagnosis was confirmed by immunohistochemical study of B-catenin with nuclear expression. Margins were positive in 8 cases. No recurrences have been observed with a follow-up in 10 patients between 20 and 1 year. Two patient had a history of infiltrating carcinoma.
Conclusion: Breast fibromatosis is a rare entity, clinically and radiologically mimicking breast cancer.
The differential diagnosis is broad and should be made with Scar, Nodular fasciitis, Dermatofibrosarcoma protuberans, Low grade fibromatosis-like metaplastic carcinoma, Myofibroblastoma and Benign phyllodes tumour.
Breast augmentation has been described as a risk factor for the development of breast fibromatosis, but has not been explicitly linked to cancer breast surgery.
A literature search showed that there have been only 9 reported cases of male breast fibromatosis
We have not confirmed the high recurrence rate in our series, as no recurrence was detected in the 8 cases with follow-up and affected edges.

E-PS-02-047
Impact of different CE-IVD IHC assays on HER2 status in breast cancer with focus on HER2-low and HER2-ultralow
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Background & Objectives: The European Medicines Agency (EMA) recently approved trastuzumab deruxtecan for treating patients with unresectable or metastatic HR-positive breast cancer (BC) that is HER2-low or HER2-ultralow. HER2 status should be determined using a CE-IVD-approved immunohistochemistry (IHC) assay. While staining differences among IHC-assays are well known, a direct comparison of the three main CE-IVD-approved assays is lacking. Additionally, previously published comparisons provide limited information on analytical performance due to post-analytical variability in the studies.
This study evaluates the analytical performance of three most frequently used CE-IVD-approved HER2 IHC-assays and their clinical implications for categorizing HER2-low and HER2-ultralow BC.
Methods: Two tissue microarrays (TMAs) were constructed for other quality control studies, including triple-negative and ductal BC. Serial sections, minimizing tumour heterogeneity, were stained with three CE-IVD approved IHC-assays: PATHWAY rmAb 4B5, 790-2991 (Ventana/Roche), HercepTest pAb, SK001 (Dako/Agilent) and HercepTest rmAb DG44, GE001 (Dako/Agilent). All BCs were scored as HER2 0, ultralow, 1+, 2+ or 3+. The amplification status was available for HER2 2+ cases based on fluorescence in situ hybridization of the original tissue.
Results: In total 109 BCs were analysed. A 97% concordance was observed across all three assays, classifying samples into the classical two groups: HER2 negative (0, ultralow, 1+, 2+ unamplified) and HER2 positive (3+, 2+ amplified). For HER2-low and HER2-ultralow a low inter-assay agreement was seen as the HER2 0 classification differed between assays: PATHWAY classified 34% (37 samples) as HER2 0, compared to 25% (27 samples) with HercepTest rmAb and 31% (34 samples) with HercepTest pAb.
Conclusion: This study shows strong concordance among the three IHC assays using the classical interpretation, which classifies BC as HER2 positive or negative. However, under the indication, where only HER2 0 patients are untreated, assay choice affects treatment decisions, with PATHWAY rmAb classifying more patients as HER2 0 compared to the two HercepTest assays.

E-PS-02-048
Undifferentiated pleomorphic sarcoma of the breast: a case report and review
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Background & Objectives: Undifferentiated pleomorphic sarcoma (UPS) of the breast is a rare tumour. Histologically, it is composed of pleomorphic cells with epithelioid and spindle cell morphology, histiocytoid features with vacuolated cytoplasm, and karyorrhectic giant cells. The tumour exhibits areas of necrosis and frequent mitotic activity. Due to its rarity, we present this case to contribute to the literature.
Methods: Examination included formalin fixation and paraffin embedding (FFPE) of the tumour tissue. Haematoxylin and eosin (H&E) staining was performed to evaluate cellular morphology, necrosis, and mitotic activity. Immunohistochemical staining was conducted using a panel of markers, including desmin, SMA, caldesmon, S100, myogenin, MYOD1, CD34, PanCK, CDK4, MDM2, HMB45, H3K27ME3, ALK, and CD30, to exclude other differential diagnoses and confirm the diagnosis of UPS.
Results: A 52-year-old female presented with a palpable mass in the left breast. Histological examination revealed pleomorphic cells with epithelioid and spindle morphology, frequent mitoses, and areas of necrosis. Immunohistochemical analysis was negative for desmin, SMA, caldesmon, S100, myogenin, MYOD1, CD34, PanCK, CDK4, MDM2, HMB45, H3K27ME3, ALK, and CD30. Based on these findings, a diagnosis of **undifferentiated pleomorphic sarcoma of the breast** was established.
Breast UPS is an extremely rare malignancy, with only a few cases reported in the literature. Cases have been observed in patients aged 22-76 years, with tumour sizes ranging from 1 to 17 cm. Most diagnoses occur within months of symptom onset. Our case involved a 52-year-old patient with a 7 cm tumour.
Conclusion: Undifferentiated pleomorphic sarcoma of the breast is a rare neoplasm that shares morphological similarities with UPS in other anatomical locations. Due to its rarity, further case reports are needed to better understand its behaviour and optimal management.

E-PS-02-049
Glycogen-rich carcinoma of the breast: a report of two new cases
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Background & Objectives: Glycogen-rich carcinoma (GRCC) of the breast is a rare histological variant (pattern) of invasive breast carcinoma of no special type. It is characterized by tumour cells with abundant, clear, glycogen-filled cytoplasm. Reported expression

levels of steroid receptors (Estrogen receptor/ER/ and progesterone receptor/PR/) and HER2 vary in the literature.
Methods: We present two new cases of GRCC in a 66-year-old and a 51-year-old patient.
Results: Both tumours displayed predominantly solid growth patterns with clear, PAS-positive/PAS-D-sensitive cells. In Case 1, the tumour had moderate cellular atypia with low mitotic activity (grade 2). Immunohistochemically, it was ER-positive, PR-negative, and HER2-positive (score 3+). In contrast, Case 2 showed high mitotic activity (grade 3) and was triple-negative (ER-negative, PR-negative) with a low HER2 phenotype (score 1+). Staging revealed pT1cN0 disease in Case 1 and pT2N0 in Case 2. Both patients underwent primary surgery with axillary dissection, followed by adjuvant systemic therapy. Case 1 also received anti-HER2 and endocrine treatments.
Conclusion: GRCC is heterogeneous in its clinical presentation and molecular features. However, its management predominantly depends on the tumour's pathological and molecular profiles. Further follow-up will be necessary to determine if this rare variant of invasive breast carcinoma demonstrates a distinct clinical course compared to other breast cancers.

E-PS-02-050
Mismatch repair protein expression in breast cancer
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Background & Objectives: Breast cancer (BCa) is the leading cause of cancer diagnosed in women. Multifactorial risk factors including increased body mass index (BMI), obesity, alcoholism, smoking and hyperoestrogenic states have been postulated. Mismatch repair (MMR) has been a causative germline alteration in several cancers. BCa exhibiting deficient-MMR (dMMR) often display unique molecular features and tend to have higher mutational burden, potentially influencing response to therapy. Few reports indicate that dMMR occurs in a small subset of BCa, with a prevalence of approximately 1-3%.
Objectives:

- To assess the prevalence of mismatch repair deficiency in patients with breast carcinoma
- To correlate mismatch repair deficiency with clinicopathological and molecular profile of breast carcinoma in Indian patients.

Methods: A total of 42 cases of histologically proven BCa were reviewed for histopathology, hormonal immunohistochemistry and socio-demographic variables were noted. MMR expression for all 4 MMR antibodies were studied.
Results: A total of 42 cases of invasive ductal carcinoma were analysed. All the patients were females and with a mean age of 47. Of the 42 cases, core biopsies were done in 36 cases, in 14 cases core biopsies were followed by modified radical mastectomy and in the other 6 cases, only modified radical mastectomy was done. Immunohistochemistry for hormonal profiling revealed that of those 42 cases, 2 cases were Luminal A, 18 cases were Luminal B, 13 cases were HER2 enriched and 9 cases were triple negative BCa. Simultaneously, immunohistochemistry for mismatch repair showed that PMS2 and MSH6 was deficient in 2 out of 42 cases.
Conclusion: MMR deficiency testing done in the Western population, are noted in about 1-3 % of cases in previous studies. In the present study, MMR deficiency was noted in 4.7 % cases, however, owing to limitation of small size, further studies are needed to assess the frequency of alteration of MMR system.

E-PS-02-052
Expression of SOX17 in triple negative breast carcinomas
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Background & Objectives: Triple-negative breast carcinoma (TNBC) is a heterogeneous group of tumours defined by the absence of oestrogen receptor and progesterone receptor expression, and HER2 overexpression. Diagnostic challenges often arise, particularly in metastatic settings, where differentiation from other malignancies is critical. PAX8, commonly used as a marker of müllerian origin, may be expressed in up to 40% of TNBCs depending on the clone, limiting its specificity. SOX17, a transcription factor recently proposed as a diagnostic marker, is expressed in a majority of endometrial and ovarian carcinomas, including mesonephric-like carcinoma. This study aimed to evaluate SOX17 expression in TNBC.
Methods: Tissue microarrays (TMAs) containing 308 TNBCs (triplicate 1 mm cores) were immunostained for SOX17, PAX8 (SP348) WT1 (6F-H2), GATA3 (L50-823), and TTF1 (SPT24) using standardized protocols and scored using a modified Allred scoring system. Tumours were classified histologically per WHO guidelines.
Results: SOX17 expression was identified in only 1 of 308 TNBCs (0.3%), limited to focal positivity (<5% of tumour cells, weak to moderate intensity). This tumour, classified as invasive carcinoma of no special type, also expressed GATA3 and WT1 but was negative for TTF1 and PAX8. Endothelial cells exhibited consistent SOX17 positivity, serving as an internal control. Interpretation of SOX17 was occasionally challenging, in distinguishing endothelial cells from neoplastic cells of spindle cell metaplastic carcinomas.
Conclusion: SOX17 is absent in 99.7% of TNBCs, supporting its utility as a discriminatory marker when differentiating TNBC from endometrial or tubo-ovarian carcinomas. In the appropriate clinical context, SOX17 expression may aid in identifying a non-mammary origin. However, interpretation requires caution, particularly in metaplastic carcinomas, and recognition of non-specific staining in endothelial cells is essential to validate immunostain adequacy.

E-PS-02-053
Beyond HER2 'Negative': Do We Need to Do More?
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Background & Objectives: Breast cancers are currently classified as HER2-positive or HER2-negative based on the evaluation of HER2 status using immunohistochemistry (IHC) and/or in situ hybridization (ISH). Recent clinical trials suggest that patients within the HER2-negative group (those with low or ultralow levels of expression) may benefit from HER2-targeted therapies. This study investigates whether HER2 subgroup classification changes when IHC is performed on multiple tumour blocks and/or metastatic lymph nodes.
Methods: Clinicopathological data from 74 breast cancer patients, initially scored as HER2 '0' per ASCO-CAP guidelines in their pathology reports, were retrieved. Patients with fewer than three formalin-fixed paraffin-embedded tumour blocks and those who received neoadjuvant therapy were excluded. HER2 IHC was performed on two additional tumour blocks and the largest metastatic lymph node (n=24) if present. The original HER2-stained slide and the newly stained additional slides were independently scored by three pathologists and categorized into subgroups based on HER2 expression levels.
Results: HER2 assessment on multiple blocks led to the reclassification of 9.5% (n=7) of cases as '1+' and 9.5% (n=7) as '2+,' requiring ISH. Additionally, within the '0' group, 31.1% (n=23) of cases could be

categorized as 'HER2-ultralow.' Testing the largest metastatic lymph node did not provide additional information beyond what was already obtained from analysing two additional primary tumour blocks.
Conclusion: Despite a limited sample size, reassessing HER2 on multiple tumour blocks led to a 19% reclassification rate from '0' to '1+' or '2+.' This suggests that evaluating more than one tumour block could improve the identification of patients eligible for HER2-directed therapies in the lower end of the HER2 expression spectrum.

E-PS-02-054

Expression of miR-21 and miR-127 in metastatic breast carcinoma, primary breast tumour, and normal breast tissue among patients from Tondo Medical Centre, Philippines

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Background & Objectives: Breast carcinoma is the most prevalent cancer in women globally and locally. Great strides have been made with regards to its treatment, however, there are still patients who succumbed to aggressive types of breast cancer (i.e. metastasizing breast carcinoma). This study aims to investigate the role of microRNAs (miRs) in metastatic and primary breast carcinoma, which may identify potential targets for therapy.
Methods: RNA was extracted from formalin-fixed, paraffin-embedded (FFPE) tissues of the primary breast tumour, normal breast tissue, and lymph node metastatic lesion among four (4) Tondo Medical Centre patients with breast carcinoma with lymph node metastasis. Expression of miR-21 and miR-127 was determined using reverse transcriptase and quantitative polymerase chain reaction (qRT-PCR). Cycle threshold (C_T) values were correlated with histopathologic data between the three groups.
Results: All four (4) patients, aged 43 to 63 years old, had primary breast carcinoma with Nottingham Histologic Score II. Tumour sizes ranged from 3.0 cm to 8.0 cm. Three of four primary tumours expressed miR-21. The primary tumour without miR-21 expression had the smallest tumour size (3.0 cm). All primary tumours did not express miR-127. One of four normal breast tissues expressed miR-21. Interestingly, this normal breast tissue had co-expression of miR-127 consistent with its tumour suppressor role. One of four metastatic (lymph node) lesions expressed miR-21. Of note, this patient had the most number of lymph node metastases (11 out of 13 or 84.62% positive). The remaining three only had 21.05% to 40% positive lymph node metastases. All four metastatic lesions were negative for miR-127.
Conclusion: The results suggest the role of miR-21 in promoting tumour growth and metastasis, which can be a potential target in the development of an alternative therapy. The possible tumour suppressor activity of miR-127 against miR-21 needs further investigation.

E-PS-02-055

A rare case of malignant melanoma masquerading as a breast tumour

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Background & Objectives: The histopathological diagnosis of malignant melanoma requires not only the fulfillment of morphological criteria: immunohistochemical and genetic analyses are also necessary in poorly differentiated cases. We report a case of melanoma with no Melan-A and HMB-45 immunoreactivity, extensively involving the breast parenchyma.
Methods: The radiologist reported a breast mass of 14 cm in diameter infiltrating most of the left breast and a lesion above the left clavicle of a 42-year-old woman. The lesion had radiologically sharp contours. A core needle biopsy was performed: histopathological examination showed a tumour consisting of enlarged tumour cells with irregular nuclei and prominent eosinophilic nucleoli in several foci, surrounded by myxoid stroma. The mitotic activity was moderate. Morphological findings raised the possibility of malignant melanoma, clear cell sarcoma and epitheloid malignant peripheral nerve sheath tumour (MPNST). Extended immunohistochemical analysis and additional molecular analysis have also been performed on formaline-fixed paraffin-embedded (FFPE) tissue blocks.
Results: Immunohistochemical analysis showed that tumour cells were strongly and diffusely positivity for vimentin, S100, PRAME and SOX-10 and focal expression of pan CK was also observed. The tumour was negative for ER-receptors, PR-receptors, HER2, Melan-A and HMB-45. Subsequent immunoreactions indicated negative, desmin and Myf-4 reactions. Neither BRAF (V600E) positivity nor INI1 deficiency were detected. Fluorescent in situ hybridization (FISH) was preformed to analyse the translocation of the EWSR1 gene: the lack of the translocation suggested the exclusion of clear cell sarcoma.
Conclusion: As no epidermal involvement was found after a comprehensive dermatological examination, further investigations are needed to determine the exact origin of this tumour. However, primary cutaneous dermal malignant melanoma is an acceptable diagnosis, and the preserved INI1 expression does not completely exclude or strengthens the diagnosis of MPNST.

E-PS-02-057

HER2-low status in invasive lobular carcinoma: a retrospective study at the Medical University of Vienna

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Background & Objectives: Invasive lobular breast cancer (ILC) diagnosis relies on morphological features like dyscohesive growth pattern, typically linked to bi-allelic CDH1 loss, which encodes for the cell-adhesion molecule E-Cadherin. Yet, similar morphology can arise from other genetic changes as well. This study examined the link between loss of E-Cadherin expression and HER2 expression in invasive lobular breast cancers, assessing their impact on DFS and OS.
Methods: We studied 162 patients, aged 32-87, diagnosed with primary invasive carcinoma with lobular morphology at the Medical University of Vienna between 2005-2012 over a 13- to 20-year follow-up. Diagnostics followed current WHO guidelines, with HER2 expression assessed per ASCO/CAP standards. E-Cadherin expression was evaluated via immunohistochemistry, according to current ESMO guidelines. Association between HER2, E-Cadherin expression and clinicopathological parameters was studied by chi^2 test. Disease-free survival (DFS) and overall survival (OS) were analysed using the log rank test, based on E-Cadherin and HER2 expression.

Results: E-Cadherin expression was absent in 106 (65.4%) tumours with lobular morphology. These tumours displayed a significantly higher expression of ER/PR and lower grade and pT stage ($p<0.05$). Ki67 proliferation rate was generally lower in E-Cadherin negative tumours, although not statistically significant ($p=0.1$). Low HER2 expression was more common in tumours with loss of E-Cadherin expression (60.9% vs. 39.1%), though not statistically significant ($p=0.293$). Low HER2 expression did not significantly affect DFS or OS, regardless of E-Cadherin expression.
Conclusion: We observed a trend toward increased incidence of low HER2 expression in breast carcinomas lacking E-Cadherin, without impacting DFS or OS in long term follow-up. Larger cohort studies are warranted to validate our results.

E-PS-02-058
Breast Desmoid Tumour: a retrospective study of 18 cases with review of the literature
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Background & Objectives: Breast desmoid tumour (BDT), also known as aggressive fibromatosis, is a rare benign myofibroblastic proliferation characterized by aggressive behaviour and a high recurrence rate. Its clinical presentation often mimics malignancy, and pathology represents the gold standard for diagnosis. A history of trauma or prior surgery is considered the main risk factor. The recommended treatment is wide local excision with clear margin. This study aims to analyse the histopathologic features, treatment approaches and essential differential diagnosis of this rare neoplasm.
Methods: We conducted a retrospective study of 18 cases of BDT diagnosed at Pathology department B over the past 20 years (2005-2025).
Results: The cohort consisted of 13 female patients, with a mean age of 50 years (range: 26–82 years). Most patients had no risk factors, although two had undergone prior procedures on the ipsilateral breast. The type of procedure performed included local excision for three patients, lumpectomy for seven patients and biopsy only was available for three patients.
Among patients who underwent surgery, five cases were purely intraparenchymal while four cases involved the chest wall. The margin status was positive in two cases, negative in six and close in two cases. Pre-operative biopsy was performed in seven cases, with three confirming the diagnoses of BDT. Three patients proceeded directly to surgery with no preoperative percutaneous biopsy.
BDT diagnosis was made by histology alone in two cases and with both histology and immunohistochemistry in 11 cases. Additionally, Cutaneous invasion was observed in two patient and one patient had bifocal BDT.
Conclusion: BDT is a rare neoplasm that predominantly affects females. The principal differential diagnosis includes fibromatosis-like metaplastic breast carcinoma, scar tissue, myofibroblastoma and nodular fasciitis. Immunohistochemical staining for beta-catenin in association with histological features is the key for diagnosis.

E-PS-02-059
Prognostic significance of ROR1, BMI-1 expression and PIK3CA mutation in luminal breast cancer
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Background & Objectives: Luminal breast cancer (BC), defined by hormone receptor expression, accounts for approximately 70% of all breast cancers. While endocrine therapy improves prognosis, a subset of patients experiences disease progression due to underlying molecular alterations. This study aimed to evaluate the prognostic relevance of ROR1 and BMI-1 protein expression (assessed by immunohistochemistry) and PIK3CA gene mutations (detected by PCR) in patients with luminal HER2-negative BC receiving aromatase inhibitors, with an emphasis on relapse-free survival (RFS).
Methods: The study included 80 postmenopausal women with primary operable luminal HER2-negative BC (T1-2N0-1M0) treated with surgery, radiotherapy, and adjuvant hormone therapy using aromatase inhibitors. Immunohistochemistry was performed to detect ROR1, BMI-1, and cyclin D1 expression in tumour tissues. PIK3CA mutation status was determined using real-time PCR. Statistical associations were analysed using Kaplan-Meier survival curves, χ^2 test, and Cox's F-test ($p<0.05$ considered significant).
Results: ROR1 and BMI-1 expression was observed in 57.5% and 82.5% of tumours, respectively. High expression of both markers was associated with the luminal B subtype. PIK3CA mutations were detected in 30% of cases and were significantly linked to reduced 5-year RFS ($p=0.03$). Cyclin D1 overexpression (in 37.5% of tumours) was strongly associated with ROR1 expression ($p=0.0003$). Co-expression of ROR1 and BMI-1 showed a trend toward more aggressive disease. BMI-1 expression was confirmed in all tumours from patients who experienced relapse.
Conclusion: ROR1 and BMI-1 protein expression, along with PIK3CA mutations, represent clinically relevant biomarkers in luminal BC. Their expression correlates with adverse features such as the luminal B subtype and disease progression. These findings support the integration of immunohistochemical and genetic profiling into clinical practice to enhance risk stratification and guide targeted treatment strategies. Future research should focus on combining PI3K inhibitors with endocrine therapy to overcome resistance and improve survival outcomes in hormone receptor-positive BC.

E-PS-02-060
Breast cancer with choriocarcinomatous differentiation: a case description and review of management and prognosis
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Background & Objectives: Breast cancer with choriocarcinomatous differentiation is an extremely rare variant, with only 16 cases reported by 2022, half of which are triple-negative. This subtype is characterized by elevated human chorionic gonadotropin (hCG) levels and presents clinically as a conventional breast carcinoma. Treatment usually involves complete surgical excision followed by chemotherapy, but there is no standardized protocol. The prognosis is poor, with survival often limited to a few months due to lymphatic and distant metastases. A key distinction in diagnosis is between primary invasive breast carcinoma with choriocarcinomatous differentiation and metastatic choriocarcinoma in the breast. The former has a poor response to chemotherapy, while the latter responds more favorably.
Methods: A case study of a 62-year-old woman diagnosed in 2021 with bilateral invasive ductal carcinoma (triple-negative, stage IV) is described. She underwent treatment, but in 2023, surgery revealed affected margins. Disease progression continued, and by 2024, her hCG levels rose to 46,714 mU/ml, with metastases in the lungs, liver, and axillary lymph nodes. She passed away the same year.
Results: We analysed 4 cylinders of breast mass with a whitish coloration and elastic consistency, measuring 0.1 cm in diameter,

and ranging in length from 1.4 cm (smallest) to 2 cm (largest). The diagnosis was grade 3 invasive ductal carcinoma with choriocarcinomatous differentiation (score 8: 3+3+2), with an intratumoral lymphocytic infiltrate of < 1%. Giant cells positive for immunohistochemical staining of hCG were identified in the tumour. Molecular study by NGS revealed the p.E542K variant of PIK3CA and the p.E286V variant of TP53.
Conclusion: This variant is characterized by highly atypical cancer cells resembling choriocarcinoma, mixed with epithelial or mesenchymal components. It presents as an aggressive, highly malignant ductal carcinoma with a very poor prognosis, leading to rapid metastases and early mortality. Surgery remains the primary treatment, though no effective chemotherapy regimen has been established.

E-PS-02-061
Primary angiosarcoma of the breast in a breastfeeding woman: a case report
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Background & Objectives: Primary angiosarcoma (PAS) is defined as a malignant primary endothelial neoplasm of the mammary parenchyma, not associated with radiation exposure. It is extremely rare, accounting for less than 0.05% of all primary malignancies of the breast. A pathologist plays a key role in diagnosis and in establishing prognosis by determining the histologic grade.
Methods: A 32-year-old breastfeeding woman presented with a palpable, soft, elastic, mobile left breast mass that had been enlarging for 4 months without axillary lymphadenopathy. She had given birth 8 months ago to a female, full-term newborn. She had no personal history of breast surgery, breast irradiation, long-term hormonal use and no family history of malignancy. Ultrasonography revealed a 6.5 cm lobulated hypoechoic formation in the upper lateral quadrant. Due to lactation and the overall heterogeneous echostructure of both breasts, the described formation was initially interpreted as a probably benign finding (BI-RADS 3). Cessation of lactation was proposed. A control examination after 2 months showed a 10 cm mass. Because of the significant enlargement, a core needle biopsy (CNB) of the mass and fine needle aspiration biopsy (FNAB) of the lymph node were performed.
Results: The case was diagnosed as grade 3 PAS without axillary metastasis. Microscopic examination revealed interanastomosing vascular channels filled with erythrocytes, lined with pleomorphic endothelial cells, with infiltrative growth through normal structures. There were punctate necrotic foci, blood lakes, and irregular mitoses. The tumour was positive for vimentin, CD31, CD34, and Factor VIII, negative for AE1/AE3, with Ki67 above 90%, and no detected C-MYC amplification or NTRK fusion. Radical mastectomy was performed, confirming our diagnosis (PAS, pT3N0). The patient underwent three cycles of Adriamycin chemotherapy and radiotherapy.
Conclusion: We report a case of PAS in a breastfeeding woman, with a full description of clinical manifestation, radiology, histology, next-generation sequencing results, and treatment.

E-PS-02-062
Metastatic lobular carcinoma identified within a uterine polyp and fallopian tubes, representing the initial presentation of a previously undiagnosed breast malignancy
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Background & Objectives: Metastatic breast carcinoma involving the female gynaecological system represents an uncommon pathology. A review of accessible PubMed data spanning 1983 and 2024 identified only 23 reported cases of breast cancer metastasizing to uterine polyps. Notably, most of these cases were associated with tamoxifen therapy and morphologically were compatible to lobular carcinoma.
Methods: This case describes a 52-year-old woman with no significant medical history who presented with menorrhagia and an ultrasound diagnosis of a uterine polyp. She underwent a total hysterectomy and bilateral salpingo-oophorectomy. Macroscopic examination identified a 5 mm intrauterine polyp, with no additional structural abnormalities observed in the uterine body, cervix, or adnexal structures. Tissue samples were subsequently reproduced and processed for histological evaluation in accordance to established laboratory protocols.
Results: Within the uterine polyp, against a background of mild fibrosis and interspersed partially atrophic endometrial glands, nests and cords of round atypical cells displaying hypochromatic nuclei and scarce mitotic activity were identified. Similar linear cords and scattered individual cellular elements were also observed bilaterally in the otherwise unaffected walls of the fallopian tubes. Immunohistochemical staining of the target cellular population revealed phenotypic characteristics, including diffuse positivity for CK7, GCDFP-15, GATA3, and ER, findings consistent with metastatic breast carcinoma. Clinical imaging conducted after the histopathological report confirmed the presence of a mass in the breast.
Conclusion: Given the potential for metastatic cells to infiltrate endometrial polyps as well as seemingly unaffected regions of the uterus, pathologists should perform a comprehensive examination to prevent diagnostic pitfalls.

E-PS-02-063
Radial danger: radial scars of the breast- a diagnostic and management dilemma and a university pathology department's 15-year experience
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Background & Objectives: Radial scars/complex sclerosing lesions (RSL) of the breast are benign lesions with glandular structures in fibroelastotic stroma, with or without proliferative epithelial changes. They often pose a radiology dilemma as they mimic breast carcinoma on imaging and induce controversial management strategies. We present a recent case of a radial scar diagnosed on a core needle biopsy, and the statistical analysis' results of diagnosed radial scars over a 15-year period in a University Pathology Department, to raise awareness.
Methods: A tru-cut needle biopsy of a suspicious lump in the left breast of a 44-year old female was performed, and the sample was sent to the Pathology laboratory for histopathological examination. Immunohistochemical stains were performed. We reviewed the histopathological reports of radial scars over a 15-year period and performed statistical analysis.
Results: The histopathological examination revealed lobulocentric architecture with dense hyalinized stroma and after the immunohistochemical evaluation the presence of myoepithelial cells was confirmed. The findings were consistent with radial scar of the breast.
The statistical analysis revealed that in 5 cases (38,5%)the radial scar was the only finding, 2 (15,3%) had concomitant ductal papillomatosis and intraductal papilloma, 3 (23%) had additional atypical ductal hyperplasia, 5 (38,5%) had DCIS and/or invasive ductal carcinoma (4 with negative lymph nodes and 1 with positive lymph nodes). There were two peaks in the incidence of radial scars, one on the 4th and the other on the 6th decade of life.
Conclusion: These lesions comprise both a possible histological and imaging pitfall. The histopathological evaluation may underestimate

atypical and malignant lesions, due to tissue size limitations and pathologists should be aware of the potential danger. As the management of radial scar and complex sclerosing lesion detected on mammography remains controversial, the need for more systematic and retrospective reviews, as well as patient long-term follow-up, becomes imperative.

E-PS-02-064

Spontaneous regression of invasive lobular carcinoma: a case report

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Background & Objectives: Spontaneous regression (SR) of oestrogen receptor (ER)-positive invasive lobular carcinoma (ILC) of the breast is an exceptionally rare phenomenon, with very few cases documented in the literature. The present study aims to report a case of SR in ER-positive ILC, potentially associated with hormonal therapy for endometriosis.

Methods: A 47-year-old woman, receiving progestin-based therapy for endometriosis, developed a parareolar breast mass associated with ipsilateral axillary lymphadenopathy. A core needle biopsy (CNB) confirmed ER-positive, progesterone receptor (PR)-positive, HER2-negative ILC, grade 2. Fine-needle aspiration cytology (FNAC) of an ipsilateral axillary lymph node was positive for carcinoma. The patient subsequently underwent quadrantectomy and axillary lymph node dissection.

Results: Histological examination of the surgical specimens revealed only minimal residual foci of ILC within the breast tissue, accompanied by marked lymphocytic infiltration. Axillary lymph node dissection identified necrotizing epithelioid granulomas and isolated tumour cells (ITCs) limited to the nodal capsule, without evidence of viable metastatic carcinoma.

Conclusion: The observed spontaneous regression may be associated with the hormonal therapy administered for endometriosis, which likely induced a hypoestrogenic state, potentially facilitating an immune-mediated response. Progestins' anti-estrogenic effects could have reduced oestrogen-mediated immunosuppression, enhancing immune recognition and clearance of tumour cells. The presence of necrotizing granulomas supports the hypothesis of immune activation. This case suggests a potential link between hormonal modulation and SR of ER-positive ILC, encouraging further studies on the interplay between endocrine therapy and immune mechanisms in breast cancer.

E-PS-02-065

Atypical myofibroblastoma in a young patient – case report

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Background & Objectives: Myofibroblastoma (MFB) of the breast is a rare, benign mesenchymal tumour composed of spindle cells with myofibroblastic differentiation. It belongs to the spectrum of benign spindle cell tumours and originates from hormonally responsive mammary stromal cells. Myofibroblastoma typically presents as a slow-growing, painless, non-tender mass. It is most commonly observed in older men (median age 60–70 years) and postmenopausal women.

Methods: A 19-year-old female patient presented for evaluation due to a tumour-like mass she had palpated in her left breast. Clinical and ultrasound examinations revealed a well-defined tumour with benign characteristics, most consistent with a fibroadenoma. However, histopathological findings from a core needle biopsy suggested a mesenchymal tumour classified as B4. A wide local excision of the left breast tumour was subsequently performed, and the specimen was sent for pathological examination.

Results: Macroscopic examination revealed a relatively well-defined, whitish tumour with a whorled structure, elastic consistency, and a glassy sheen, measuring 20 mm in diameter. Microscopic examination showed that the tumour consisted primarily of spindle-shaped cells, with large, pleomorphic atypical cells diffusely distributed among them, along with occasional multinucleated floret-like cells. Mitoses and necrosis were not observed. Immunohistochemical analysis demonstrated expression of CD34 in tumour cells, along with positivity for ER, PR, and AR, with an absence of Desmin expression. Based on histopathological and immunohistochemical findings, the tumour was classified as atypical myofibroblastoma.

Conclusion: Atypical myofibroblastomas are generally considered benign, with a low risk of recurrence or metastasis. However, due to their histological overlap with other mesenchymal neoplasms, accurate diagnosis is crucial to avoid overtreatment or misclassification as a more aggressive tumour. Surgical excision remains the standard treatment. This case highlights that even young women can develop this rare tumour, emphasizing the importance of considering myofibroblastoma in the differential diagnosis of breast masses in younger patients.

E-PS-02-066

Primary breast sarcomas: a 20-year experience

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Background & Objectives: Primary breast sarcomas are exceptionally rare, with an estimated incidence of 17 cases per million female patients per year. A limited number of published clinicopathologic series on these pathologies currently exist. We present an analysis of the pathologic characteristics of the cases of primary breast sarcomas examined in our Pathology Department over the prior 20-year period.

Methods: Pathology reports with a diagnosis of primary breast sarcoma were retrieved from our Department's files, from 2004 to 2024. Only complete reports and only excision specimens were included. All reports and tissue slides underwent a separate review from a different than the diagnosing pathologist. Subsequently, patient records were accessed to determine patient characteristics.

Results: In total, 13 patients were identified. All 13 (100%) were female. Median age at diagnosis was 70 years (IQR 21 years). The type of specimen was local excision for 6 patients (46.2%) and mastectomy for 7 patients (53.8%). The right breast was affected in 8 patients (61.5%), while the left breast in 5 patients (38.5%). Median maximal dimension of the tumour was 5.5 cm (IQR 6.25 cm). The histopathologic diagnosis was angiosarcoma in 5 cases, malignant fibrous histiocytoma in 2 cases, low-grade myofibroblastic sarcoma in 2 cases, well-differentiated liposarcoma in 1 case, leiomyosarcoma in 1 case, stromal sarcoma NOS in 1 case and sarcoma NOS in 1 case. Additional variables were also measured and analysed.

Conclusion: Primary breast sarcomas are rare, with the understanding of their characteristics, epidemiology and management stemming mainly from case series of major cancer centres. Their management is challenging. Our study extends the available literature and enhances the knowledge surrounding these rare pathologies.

E-PS-02-067

A case report of a rare type of biphasic breast lesion

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Background & Objectives: Periductal stromal tumour (PDST) is a biphasic fibroepithelial lesion: the periductal spindle-cell stroma and the lacking leaf-like architecture of the epithelial component distinguish it from phyllodes tumours. In cases of incomplete resection recurrence can occur, and beyond, sarcomatoid transformation has also been detected in low number of cases. We present a 30-year-old woman with a 16 mm lobulated lesion in the left breast with uncertain radiologic dignity. The histological diagnosis based on ultrasound-guided core needle biopsy.
Methods: Formalin-fixed paraffin-embedded (FFPE) tissue blocks were prepared from biopsies followed by haematoxylin-eosin staining and immunohistochemistry (IHC).
Results: Microscopic examination showed a fibroepithelial proliferation with stromal spindle-cell hypercellularity around the breast ducts. The abscence of the epithelial leaf-like growth-pattern was characteristic. The immunohistochemical reactions showed positivity for both smooth muscle actin (SMA) and CD34. The nuclear negativity of β-catenin excluded the possibility of fibromatosis. The immunoreactivity against desmin was also negative. The proliferation activity of the stromal cells presented less than 1% (Ki-67). The CK14- and p63-positivity supported the integrity of the myoepithelial cell layer.
Conclusion: The PDST of the breast is a rare biphasic entity accounting for less than 1% of breast carcinomas. The negativity for β-catenin excluded the possibility of fibromatosis. We suggested complete removal with wide surgical margins to avoid the local recurrence and potential malignant transformation. Additional IHC examinations are in progress to investigate further breast tumour-related markers. Presentation of this case indicates that PDST should be kept in mind as a differential diagnosis of biphasic stromal-predominant lesions.

E-PS-02-068

Siglec-15 expression in breast cancer and its association with clinical and pathological features

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Background & Objectives: Immune checkpoint blockade with PD-1/PD-L1 has limited success in breast cancer (BC) patients, partly due to alternative immune checkpoint molecules. Sialic acid–binding immunoglobulin-type lectins (Siglecs), expressed on immune cells, are potential new targets for immunotherapy. Siglec-15, a member of the Siglecs family, has been reported to be expressed in in lung and gastric cancer, but its expression in BC remains unclear.
Methods: Siglec-15 expression was evaluated in 88 invasive BC samples on tumour tissue microarray (TMA) using immunohistochemistry with anti-Siglec-15 antibody (PA5-72765, Thermo Fisher Scientific, USA, 1:200). Staining intensity was categorized as negative, weak, or moderate to strong. Siglec-15 expression was correlated with patient clinical (age, neoadjuvant chemotherapy) and pathological (tumour biomarker status, histology grade, stage, and lymph node status) features.
Results: Siglec-15 was expressed in 82.9% (77/82) of BC samples. Its intensity was not influenced by patient age or neoadjuvant chemotherapy. Moderate to strong staining was more common in ER+/HER2- tumours (64.6%) compared to ER-/HER2- tumours (11.7%) (p=0.0004) and in grade 1 and grade 2 tumours (66.7% and 65.2%) compared to grade 3 tumours (27.2%) (p=0.013). For pT1 and pT2 tumours, there was no significant difference in moderate to strong staining (52.8% vs. 60%), but pT1 tumours had fewer negative stains (5.5%) and more weak stains (41.7%) than pT2 tumours (23.3% negative and 16.7% weak staining) (p=0.026). Siglec-15 intensity was not associated with lymph node stage.
Conclusion: Siglec-15 is widely expressed in invasive BC, particularly in ER+/HER2- and lower-grade tumours. Further studies with larger cohorts are needed to confirm these findings and assess the potential of Siglec-15 as an immunotherapy target.

E-PS-02-069

Clinicopathological characteristics of HER2-low breast cancer in Latvia: a single centre experience

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Background & Objectives: HER2-low breast cancer (BC) was defined as those with a HER2 immunohistochemical (IHC) score of 1 + or 2 + without ERBB2 amplification in most of clinical trials. Previous studies showed that immunohistochemical HER-2 (2+score) expression combined with a negative HER-2 status on in situ hybridization was found to be an adverse prognostic factor. The aim of our study was to evaluate the clinical and histopathological characteristics in patients with HER-2 low breast cancer (IHC 2+score).
Methods: 98 patients undergoing core needle biopsy of BC in 2023-2024 in Riga East University Hospital with subsequent histopathological examination were enrolled in the study. Histopathological, immunohistochemical and chromogenic in situ hybridisation (CISH) examination was performed.
Results: 98 patients with breast cancer with IHC 2+ score HER-2 expression were enrolled in the study. The median patient age was 66 ± 12.54 years. The positive ER expression (>10.0%) was observed in 86.59% of cases, whereas the positive PR expression was observed in 72.16% of cases. The median Ki-67 index was 25 ± 24. 10%. In 62.88% of cases these tumours were Grade 2 tumours, whereas Grade 3 tumours were found in 16.49 % of cases.
The association between the tumour Grade, Ki-67 and immunohistochemical HER-2- (2+) expression have not been found.
Conclusion: In this study, HER2-low BC accounted for 94.9% of all tumours, with the vast majority (86.59%) being hormone (HR) positive.
Our data showed the complex characteristics of HER2-low BC, to which HR status is closely related, however associations between IHC 2+ score HER-2 expression and patient age, tumour grade and Ki-67 index has not been observed.

E-PS-02-070

Integrated analysis of triple-positive breast cancer: BC360-based PAM50 transcriptomic profiling, *FGFR1–4* expression and genomic characterization with clinico-pathological correlation

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Background & Objectives: Triple-positive breast carcinoma (TPBC; ER+/PR+/HER2+) represents a biologically diverse subset of breast cancer that often eludes precise therapeutic stratification. This study aimed to characterize TPBC through an integrated clinico-pathological assessment, BC360-based PAM50 transcriptomic profiling, and comprehensive FGFR1–4 analysis at the proteomic, transcriptomic, and genomic levels.
Methods: A total of 134 patients with treatment-naïve invasive breast carcinoma of no special type, diagnosed between 2012 and 2021, were retrospectively recruited. Pathological samples were reviewed per current WHO criteria, and clinical data were collected. IHC was used to assess ER, PR, HER2, and FGFR1–4 expression in FFPE tissue. Transcriptomic profiling of 121 tumours was performed using the NanoString® BC360™ panel for PAM50 subtyping, *FGFR1–4* mRNA quantification, and pathway signature analysis. Additionally, *FGFR1–4* were NGS-sequenced using a QIAseq targeted DNA/RNA custom panel (Qiagen) on the Illumina platform.
Results: Among 134 tumours, 38 (28.4%) were classified as TPBC. PAM50 subtyping revealed marked heterogeneity, with TPBCs distributed across luminal A (50%), luminal B (23.7%), and HER2-enriched (26.3%) subtypes. HER2-enriched and luminal B tumours were associated with higher histological grade, increased proliferation (Ki-67), and inferior disease-free and overall survival comparing to luminal A tumours. *FGFR1–4* mRNA and protein expression varied significantly across subtypes: FGFR4 was most prominent in HER2-enriched tumours, whereas FGFR1 expression was more abundant in luminal A/B subtypes. Transcriptomic analysis via BC360 revealed several distinct molecular signature profiles in TPBC compared to other immunophenotypes. Targeted NGS of *FGFR1–4* was successfully completed in all TPBC cases with data being analysed.
Conclusion: Triple-positive breast cancer is molecularly heterogeneous and cannot be fully defined by immunophenotype alone. Integrating PAM50 subtyping with FGFR1–4 protein and genomic profiling identifies prognostically and therapeutically relevant subgroups. These results support routine molecular testing, especially PAM50, to guide proper stratification and personalized treatment in TPBC.

Funding: This research was funded by: 1) The Polish National Science Centre grants PRELUDIUM no. 2018/29/N/NZ4/02384 (to MB), OPUS no. 2020/39/B/NZ4/02696 (to HMR), and Sonata Bis no. UMO-2018/30/E/NZ3/00222 (to RS); 2) The National Centre for Research and Development grant LIDER no. 0188/L-13/2022 (to MB); 3) The Medical University of Lodz Rector's scientific grant within the BRaIn Internal Grant Program no. 503/1-034-03/503-90-105 (to MB); 4) The Polish Ministry for Science and Higher Education "Perly Nauki" Grant no. PN/01/0017/2022 (to AZ)

E-PS-02-071

Validation of a triple negative breast cancer patient stratification strategy for neoadjuvant chemotherapy utilizing FOXC1 immunohistochemistry

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Background & Objectives: Neoadjuvant chemotherapy (NACT) in the setting of early-stage triple negative breast cancer (TNBC) to obtain pathologic complete response (pCR) is accepted standard of care. However, there is currently no effective patient stratification strategy (PSS) to determine predicted responders (PR)/non-responders (PNR) to NACT in TNBC.
Methods: TNBC patient samples from a NACT trial NKI dataset (n=178) was analysed for FOXC1 (plasticity marker) and MKI67 (proliferation marker) RNA expression values, correlated with observed pCR and used to develop an AI-enabled prediction algorithm using an iterative knowledge-driven engine. For the validation study, real-world TNBC patients (n=40) who had undergone NACT treatment at Tata Medical Centre (TMC) Kolkata were identified from the breast cancer database and FOXC1 immunohistochemistry (IHC) was performed using the VERESCA FOXC1 CE-Marked kit (Onconostic Technologies, Inc.) using validated protocols already reported (ECP 2024) along with standard MIB1 Ki67 IHC on the patients' pre-treatment core needle biopsy FFPE tissues on a Leica Bond III auto-stainer. The proprietary AI-enabled algorithm developed using the training dataset was then tested using the validation dataset.
Results: PNR as well as 2 categories of PR (moderate + high) were correctly predicted on the basis of FOXC1 and MKI67 expression values in both the training (Sensitivity 97% overall, $p<0.0001$ high PR group) and validation (Sensitivity 85% overall, $p<0.024$ high PR group) datasets with a high level of accuracy, regardless of whether RNA or protein expression were utilized as data inputs.
Conclusion: Routine IHC detection of FOXC1 utilizing the VERESCA FOXC1 kit affords a highly cost-effective PSS when considering NACT in early-stage TNBC. In conjunction with the VERESCA FOXC1 test's predictive utility for neoadjuvant chemoimmunotherapy (ESMO IO 2022), the test presents a pragmatic approach to achieve Precision Oncology goals in early-stage TNBC for both PR and PNR patients to either chemotherapy or chemoimmunotherapy regimens.

E-PS-02-072

Unmasking the unusual: metastatic malignant peripheral nerve sheath tumour, Ewing sarcoma, and melanoma to the breast

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Background & Objectives: Metastasis to the breast from extramammary malignancies is a rare occurrence, making up only a small fraction, just 0.5-5% of all malignant breast lesions. Melanoma is recognized as one of the most common neoplasms metastasizing to the breast, in contrast with Ewing sarcoma and malignant peripheral nerve sheath tumour (MPNST), which are exceedingly uncommon in this setting. We report three cases, one of metastatic MPNST, one of Ewing sarcoma and one of melanoma as metastases to the breast, the diagnoses of which were confirmed through histopathology and immunohistochemistry.
Methods: All three patients had undergone initial surgical treatment for their primary respective malignancies. Approximately 12-24 months following their surgical treatment, during screening mammography, the three patients' imaging findings indicated a breast mass. The differential diagnosis led to the dilemma of a primary breast malignancy versus a metastasis, based on their patient history, and warranted breast biopsy samples for further evaluation.
Results: All patients were female, with ages of 20 - 68 years. The tumour size ranged from 2.2 - 15.5 cm. One patient underwent simple mastectomy and two patients were treated with local excision. The excision specimens were analysed by the Pathology team, which confirmed the final diagnoses of metastatic Ewing sarcoma, melanoma and malignant peripheral nerve sheath tumour (MPNST) to the breast.

Conclusion: Metastases to the breast are rare. These entities have the ability to radiographically mimic primary breast carcinoma but also cause differential diagnostic challenges in pathologic examination. Performing clinicopathologic correlation and providing a complete patient history are of utmost importance, so that misdiagnosis and inappropriate management can be avoided.

E-PS-02-073

Prognostic significance of fibrosis in the tumour stroma in triple negative breast carcinoma

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Background & Objectives: Breast carcinoma continues to be the most common cancer and cause of death in women worldwide. Tumour microenvironment is an important pathological finding in all known solid cancers, both in terms of prognostic and treatment options. Stromal fibrosis is responsible for the treatment resistance of tumour cells by preventing oxygen circulation and drug transport around the tumour. Our aim in this study is to evaluate the relationship between fibrosis and histopathological findings in triple negative breast carcinomas.
Methods: Our study included 27 cases who were operated on for breast carcinoma between 2018-2025. Masson-Trichrome histochemistry was applied tumour-containing blocs. For each case, fibrosis was recorded as diffuse or focal. The largest fibrotic focus size was measured. The relationship between the extent of fibrosis and histopathological data was investigated. SPSS IBM 21.0 was used for statistical analysis.
Results: When the fibrosis size threshold value was taken as 15 mm, a significant difference was found between tumour size, age, and Ki-67 proliferation index values. Patients were younger in the fibrosis >15 mm group ($p<0.05$), tumour size was larger in the fibrosis>15 mm group ($p<0.05$), Ki-67 proliferation index was lower in the fibrosis>15 mm group ($p<0.05$). Since most of the cases had high nuclear and tumour grades, no statistical difference was found between these findings.
Conclusion: The tumour microenvironment is a wide area of research that also affects the treatment of the disease. Triple negative breast carcinoma is also in a poor prognostic group. We believe that the presence of fibrosis, which can affect the treatment process and prognosis of the disease and is quite easy to evaluate histopathologically, can be more clearly demonstrated with studies conducted with a larger number of cases.

E-PS-02-075

Idiopathic granulomatous mastitis: from aetiology toward therapeutic approaches

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Background & Objectives: Idiopathic granulomatous mastitis (IGM) is an evolving problem with no definitive treatment guidelines. Its pathogenesis is thought to involve ductal pathology. Excision of the sinus or fistulous tract, combined with lesion's wide local excision (WLE), may provide a curative approach.
The objective was to explore the underlying aetiology of IGM and assess the effectiveness of WLE with total or partial duct excision as a treatment modality.
Methods: Retrospective study conducted over four years (2021–2023) at a single institution, involving 13 patients diagnosed with IGM. The patients were divided into three groups : Group A received steroid therapy, Group B underwent WLE alone and Group C received WLE with total or partial duct excision.
Preoperative investigations were conducted, and postoperative follow-up ranged from 6 months to 2 years. Histopathological examination (HPE) of excised tissue was performed to confirm the diagnosis and assess the nature of the disease.
Results: HPE was identified as the most reliable diagnostic tool for confirming IGM. The results demonstrated varying recurrence rates across the groups: Group B (WLE alone) had the highest recurrence rate (76.3%). Group A (steroid therapy) had a recurrence rate of 39%. Group C (WLE with duct excision) had the lowest recurrence rate (4.6%).
Statistical analysis showed that patients in Group C had a significantly lower chance of recurrence compared to both Group A and Group B ($p < 0.05$). HPE of excised ducts from patients in Group C revealed ductal disruption, leakage, and periductal granulomas in 70% of cases.
Conclusion: IGM is primarily a disease of the mammary ducts. WLE combined with total or partial duct excision is an effective and curative approach for patients who do not respond to steroid therapy or WLE alone. This approach should be considered a viable treatment option for non-responding IGM cases.

E-PS-02-076

Primary mucinous cystadenocarcinoma of the breast with coexisting invasive ductal carcinoma: a case report and literature review

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Background & Objectives: Mucinous cystadenocarcinoma (MCA) of the breast is an exceptionally rare subtype of primary breast carcinoma, newly recognized in the WHO 5th edition classification. Due to its extreme rarity and histological resemblance to mucinous tumours of the ovary and pancreas, distinguishing MCA from metastatic disease is crucial for accurate diagnosis. We reported a rare case of primary breast MCA with an adjacent microscopic focus of invasive ductal carcinoma (IDC), highlighting its diagnostic, histopathological, and immunophenotypic features. Additionally, we compare our case with previously reported cases to contribute to the limited literature on this entity.
Methods: 76-year-old woman presented with mass in the left breast. MRI revealed a 30×25 mm multilocular, predominantly cystic BI-RADS 4A lesion. Core needle biopsy suggested "at least high-grade ductal carcinoma in situ (DCIS)." Patient underwent breast-conserving surgery and sentinel lymph node biopsy; no metastasis was detected intraoperatively. Gross examination revealed a 3.5 cm, mucin-rich, heterogeneous mass. Histopathological analysis demonstrated cystic structures with papillary projections lined by columnar mucinous epithelium, consistent with MCA, adjacent to a microscopic IDC focus. Immunohistochemical analysis was performed to further characterize the tumour.
Results: The MCA component was quadruple-negative with a Ki-67 index of 5–10%. IDC area exhibited weak ER positivity, PR negativity, AR positivity, HER2 0, and a Ki-67 index of 10–15%. No lymph node metastasis was detected. At the 6-month follow-up, the patient remained disease-free.
Conclusion: Despite its quadruple-negative phenotype, MCA appears to follow an indolent clinical course. The coexistence of IDC with distinct receptor status suggests potential divergent differentiation, raising questions about the tumour's histogenesis and biological behaviour. Given its rarity, this case underscores the importance of thorough histopathological and immunohistochemical evaluation to differentiate primary breast MCA from metastatic mucinous tumours. Our findings add to the limited knowledge surrounding this rare entity and highlight the need for further research.

E-PS-02-077

Comparative study of the Nottingham Prognostic Index (NPI) in breast cancer patients at a public hospital in southern Brazil

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Background & Objectives: Breast cancer treatment relies on prognostic tools. In Brazil, women treated in the public system have limited access to expensive tests. Low-cost methods, such as the Nottingham Prognostic Index (NPI), may be promising. This study evaluates the application of the NPI, aiming to classify prognostic subgroups with variables.
Methods: Cross-sectional study to analyse the prognostic profile of women with breast cancer in a public hospital between 2020 and 2021. The variables were: age, size, lymph node metastasis, histological grade and immunophenotypic subtypes. Ages were grouped into three categories, and the NPI was calculated.
Results: G1: 14 patients aged between 18 and 49 years, G2: 28 aged between 50 and 69 years and G3: 5 aged 70 years or older. G2 had lower NPI and mean tumour size. 17.02% were histological grade I, 42.55% II and 40.43% III. The mean NPI of patients without lymph node metastasis was 3.66, and that of patients with metastasis was 5.07 (NPImín) and 6.07 (NPImax). Based on Todd et al, 1987, the NPI was subdivided into three prognostic groups, with overall survival rates at five years: good, intermediate and poor. In the sample, 9 patients were classified as having a good prognosis (NPI $\leq$ 3.4), 28 as intermediate (NPI $>$ 3.4 and $\leq$ 5.4) and 10 as poor (NPI $>$ 5.4). Of the sample, 5 were of the Luminal A subtype (10.64%) and 22 were of the Luminal B/HER2- subtype (46.81%), with the Luminal A and Luminal B/HER2- subtypes presenting lower mean NPI values, demonstrating a more favourable prognosis in relation to the other subtypes.
Conclusion: The main findings indicated that the NPI has good prognostic capacity in HR-positive/HER2-negative immunophenotypes. Patients undergoing mammographic screening had better prognoses. The robustness of the NPI in different populations was identified, as well as its importance as a low-cost tool applicable in clinical practice.

E-PS-02-078

Prevalence and reproducibility of HER2 immunohistochemistry scoring in breast cancer: insights from a Portuguese tertiary healthcare institution

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Background & Objectives: With the rise of new therapeutic schemes for metastatic breast cancer (BC) patients, accurate evaluation and correct categorization of HER2 status gains further clinical relevance, specifically for HER2-low and HER2-ultralow groups. Our main goal is to characterize the distribution of different HER2 groups, in all BC biopsies registered over a year, in a tertiary centre in Portugal, with additional re-evaluation of HER2 immunohistochemistry (IHC) scores 0 and 1+ to determine the reproducibility of results.
Methods: Pathology reports of 155 BC biopsies, registered from January 2nd to December 31st 2024, were analysed, HER2 IHC scores were extracted and its distribution was established. Re-evaluation of HER2 IHC scores 0 and 1+ was undertaken, using the ASCO/CAP 2018 guidelines, while keeping in mind the extended therapeutic eligibility criteria, allowing comparison between previously recorded scores and re-evaluated scores.
Results: Previously recorded cases with HER2 IHC scores 0, 1+, 2+ and 3+ prevalence was 47% (n=72), 21% (n=33), 18% (n=28) and 14% (n=22), respectively. Re-evaluated HER2 IHC scores 0, 1+, 2+ and 3+ prevalence was 45% (n=70), 20% (n=30), 21% (n=33) and 14% (n=22), respectively. Concordance rates were significantly higher for the HER2 0 group (87.5%) than for the HER2 1+ group (57.6%); particularly, the re-evaluation of HER2 IHC 0 cases allowed the identification of 9 additional HER2 IHC 1+ cases (HER2-low) and 14 HER2 IHC>0 <1 (HER2-ultralow); re-evaluated HER2 IHC 1+ cases revealed additional discrepancies with previous scores, leading to 5 "newly" identified HER2 IHC +2 cases and another 7 cases as HER2 IHC>0 <1 (HER2-ultralow).
Conclusion: Despite the relatively limited number of cases included in our study and considering clinical management implications, initial results indicate that reproducibility of results need to be improved through different strategies, such as HER2 scoring training or consensus meetings. Further analysis is being performed to determine inter-observer reproducibility.

E-PS-02-079

Accuracy of cytological assessment in detecting HER2-low status in primary and metastatic breast carcinoma

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Background & Objectives: HER2-low breast cancer nowadays is a significant clinical subtype that expanded therapeutical options, especially with the introduction of anti-HER2 antibody–drug conjugates. Fine-needle aspiration cytology (FNAC) is a minimally invasive technique useful when core needle biopsy (CNB) is not a possible choice. The aim of this study is to assess accuracy of HER2-low status detection from cell blocks (CBs) obtained through FNAC, in comparison to the respective histological specimens.
Methods: We selected 46 cases of invasive breast carcinoma diagnosed via FNAC at Vanvitelli Hospital and we collected data related to evaluation of immunocytochemistry (ICC) analysis for oestrogen receptor (ER), progesterone receptor (PR), and HER2 on FNAC-derived CBs. Then, we compared evaluation with the assessment of corresponding histological specimens. For case with HER2-2+ evaluation we performed a fluorescence in situ hybridization (FISH). Finally, we calculated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), and we evaluated diagnostic accuracy through ROC curve analysis.
Results: The 46 examined cases show the following data: average age: 62 years, 73.9% was primary breast carcinoma, while 26.1% was metastatic cases.
The ICC and IHC results showed a strong agreement for ER (Cohen's K: 0.81) and a moderate agreement for PR (K: 0.51). Regarding to HER2-low cases (1+ or 2+ without amplification), ICC demonstrated high specificity (92.9%) and PPV (95%), with moderate sensitivity (59.4%) and NPV (50%). The ROC analysis produced an AUC of 0.76, indicating good diagnostic accuracy.
Conclusion: FNAC-derived CBs represent a valid alternative to histological samples in the assessment of HER2-low breast cancer, particularly when CNB is not available. While a positive ICC result (1+ or 2+) is highly predictive of HER2-low status, a negative result (0) may warrant

further investigation due to moderate sensitivity. Cytological evaluation can support therapeutic decision-making in selected clinical contexts.

E-PS-02-080

Solid-basaloid adenoid cystic carcinoma of the breast: TRPS1 expression and clinicopathological findings in two cases

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Background & Objectives: Adenoid cystic carcinoma (ACC) of the breast is a rare malignancy, accounting for <0.1% of invasive breast neoplasms. The rare solid-basaloid (SB) pattern, first described in 2002, has been recently evaluated for TRPS1 expression, a new histochemical marker of breast origin. This study reviews clinicopathological features of ACC-SB cases diagnosed in our institution.
Methods: We review all pathological reports of ACCs of the breast, recorded in our institution since 2005. The inclusion criteria were the presence of a reported triple-negative invasive carcinoma with a solid-basaloid pattern in biopsy, with more than 90% SB pattern in the gross specimen and in which other differential diagnosis had been excluded (namely small cell carcinoma). The clinical data was reviewed, histological slides reassessed, and TRPS1 expression evaluated.
Results: Among 12 ACC codified cases in system, two met SB criteria (16.7%).
Both females with a median age of 85 years (range: 82 - 89); had a solitary lesion on their left breast.
Biopsies showed an invasive carcinoma composed of basaloid cells with scant cytoplasm, with focal nucleoli in one case, no necrosis and 2 mitosis/mm^2.
The surgical specimens revealed tumours with 30 and 75mm in highest dimension, yellow, firm and spiculated. Histologically, extensive vascular invasions were present in both cases, as well as an increased mitotic activity when compared to the biopsy (2 versus 7 -18 mitoses/mm^2). One patient had lymph node metastasis.
Both tumours were triple negative; TRPS-1 diffusely strong positive; synaptophysin and INSM-1 negative.
Conclusion: ACC-SB is a rare invasive breast carcinoma requiring immunohistochemistry for differential diagnosis. Consistent with literature, our cases showed 100% TRPS1 positivity and no neuroendocrine marker expression.
Due to the low number of reported cases in series, the prognosis for SB remains unclear, with divergent findings in literature. In our cases, there was no disease progression at six-month follow-up.

E-PS-02-081

The impact of the COVID-19 pandemic on the diagnosis of breast cancer in a public reference hospital in southern Brazil

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Background & Objectives: The COVID-19 pandemic has had a devastating effect on the world population, especially for patients with chronic diseases. One of the most affected groups was cancer patients, because due to the restrictions and cancellations of elective surgeries and exams, considered as non-priority care. In response to the efforts directed to the care of patients at high risk of morbidity and mortality related to COVID-19 infection, there was a decrease in care considered non-emergency. During this devastating scenario of the year 2020, cancer has not changed the prevalence, and despite the pandemic the disease continued to exist. Breast cancer, the high incidence among women in Brazil, represented a strong financial impact on public health systems.
Methods: The aim of the study was to evaluate the relationship between the effect of the Covid-19 pandemic on the diagnosis of breast carcinoma in the population treated at a public hospital, comparing the years 2019 (pre-pandemic) with the year 2020 and the year 2021, after implementation of vaccination of the adult population.
Results: Variables extracted from the SISMAMA program "cancer information system", available on the Ministry of Health platform online, were categorized and coded and included gender, age, benign x malignant diagnosis. The frequencies were calculated. In the triennium (2019-2021), 1,091 patients were treated for the investigation or treatment of breast lesions. Of these, 882 were biopsies in women over 18 years of age, 293 cases of cancer, divided into 130 diagnoses in 2019, 75 in 2020 and 88 cases in 2021.
Conclusion: It can be concluded with the number of biopsies in 2019 (pre-pandemic) compared to the years 2020 (pandemic) and 2021 (vaccine era) had a significant reduction in the number by up to 33% and that the number of malignancy diagnoses had a reduction of up to 42% of cases between 2021 compared to 2020.

E-PS-02-082

Importance of ER, PR, HER2, Ki67, CK19, CD8 and PD-L1 biomarkers for diagnosis, prognosis and assessment of metastasis risk in patients with breast carcinoma

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Background & Objectives: Breast cancer (BC) has a high incidence among women worldwide. Metastatic disease is the leading cause of death, and one of the main causes of metastasis is dormant cells in the circulation. There is evidence that these cells develop mechanisms to escape the host immune response; therefore, they are associated with more aggressive immunophenotypes of the disease. Subtypes with worse prognosis also express some proteins related to the immune response, such as PD-L1. Therefore, understanding the associations between parameters and protein expression products is essential to establish alternatives that aid in the diagnosis and treatment of BC. Protein expression products have gained prominence in BC research, but the associations of these biomarkers have not yet been investigated.
Methods: To evaluate the importance of the joint analysis of the biomarkers ER, PR, HER2, Ki67, CK19, CD8, PD1, CTLA-4 and PD-L1 for the diagnosis, prognosis and assessment of the risk of metastasis in patients with breast carcinoma. The biomarkers were studied by flow cytometry or immunohistochemistry (IHC) methodologies.
Results: PDL1 by IHC was associated with subtypes with worse prognosis. Of all leukocytes present in peripheral blood, GD T lymphocytes were reduced in samples with CDI. There was a decrease in NKT cells and a decrease in the proportion of CD4/CD8 T lymphocytes in histological samples. The population of DN T lymphocytes is slightly increased in the luminal A subtype and increases in the HER2 and TBNC subtypes. TCD4 and TCD8 lymphocytes in the peripheral blood of patients with BC showed increased expression of the biomarkers CTLA4 and PD1 compared to the control. Regarding the investigation of circulating tumour cells (CTC), they were detected in 6.38% of cases.
Conclusion: This investigation shows the importance of joint assessment of biomarkers and the ability of flow cytometry to detect CTC safely and quickly for monitoring BC.

E-PS-02-083

Tubular adenosis of the breast: a case series with radiological/ pathological correlations

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Background & Objectives: Tubular adenosis (TA), originally described by Oberman in 1984 and subsequently characterized by Lee et al. in 1996, is a rare lesion of the breast that may mimic invasive carcinoma both radiologically and histologically.

TA is characterized by a non-lobulocentric, haphazard proliferation of elongated, narrow, and sometimes branching tubules lined by bland-looking ductal cells, surrounded by an intact myoepithelial layer.

The present study aimed to report the radiological and pathological features of a series of 8 TA cases to better understand its features.

Methods: Eight cases of breast TA were retrieved from the files of the Breast Unit at Bellaria Hospital (Bologna, Italy) diagnosed from 2010 to 2024.

All patients underwent a mammogram and then a vacuum-assisted biopsy and/or surgery.

The specimens were formalin-fixed and paraffin-embedded according to routine procedures.

The radiologic images were reviewed alongside the histology.

Results: Of the eight cases, in 1/8, FA was observed close to an infiltrative lobular carcinoma, and in 1/8, FA was associated with infiltrative carcinoma of non-special type.

In 4/8 cases, FA was close to foci of in situ lobular neoplasia, whereas 3/8 cases were associated with in situ ductal carcinoma. In three out of 8 cases, benign lesions were observed.

The comparison with radiological images revealed that the three cases with benign lesions had been classified as BI-RADS 3, whereas the other five cases had been described as BI-RADS 5.

All patients are alive and free of disease.

Conclusion: TA is a poorly known entity and may be confusing radiologically, leading to biopsies, but also histologically.

It should be taken into consideration in the differential diagnosis when seeing haphazardly arranged tubules that infiltrate fat but maintain myoepithelium.

TA can be associated with in situ or invasive carcinoma and the hypothesis of whether it has premalignant potential requires further research.

E-PS-02-084

Breast cancer: MAF as a predictive biomarker in treatment with adjuvant biophosphonates

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Background & Objectives: MAF (v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog- an AP-1 family transcription factor) amplification correlates with poor prognosis and bone metastasis in breast carcinomas (BC), also interfering with biophophonates metabolism, usually prescribed in postmenopausal women with early-stage BC when bone metastases control is important to reduce skeletal–related events and improving life quality. We present preliminary testing of MAF by applying FISH.

Methods: A series of ten FFPE sections of primary BC and a case of lymph node metastases *were evaluated for MAF* amplification using fluorescence in situ hybridization (FISH), MAFTEST (Inbiomotion, Barcelona, Spain). DAPI counterstain was applied, and images were acquired with a Leica DM 5500B microscope. The recommended score for *MAF* amplification, defines a mean number of 2.5 or more *MAF* copies per nucleus.

Results: The MAF status of the 11 tumour samples retrieved between December 2024 and March 2025 was based on tumour haematoxylin-eosin sections for selection of tumoral areas; patients mean age was 55 years (38-68). MAF-FISH was negative in all the 11 breast cancers samples. This result did not correlate with Nottingham Score, as five cases were G1 and the same number G2; as well as high oestrogen receptor and progesterone receptor immunohistochemistry.

Conclusion: The analysis of MAF status, committed the benefit from bisphosphonates therapy in the presented analysed cases. The implementation of MAF FISH as a predictive test into clinical practice, benefits 80% of younger women who have not reached menopause and who are currently excluded from treatment with adjuvant biophosphonates as shown in the literature.

According to the available data (AZURE trial), MAF biomarker selects a benefiting subgroup, including younger premenopausal patients currently excluded as mentioned.

E-PS-02-085

An immunohistochemical analysis of tumour associated interleukins in breast carcinoma

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Background & Objectives: The pathogenesis of Breast Cancer (BC) is multi-factorial. Several interleukins are particularly relevant in the development and progression of cancer. The aim of this study is to evaluate the immunoexpression of TGF-beta2, IL-1A, IL-17, IL-19, and IL-20 as prognostic factors in BC.

Methods: All cases operated for modified radical mastectomy from 2018 to 2021 were collected. Immunohistochemistry was performed on representative FFPE tissue for TGF-beta2, IL -1A, IL-17, IL- 19, IL- 20. The H score was obtained, giving a range of 0 to 300. Clinicopathological details were obtained. Statistical analysis was done by using SPSS software.

Results: The expression of tTGF-Beta2 was more in post chemotherapy related BCs compared to naïve chemotherapy BCs (Mann-U test- p- 0.0034). Rest all other interleukins expression in naïve and post chemotherapy BCs are statistically insignificant. In naive chemotherapy cases, the low expression of IL1A was associated with negative hormonal receptors status(p value 0.011) and high IL19 expression was associated with higher stage disease (p-0.023). However, in rest other prognostic parameters were insignificant. In post chemotherapy cases, T size of the tumour showed significant association with IL 1A expression (p-0.037), while only HER2 overexpression showed significant association with IL 17 expression (p-0.046). However, in rest other prognostic parameters were insignificant.

Conclusion: IL1A, IL 19, IL17 displayed significant associations with certain prognostic factors of BC. Our study aimed to investigate the immunoexpression of interleukins in post-chemotherapy cases,

comparing them with chemotherapy-naive cases to identify any differences in expression. While the pathogenic role of interleukins in breast cancer progression and development is established, further research is needed to fully understand their implications and potential therapeutic applications in breast cancer treatment.

Funding: Department of Science and Technology, Government of India

E-PS-02-086

Microglandular adenosis-associated breast carcinoma: a case series highlighting shared immunophenotype, distinct morphological features, and genetic analysis

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Background & Objectives: Microglandular adenosis (MGA)-associated breast carcinoma is a rare and diagnostically challenging entity, often exhibiting a triple-negative phenotype. This case series presents two such patients, highlighting their distinct histopathologic features and shared immunophenotypic profiles.
Methods: We retrospectively analysed the clinicopathologic and immunohistochemical findings of two patients diagnosed with MGA-associated breast carcinoma. Histologic evaluation was performed on biopsy and surgical specimens, and immunohistochemical profiling was conducted to assess diagnostic markers, including ER, PR, HER2, S100 and Ki-67. In addition next-generation sequencing (NGS) was carried out to identify potential pathogenic mutations and molecular alterations in both cases.
Results: The first patient was a 50-year-old female diagnosed with high-grade (grade III) invasive ductal carcinoma arising in a background of MGA. The second patient, a 29-year-old female at 38 weeks of gestation, was diagnosed with bilateral breast tumours, including an invasive carcinoma arising in MGA in the left breast. Both cases exhibited a triple-negative phenotype (ER-, PR-, HER2-) and high proliferative activity (Ki-67: 50–60%).
Conclusion: MGA-associated breast carcinoma may present with diverse morphologic features. Recognizing MGA as a potential precursor lesion is crucial for accurate diagnosis and appropriate clinical management. Despite their rarity, such tumours warrant publication in small case series, as they offer valuable insights into clinicopathologic characteristics, support refinement of diagnostic criteria, and contribute to the development of evidence-based management strategies.

E-PS-02-087

Frequency of HER2-low breast cancer at Fundación Santa Fe de Bogotá

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Background & Objectives: HER2-low expression represents an emerging subgroup with significant therapeutic implications. This study aims to determine the frequency of HER2-low among primary and metastatic breast carcinomas treated at Fundación Santa Fe de Bogotá (FSFB) between 2019 and 2023, assessing its histologic distribution.
Methods: A retrospective observational cohort study based on the review of medical records and pathology reports of breast cancer patients managed between 2019 and 2023. A total of 786 cases with HER2 immunohistochemistry performed at the FSFB pathology laboratory were analysed, evaluating HER2 classification and its association with histologic subtypes and tumour location.
Results: A total of 411 primary carcinomas were identified, of which 87% were HER2-negative (0, 1+, 2+ with negative ISH), and among these, 46% were classified as HER2-low. Of the HER2-low tumours, 77% were hormone receptor (HR)-positive and 73% corresponded to invasive ductal carcinoma. Additionally, 82% were Nottingham grade 2. Among 78 metastatic cases, 74% were HER2-negative, with 30% of them being HER2-low. The most frequent metastatic sites were non-visceral (67%), visceral (62%), and central nervous system (25%). The frequency of HER2-low in this cohort was lower compared to previous reports in the literature (46% vs. 60%).
Conclusion: This study demonstrates that nearly half of HER2-negative breast carcinomas in this population are HER2-low, which has important therapeutic implications due to the use of antibody-drug conjugates (ADCs). Reassessment of biomarkers using updated criteria is essential to determine eligibility for novel therapies. These findings underscore the need for a multidisciplinary approach to optimize clinical management and outcomes in patients with HER2-low breast cancer.

E-PS-02-088

Histologic and molecular approach to distinguish grade 3 well-differentiated neuroendocrine tumour from poorly differentiated neuroendocrine carcinoma of the breast

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Background & Objectives: Under the most recent WHO classification, all breast neuroendocrine neoplasms are graded based on Nottingham histologic grading scheme. It is difficult to distinguish grade 3 (G3) well-differentiated neuroendocrine tumour (NET) from poorly differentiated neuroendocrine carcinoma (NEC). However, given the treatment difference between these two neoplasms, it is critical to classify these neoplasms accurately.
Methods: Thirteen high-grade neuroendocrine neoplasms of the breast were identified in our surgical pathology file. All cases were graded as G3 based on Nottingham histologic grade. Tumour necrosis, mitosis, Ki-67 proliferation rate, expression of retinoblastoma protein (Rb) and p53 aberrant expression or *Rb* and *TP53* gene mutation were evaluated in each case.
Results: Three of 13 cases revealed Rb protein loss, or p53 abnormal expression or *Rb* and/or *TP53* gene mutation. These 3 cases also demonstrated much higher Ki-67 proliferation rate (>50%), and larger area of tumour necrosis, compared to the remaining 10 cases.
Conclusion: Similar to the pancreas, evaluating Rb, p53 and Ki-67 by immunohistochemistry and/or molecular studies may help to distinguish high-grade (G3) well-differentiated NET from poorly differentiated NEC in the breast. However, due to the rarity of these breast neoplasms, additional studies with larger cohort are warranted.

E-PS-02-089

Estrogen receptor and androgen receptor co-expression in primary and metastatic breast cancer

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Background & Objectives: Oestrogen receptors (ER) and androgen receptors (AR) have been used as therapeutic targets in the management of breast cancer. Studies have shown that ER was higher in tumours that metastasized to the bone as compared with tumours that

metastasized to visceral sites. In this study, our goal is to evaluate the status of hormone receptors in primary tumours, lymph node metastases and in recurrent/distant metastatic breast cancer.
Methods: Tissue microarrays of 166 paired cases of primary breast cancers and axillary lymph node metastases. In addition, 77 cases of recurrent/distant metastatic breast carcinomas including metastatic to bone marrow (n=42), liver (n=19), ovary (n=12) and small intestine/colon/omentum/perirectal (gastrointestinal) (n=4). Immunohistochemical studies were performed to evaluate tumour expression of AR and ER.
Results: Primary breast cancer and lymph node metastasis are positive for AR (63%) and ER (79%). AR positive (AR+) tumours are also positive for ER/PR. AR is expressed in 91% (31/34) of carcinomas with lobular or mixed ductal/lobular features and only in 53% (61/115) of ductal carcinomas. Majority of distant metastatic tumours express ER, being positive in 84% (16/19) of liver metastasis, 67% (8/12) of ovarian metastasis and 67% (28/42) of bone metastasis. AR is also positive in distant metastatic sites (50%) being positive in 11/19 of liver metastasis,7/12 of ovarian metastasis and 21/42 of bone metastasis. Although AR positivity is less abundant than ER positivity, an association between these two receptors is suggested by their co-expression in 95% (87/92) of primary breast cancer and in 92% of (37/40) distant metastasis.
Conclusion: AR and ER are frequently expressed in primary and corresponding axillary lymph node metastasis; and in distant metastatic sites of breast cancer. The co-expression of AR in a subset of ER positive cases may provide a potential target in the treatment of tamoxifen-resistant breast cancer patients.

E-PS-02-090
Histo-radiological correlation of BI-RADS 3 lesions in patients under 40 years old. Experience in Albania
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Background & Objectives: Pathological conditions of the breast at under 40-years old patients have a lower incidence and are mostly benign.
The histopathological recognition of their spectrum in these age groups has a diagnostic and a management importance. During the diagnosis of these lesions, we must keep in mind, in addition to the essential histopathological features, the possibility of the presence of unclear malignant potential lesions or malignant lesions, as happened in some of the cases included in our study.
With the same radiological BIRADS-3 stage diagnoses and different clinical histories, the patients in our study are part of the age group of 20-40 years. Their histopathological diagnoses include benign lesions, primary malignant disease and lesions with low potential malignant transformation (B3 lesions).
Methods: This is a descriptive retrospective study conducted at the Pathology Department of Hospital Universitary Centre "Mother Thersa". In this study have participated 50 patients aged 20-40 that were diagnosed radiologically stage BIRADS-3 and have performed tru cut biopsy and histopatologjical/ imunohistochemistry examination.
Results: After performing histopathological examination and IHC, the study results showed a predominance of fibroadenoma (62%, 31 patients), benign proliferative lesions (B3) in 22%, 11 patients) and in 16%, 8 patients, primary malignant lesion was identified (ductal carcinoma in situ in 3 patients (6%) and invasive ductal carcinoma in 5 patients (10%).
Conclusion: According to our study, lesions staged radiologically BIRADS-3 at patients aged 20-40, are diagnosed histopatologically, at the largest percentage as benign lesions (62%). However, a relatively significant number of patients were diagnosed as B3 lesions (22%) and as malignant lesions (16%) after BIRADS-3 staging, thus concluding on the importance of screening, clinical follow-up and the necessary radiological-histopathological correlation.

E-PS-02-091
Variants of invasive lobular carcinoma: diagnostic and reporting practices, impact on treatment and clinical management
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Background & Objectives: Invasive lobular carcinoma (ILC) accounts for up to 15% of breast cancers. Except classic ILC, other cytologic and architectural variants exist. This study aims to categorize ILC into variants and assess how pathology reporting on ILC variants may affect patient management and treatment strategies.
Methods: All ILC consecutive cases diagnosed since January 2023 were included in this study. We categorized tumours as variants when any cytologic or architectural variations were present. Clinical and demographic data, including tumour grade, tumour size and margin status, pathologic stage, lymph node status, distant metastasis, prognostic/predictive markers, and molecular studies were documented, and variants characteristics were compared to classic ILC group.
Results: Among 123 ILC cases, 68 were variants, and 55 classic. The most common variants were pleomorphic (27) and signet ring cells (19) and remaining were categorized as alveolar, trabecular, or solid. Pleomorphic ILC presented with a high nuclear and histologic grade ($p<0.0001$) and more frequent axillary lymph node metastases (71% vs. 45%). Distant metastases to liver, bone, brain, and orbits were commonly present in variants (12 of 68 cases) vs. classic type (2 of 55, $p=0.0426$) with pleomorphic and signet ring cells variants the most common. There were no significant differences noted between variants and classic ILC in age (61.5 vs. 64 years), tumour size (3.88 cm vs. 3.76 cm), pathologic tumour stage ($p=0.119$), margin status, and tumour focality. Lymphatic invasion was rare, even in cases with positive lymph nodes. Most tumours were ER/PR-positive, HER2-negative but five cases (2 variants and 3 classic ILC) were triple positive (ER/PR/HER2), and one variant was ER/PR-negative and HER2-positive. Ki-67 proliferation marker was higher in variants vs. classic ILC (21+/-15 vs. 12+/-9, $p=0.0029$).
Conclusion: This study highlights pathologic and molecular diversity of ILC, emphasizing the importance of reporting on type of variants that my impact on treatment and clinical management.

E-PS-02-092
Prognostic significance of p21 protein in breast cancer
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Background & Objectives: Breast cancer is the most common malignancy in women. Bearing in mind these circumstances, a review of new molecular mechanisms underlying breast cancer progression, resistance and various aspects of existing therapeutic methods would lead to new insights for biologists and clinicians. In this regard, we conducted a study covering recent advances in breast cancer biology with a focus on the *p21* protein.
Methods: The study included 147 patients diagnosed with invasive breast cancer. The presence of non-invasive lesions was noted in each invasive breast cancer and surrounding tissue. *p21* expression was determined by reading the percentage of nuclear expression in epithelial cells of invasive breast cancer and non-invasive lesions.
Results: Results showed that expression of *p21* increases with the progression of cytological changes in the epithelium; it is significantly

higher in invasive breast cancer compared to non-invasive lesions ($p<0.001$). There is a difference in *p21* expression between different molecular subtypes of breast cancer ($p=0.004$). Statistically significantly higher values of *p21* expression were observed in those breast cancers that showed overexpression of *HER2* compared to *HER2*-negative tumours ($p=0.001$). Depending on *Ki67* expression, the highest *p21* expression is in the group with high *Ki67* expression values ($p=0.019$). The increase in *p21* expression in tumour cells was accompanied by a statistically significantly reduced expression of *ER* ($p=0.015$, $\rho=-0.225$) and *PR* ($p=0.027$, $\rho=-0.205$).

Conclusion: *p21* protein plays an important role in proliferation, malignant transformation, as well as in progression from non-invasive lesions to invasive breast cancer.

E-PS-03 E-Posters Cardiovascular Pathology

E-PS-03-001

Arrhythmogenic right ventricular dysplasia as a cause of sudden death in a 58-year old woman: case analysis

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Background & Objectives: Arrhythmogenic right ventricular dysplasia (ARVD) is a genetic heterogeneous hereditary heart disease characterized by fibro-fatty replacement of the right ventricular (RV) myocardium, accompanied by severe cardiac arrhythmias, including ventricular extrasystole and right ventricular tachycardia with a high risk of sudden cardiac death.
Methods: We present a case of the sudden death of a 58-year-old woman. An autopsy was performed with tissue sampling of internal organs. Standard haematoxylin and eosin staining was used for histological examination.
Results: A 58-year-old woman died suddenly 40 minutes after admission to the hospital. The immediate cause of death was pulmonary thromboembolism. Postmortem examination revealed a probable source of thromboembolism, namely a parietal thrombus in the right ventricular cavity and phlebothrombosis of the right popliteal and tibial veins. The development of deep vein phlebothrombosis of the right leg was directly related to a one-month-old injury to the right leg. During autopsy, a predominant lesion of the right ventricle with specific pathomorphological signs was detected, which allows the diagnosis of isolated cardiomyopathy. The disease was complicated by right ventricular heart failure with thromboembolic syndrome and pulmonary heart failure, which became the immediate cause of death. The underlying disease was not diagnosed in the clinic due to the severity of the condition and the patient's short stay in the hospital.
Conclusion: In our case, the diagnosis of ARDV was a diagnosis of exclusion. The sudden death of a 58-year-old patient, the complete absence of previous medical data or anamnesis, the absence of atherosclerosis, ischemic or inflammatory myocardial damage, pronounced macroscopic changes (gray-yellow thinned wall with a fixed thrombus (and therefore, a clear zone of hypokinesis) in the dilated right ventricle) and the histological picture of transmural fibro-fatty replacement of the right ventricle myocardium allowed us to diagnose ADV.

E-PS-03-002

Application of APE1/Ref-1 in human heart tissue for evaluating Myocardial Infarction: a proof-of-concept study

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Background & Objectives: Myocardial infarction (MI) is a leading cause of mortality worldwide. Apurinic/apyrimidinic endonuclease-1/redox factor-1 (APE1/Ref-1) is a ubiquitously expressed bifunctional protein involved in oxidative stress response, DNA damage repair, and the regulation of redox-sensitive transcription factors.
Methods: Immunohistochemical staining for APE1/Ref-1 was performed on explanted hearts from individuals with different MI histories. Western blot analysis quantified APE1/Ref-1 expression in two opposing myocardial sites (anterior and inferior walls of the left ventricle). Each myocardial site was classified as infarcted or control based on the culprit artery.
Results: APE1/Ref-1 expression was more prominent in the penumbra of the infarcted wall affected by recent ischemic injury (several days prior) compared to the contralateral wall, which had been infarcted approximately four weeks earlier in the same individual. APE1/Ref-1 immunoreactivity was also observed in vascular endothelial cells and granulation tissue in addition to cardiomyocytes. However, in myocardial infarctions occurring one to two months earlier, APE1/Ref-1 was detected only in cardiomyocytes adjacent to granulation tissue. Western blot analysis demonstrated significantly higher APE1/Ref-1 expression in myocardial regions supplied by the culprit artery compared to the contralateral site.
Conclusion: APE1/Ref-1 expression varies according to the time elapsed since MI, with distinct localization in cardiomyocytes, endothelial cells, and granulation tissue. Its differential expression suggests a role of APE1/Ref-1 in myocardial injury influenced by the microenvironment. These findings indicate that APE1/Ref-1 may serve as a useful biomarker for MI assessment, particularly in determining the infarction timeline. Furthermore, they suggest its potential application in postmortem MI diagnosis during autopsy.

Funding: This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (IRIS RS-2023-00244782)

E-PS-03-003

Basilical vein aneurysm - a case report of a rare pathological entity

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Background & Objectives: Venous aneurysms are rare vascular lesions and the term is most commonly applied to dilatations of arteries. However, these lesions may occur in any part of the vascular system. Venous aneurysms were first mentioned in the literature by Osler in 1913. Our study aims to present a rare case of venous aneurysm of the right upper extremity.
Methods: We present the case of a 63-year-old man admitted in the Surgery department of Emergency Hospital Deva for symptoms of discomfort, increasing in size, easily compressible soft tissue mass on the right upper limb. The preoperative CT revealed a "cystic" lesion measuring 3,8 cm in diameter close to the basilical vein/ local venous dilatation. The lesion was excised together with the overlying skin tissue and sent to us for histological examination. The patient was discharged the second postoperative day and his further course was uneventful with great improvement.
Results: Macroscopy and microscopy revealed a lesion located in the subcutaneous tissue, as a saccular/dilated space structure developing from a venous wall, with the lumen lined by flat endothelial cells, filled with blood and thrombi, with characteristic IHC phenotype: CD31

intense and diffuse positive in the endothelial cells, without notable cytonuclear atypia, thinning the inner and middle layers of the basilical vein and replacement of the outer layer by fibrous tissue with decrease of elastic and smooth muscle fibres of the inner and middle layers. A diagnosis of primary venous aneurysm was made. Differential diagnosis includes a wide variety of upper limb soft tissue masses, mainly lipomas or other solid or cystic tumours. Preoperative diagnosis is of immense value.
Conclusion: Venous aneurysms are uncommon vascular malformations that may be identified anywhere in the body, often misdiagnosed as other soft tissue lesions.

E-PS-03-004
Analisis of risk factors affecting the development of thoracic aortic aneurysm
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Background & Objectives: To analyse the risk factors influencing the development of thoracic aortic aneurysm.
Methods: The study included 58 patients who underwent surgery for ascending aortic aneurysms between 2017 and 2024. The average age of the patients was 51.5 ± 2.7 years. The diagnosis was confirmed by transthoracic echocardiography and multispiral computed tomography with contrast. The average diameter of the ascending aorta in the widest part was 7.5 = 0.6 cm. The majority of patients were men - 53 (91%) over the age of 50 (64%).
Results: Of the 58 patients included in the study, 53 (91%) were men and 5 (9%) were women. The average age of the patients was 51.5 ± 2.7 years. More than half of the patients (32 or 55%) had a history of chronic arterial hypertension (24 or 41.3%), which was usually combined with coronary heart disease and various atherosclerotic vascular lesions. In addition, 15 (25.8%) patients were diagnosed with bicuspid aortic valve, which is known to be a congenital anomaly closely associated with an increased risk of aortic aneurysm. The third most common cause was Marfan syndrome, which was observed in 10 (17%) cases. In addition to these main causes, a small number of patients (11%) had other risk factors such as a family history of aortic aneurysm, connective tissue diseases, and trauma. The sizes of the aneurysms were different: the average diameter was 7.5 ± 0.6 cm, and the largest aneurysm was 9.5 cm.
Conclusion: The most common underlying conditions in the development of thoracic aortic aneurysm are atherosclerotic lesions of the aorta with prolonged hypertension, as well as congenital bicuspid aortic valve. Arterial hypertension plays a key role in the development of aortic aneurysm. Early detection and effective treatment of hypertension are crucial factors in the prevention of aortic aneurysm and the prevention of its serious complications.

E-PS-03-005
Study of long-term trends of morphologically-analysed inflammatory myocardial disease in 2002-2023
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Background & Objectives: Inflammatory myocardial disease, or myocarditis, is considered among one of the most common causes of sudden cardiac death in young adults with estimated prevalence at approximately 1.8 million cases per year worldwide, still leaving true epidemiological disease data in local regions inaccurate. Study objective is to determine long-term trends of myocarditis in 2003-2023 specific for local Lithuanian region.
Methods: 40 cases of suspected / confirmed myocarditis with obtained myocardial tissue processed and examined morphologically applying light microscopy in local Lithuanian pathology laboratory in 2002-2023 were selected for the study. Selected cases were analysed according to myocardial infiltrate type (lymphocytic, neutrophilic granulocyte, giant multinucleated cell), pattern (borderline, focal, diffuse), patient's sex, age, and outcomes in yearly trends. Descriptive statistics, ANOVA, and $\chi 2$ tests were applied ($p<0.05$).
Results: 77.5% (n=31) and 22.5% (n=9) women of similar age were determined in the study (47.61 (16.88) vs (45.56 (13.11) years old; F=1.808, p=0.149). Lymphocytic infiltrate was the most common infiltrate type (67.5%, n=27), and the most predominant infiltration pattern was borderline (32.5%, n=13). Non-lethal outcomes were observed in 62.5% (n=25) of morphologically-analysed myocarditis. Non-lethal outcomes of myocarditis were predominant in 2002-2005 compared to the remaining 2006-2023 yearly trends ($\chi 2=13.156$, p=0.011). Sex and age of patients, myocardial infiltrate type and pattern were similar in 2002-2005, 2006-2010, 2011-2015, 2016-2020, and 2021-2023 yearly periods ($p>0.05$).
Conclusion: Long-term trends of patient's sex, age, and outcomes, as well as, myocardial infiltrate type and pattern in 2002-2023 were characterized in cases of myocardium tissue analysed for inflammatory disease, revealing predominance of non-lethal outcomes of myocarditis in 2002-2005. Considering the study results, it can be hypothesized that long-term data analysis of morphological testing results can serve as an important ancillary tool to monitor local population trends of a clinically significant entity validated by structural tissue analysis.

E-PS-03-006
COVID-19 cardiac injury: involvement of chymase-positive mast cells
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Background & Objectives: Acute myocardial injury is observed in 22% of COVID-19 patients. Mast cell proteases play a significant role in lung damage in COVID-19, but their contribution to cardiac damage in this pathology is poorly understood. The aim of the study was to assess the density of chymase-positive cardiac mast cells (CPMCs) in patients who died due to COVID-19 and its association with troponin I level.
Methods: The study sample consisted of 60 patients (28 women and 32 men, mean age 70.0 [62.0; 72.0] years). During hospitalization blood troponin I level were measured. Cardiac tissue samples were obtained from patient autopsies. CPMCs were counted per 1 mm^2, accounting for their degranulation activity.
Results: The median troponin I in the study group was 0.1 [0.0; 0.2] ng/ml, while elevated levels of this marker were observed in 11.7% of patients. The median number of cardiac CPMCs was 0,17 [0,00; 0,85] per 1 mm^2. CPMCs with degranulation were predominant (0,17

[0,00; 0,77] per 1 mm^2), while median of CPMCs without degranulation was 0,00 [0,00; 0,00] per 1 mm^2.
Significant correlations were established between the number of cardiac CPMCs and the level of troponin I: moderate correlation with CPMCs with degranulation (r=0.6711; p=0.0000), with total number of MC of this phenotype (r=0.6558; p=0.0000) and weak correlation with CPMCs without degranulation (r=0.3101; p=0.0172).
Conclusion: The results obtained in the study suggest the involvement of CPMCs in the development of acute myocardial injury in COVID-19 patients. Possible mechanisms underlying this pathological process include the development of the inflammatory process through the activation of proinflammatory cytokines, apoptosis of endothelial cells, and stimulation of fibrosis.

E-PS-03-007

Pathohistological characteristics of semilunar valves in calcific aortic valve disease: Correlation with clinical parameters and comorbidities

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Background & Objectives: Calcific aortic valve disease (CAVD) is a progressive, irreversible fibro-calcific remodelling of the aortic valve (AoV) leaflets, leading to aortic stenosis, which is the second-most frequent cardiovascular disease in individuals over 65. Besides aging and congenitally bicuspid AoV, CAVD development is associated with common cardiovascular risk factors such as hypertension, diabetes mellitus, and dyslipidemia. Additionally, one theory suggests that CAVD shares etiopathogenic similarities with atherosclerosis. This study aimed to analyse the pathohistological characteristics of affected AoVs and their correlation with clinical parameters like stenosis severity, ejection fraction, NYHA classification, and comorbidities (obesity, hyperlipidemia, diabetes).
Methods: In this retrospective study 58 surgically removed AoV were analysed from patients diagnosed with aortic stenosis due to CAVD at the University Clinical Centre of Serbia between April and December 2023, which were processed by standard histological techniques. Overall pathological changes of affected AoV were assessed on haematoxylin-eosin slides and classified based on Warren and Yong's grading system. Statistical analysis was performed using descriptive methods and correlation tests, with significance set at $p<0.05$.
Results: The study included 30 male and 28 female patients, with a mean age of 67.9 ± 8.1 years. Most patients (75.9%) were overweight (BMI > 25). A significant correlation was found between serum triglyceride levels and inflammatory cell infiltration around calcific nodules ($p<0.011$). No significant associations were observed between histological changes and cholesterol levels, ejection fraction, or NYHA class. Patients with severe stenosis exhibited increased valvular inflammation and neovascularization ($p<0.001$).
Conclusion: Our findings suggest that triglycerides metabolism may contribute to the progression of CAVD by promoting inflammatory processes within the valve tissue. The lack of correlation between cholesterol levels and histopathological changes supports the hypothesis that CAVD may have a distinct pathogenesis from atherosclerosis, despite some shared mechanisms. Further research is needed to explore the etiopathogenic mechanisms of CAVD.

E-PS-03-008

Primary RNAlater fixation and dissection of endomyocardial biopsies for histology and molecular biology avoids discrepancies resulting from sampling errors

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Background & Objectives: On occasion of the annual meeting of the DGK 2023 in Mannheim (Germany) primary RNAlater fixation was presented to prevent the well known sampling error of myocarditis diagnoses and virological tests (low sensitivities, between 15 and 80% false negativ virological tests).
Methods: Commonly, three biopsies for histology and two biopsies for molecular diagnostics are taken. Our submitters fixed the biopsies with RNAlater and we dissected the probes for histology and molecular analyses. The diagnostic sensitivity will amount to 97%.
Additionaly we measured myofiber diameters because of their low sampling error and the importance for cadiac structure and function.
Results: **RNAlater fixation:** Between 2020 and 2024 a cohort of 263 endomyocardial biopsies were fixed with RNAlater and have been evaluated in the MVZ für Klinische Pathologie in Darmstadt. The morphologic quality after RNAlater fixation did not differ between RNAlater fixation and formalin fixation. For staining automatic standard procedures of routine histologic laboratories were used.
Myofibre diameters:

1. Increased ventricular volume and nonhypertrophic myofibres in biopsies indicate increase of **fibrous tissue or amyloid**. Absence of interstitial deposits indicate **storage diseases (Glykogenosis, Sphingolipidosis) or hypertrophy and hyperplasia of myofibres, respectively**. Morphometry of myofibre diameters is especially **successful detecting hypertrophic cardiomyopathies.**
2. Normal muscle mass (Echo, MRT, CT) and nonhypertrophied myofibers in association with ventricular dilatation (Echo, MRT, CT) indicate an **acute cardiac event rather than preexisting cardiac remodelling.**

Conclusion: For future clinicopathologic research on RNA molecules pairwise embedding of the dissected biopsies and not pooling seems to be preferred. Measurements on myofibre diameters may be usefully included.

E-PS-03-009

Takayasu aortitis complicated with aortic pseudoaneurysms and foetal death: a case report and literature review

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Background & Objectives: Pregnancy in Takayasu arteritis (TA) patients is associated with vascular remodelling and severe cardiovascular complications (aortic aneurysms, pseudoaneurysms and coronary artery disease). We report the morphology of a clinical case with multiple aortic pseudoaneurysms and foetal death.
Methods: A 32-year-old female diagnosed with TA, was hospitalized for acute cardiorespiratory dysfunction. Imaging revealed large aortic pseudoaneurysms with hemodynamical dysfunction and foetal death (unknown pregnancy of 20 weeks and 6 days). Total thoracic aortic reconstruction was performed, and foetal spontaneous expulsion

occurred. Frozen elephant trunk (FET) surgery, which uses antegrade deployment of thoracic endovascular aortic repair (TEVAR) endografts along with total arch replacement, was selected as the best surgical approach. Examination of the aorta, placenta specimens, and clinical foetal autopsy were performed.
Results: Surgical specimen composed of a thick fragment of aorta (55x35 mm) was examined and necrotizing aortitis with intimal and adventitial scarring without dissection was seen. Active inflammatory and healed lesions were seen with predominance of lymphocytes, plasmocytes, giant cells and some ill-defined granulomas. Verhoeff staining highlighted severe fragmentation of elastic fibres and no acid-fast bacili were identified. Isolated aortitis, lymphoplasmocytic aortitis and autoimmune-associated aortitis in differential diagnosis were excluded. No major alterations were found at the placenta and the post-mortem examination of the foetus revealed no malformations or foetal growth restriction.
Conclusion: This case illustrates why pregnancies in patients with TA should be considered high risk, requiring close monitoring and collaboration of different medical specialties. In this case, we highlight the importance of clinical-pathological integration, to make a correct differential diagnosis and future therapeutic management of the patient and also of the offspring.

E-PS-03-010
Quantitative assessment of myocardial vascular network density depending on cause of death
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Background & Objectives: Diseases causing death became more and more diverse and each of them can influence structural and functional changes of myocardial tissue. The authors compared the variations of myocardial interstitial capillary network density-VD between the different cardiac wall regions depending on patients' cause of death (COD).
Methods: Five epicardium-to-endocardium cross sections (left ventricle wall-LVW: anterior-LV_AW, lateral-LV_LW and posterior-LV_PW, interventricular septum-IVS and right ventricle wall-RVW) were taken during autopsy from 95 patients died with different causes of death (vascular diseases-V_P, non-vascular diseases-NV_P, and suspect/violent cause of death-S/V_Dth, named also control group-CG) in the hospital. Tissue samples were processed and immunomarked with CD34 antibody. Slides were digitized. The VD was measured with a dedicated software "in-house" designed. Average values-AV were compared using chi square test.
Results: The VD had lowest values in V_P group and highest values in CG in general and in both sexes. Its values increased from LVW to RVW in V_P group and CG and decreased in NV_P group in general and in both sexes. They also increased from LV_AW toward LV_PW in all groups of COD and in both sexes.
The VD values were higher in women than in men in CG and NV_P group and higher in men than in women in V_P group. Its values were lowest in both sexes in V_P group but highest in men in NV_P group and in women in CG.
Conclusion: The diseases causing death determine different pathways of interstitial capillary network remodelling both along the different regions of the cardiac wall and in the two sexes, the most important being the capillary density decrease in vascular diseases as compared with all other causes of death.

E-PS-03-011
Non-Infectious Aortitis: 14 years' institutional experience
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Background & Objectives: Non-Infectious aortitis (NIA) is a rare, commonly incidental finding in Thoracic Aortic specimens. Once diagnosed, patients are at higher risk of future vascular complications, including aneurysmal development. Some cases may be part of a wider systemic condition or 'clinically isolated' in nature. Appropriate pathological evaluation is therefore key to guiding appropriate patient management and follow-up.
To appraise the pathological handling and reporting of surgically resected thoracic aortic specimens in our institution to the recommendations published by the Society for Cardiovascular Pathology / Association for European Cardiovascular Pathology in 2015. To evaluate the clinical details received, surgical indications, histopathological features, and incidence of NIA.
Methods: A 'CORVU' search of the Laboratory Information Management System at the Dept. of Pathology, Cork University Hospital from January 1st 2010 to December 31st 2024 was performed, utilizing SNOMED codes for Aorta and Aortitis. Study data was collected and analysed using Microsoft Excel.
Results: 6% (n=23) of the total 416 thoracic aorta specimens received were diagnosed with NIA, all located in the ascending aorta. Thoracic aortic aneurysm repair was the most common surgical indication (61%). 43% of aneurysm patients needed concurrent valvular repair. All cases were sampled according to consensus recommendations (average of 8.3 pieces of tissue per 3.4 cassettes). Atheromatous change was identified in 74% of cases and medial degeneration in 87% of cases. Granulomatous/giant cell (GCC) pattern was the most common histopathological pattern (96%). One case had no definitive pattern diagnosed due to mixed features. Only one GCC case had a diagnosis of Polymyalgia Rheumatica included in the clinical details.
Conclusion: NIA is a rare but important entity to recognize through optimal specimen handling and reporting, to ensure appropriate follow-up for this patient cohort. Although systemic disease was identified in only one our cases to date, an extended chart review is to follow.

E-PS-03-012
Histological structure of the atrial appendages in patients with persistent atrial fibrillation after cardiac surgery
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Background & Objectives: Atrial fibrillation (AF) is one of the most common arrythmias associated with a higher risk of thromboembolism and stroke. The incidence of AF is increasing globally, especially in the elderly population. The study aimed to perform histomorphometry of the atrial appendages removed during cardiac surgery in patients with persistent AF.
Methods: Eighty atrial appendages removed during cardiac surgery were examined: 50 – from patients with AF and 30 – from patients without AF (control group). Haematoxylin and eosin, Van Gieson's, Mallory's, and Lie-staining were used for histological examination of

the paraffin sections. The severity of myocytolysis and cardiomyocyte contraction impairment, intramural oedema, fibrosis and lipomatosis of the myocardial stroma were evaluated by histostereometric method. Monoclonal antibodies to desmin, S100 and CD117 were employed as immunohistochemical markers to characterize cytoskeleton and detect telocytes.

Results: The damages of cardiac myocytes, such as myocytolysis and cardiomyocyte contraction impairment, increase in relative interstitial volume, sclerosis and lipomatosis of the myocardial stroma were more pronounced in patients with AF. The difference was statistically significant ($p<0.001$). The structure of cytoskeletal components was damaged in cardiac myocytes affected by myocytolysis. AF was also associated with an increased vascular permeability and focal lymphohistiocytic infiltrates. In AF patients, endocardial sclerosis was accompanied by mucoid oedema and mural thrombosis. Using S100 and CD117, a moderate quantity of telocytes was detected in the myocardial stroma. The number of telocytes in patients with AF was significantly lower than in the control group.

Conclusion: Mainly non-specific histopathological changes were detected in the left auricle appendages of patients with persistent AF. The most informative findings included such acute damages of cardiac myocytes as myocytolysis, contractures and wave-like deformation, amid interstitial oedema and increased vascular permeability. Chronic changes (cardiosclerosis and stromal lipomatosis) were also more common in the AF patients.

Funding: This work was supported by the Ministry of Education and Science of the Russian Federation within the framework of the state order No 123030700101-2

E-PS-03-013

Early and late complications of stenting and coronary artery bypass grafting

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Background & Objectives: Stenting and coronary artery bypass grafting (CABG) are among the most widely used methods of treating coronary heart disease.

Methods: The autopsy results of 119 patients who underwent stenting (59 cases) or ABG (60 cases) after diagnosis of myocardial ischemia were studied.

Results: Men were 2.5 (71.2%) times more likely to undergo stenting and 2.7 times (72.7%) more likely to undergo ABG compared with women (28.8% and 27.3%). The most frequently performed stenting of the anterior interventricular artery (AIA) and the formation of an Aortic graft -AIA. Stenting of 2 or more arteries was performed in 22%, and the use of 2 or more grafts for ABG was performed in 89%. The peak of stenting deaths was observed from the day of stent placement to 10 days, the second peak was from 6 months to 2 years. With ABG, the first peak was from the day of surgery to 1 month, and the second peak occurred for a period of 10 years or more after ABG.

Deaths on the first day were associated with early complications: damage during puncture of the main artery, stent deformation, acute arterial thrombosis, occlusive dissections. With ABG, all patients underwent bypass surgery due to a violation of the adequate functioning of grafts- thrombosis.

In the first 10 days after stenting, patients died from acute coronary artery thrombosis, occlusive dissection, and myocardial infarction. During ABG, bypass thrombosis, bleeding from the internal thoracic artery, acute cerebrovascular accident, iatrogenic complications, reperfusion complications, and technical complications were recorded. Late complications of stenting included thrombosis, restenosis, and neointimal hypertrophy. With ABG performed for 5 years or more, shunt dysfunction with the development of atherosclerosis and stenosis, venous bypass thrombosis were determined.

Conclusion: Conducting autopsy examinations helps to detail the causes of death and is aimed at preventing complications.

E-PS-03-014

A comprehensive clinical and histological approach to the diagnosis and treatment of cardiomyopathy after radiation therapy

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Background & Objectives: Overall, malignant neoplasms (MN) are considered as one of the biggest health challenges worldwide. A key modality of MN treatment is radiation therapy (RT).

Histopathological evaluation, characterizing the severity of fibrosis, plays an important role in clinical settings for the timely therapy revision in patients with heart diseases and for the cardiac surgery risk assessment. The study objective is to assess the contribution of a comprehensive clinical and morphological approach to the diagnosis and treatment of radiation-induced heart disease.

Methods: From January 2012 to December 2024, surgery was performed on 39 patients with radiation-induced heart disease, 26 (66%) of whom were women. RT was conducted for Hodgkin lymphoma in 25 (64%) cases, breast cancer in 10 (24%), and mediastinal teratoblastoma in 1 case. The time interval from the completion of RT course to cardiac surgery was 26.2 ± 11.4 years. Haematoxylin and eosin, picrofuchsin acc. to van Gison, Lee's and Mallory's stains were used for staining all sections.

Results: The heart valve surgery was performed in 36 (92%) patients, one-stage coronary artery bypass surgery – 8 (20%), and subtotal pericardiectomy – in 3 patients.

Histopathological assessment of the surgical specimens revealed that the epicardium contained large areas of coarse fibrosis with the sites of angiomatosis. In most cases the fibrotic areas were associated with haemorrhages, sometimes in combination with lymphohistiocytic infiltration. Extensive vacuolization of sarcoplasm was present in cardiomyocytes in the subepicardial regions.

Conclusion: It is crucial to continue the investigation of histopathological patterns associated with the development of radiation-induced restrictive cardiomyopathy which not only complicates the clinical course of CHF and the choice of optimal medical therapy but also influences the timeline of cardiac surgery. Our histological data prove that the healthy heart tissues and structures are replaced by collagen and fibrin with the further formation of coarse fibrosis and calcification.

E-PS-03-015

Unexpected, sudden and deadly aortic aneurysm complication

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Background & Objectives: Aortic Aneurysm is responsible for relevant morbidity and mortality. Globally, aorta aneurysm-related deaths rose by 74.2% from 1990 to 2021, getting up to 153,927 deaths (2021). The authors aim to present a deadly aneurysm complication, discovered during medico-legal postmortem investigation.

Methods: A 73-years old male died suddenly, without history of personal or familial pathological antecedents. A postmortem study was

performed at a Branch of our National Medico-Legal and Forensic Sciences Institute, which included autopsy with toxicological and anatomo-pathological examinations.
Results: Relevant autopsy findings were 1100 cc of blood inside the intestine lumen, adherence of the duodenum wall to an abdominal aorta aneurysm (11cm diameter), a hole at the duodenum mucosa extending to the inner cavity of the aneurysm through a linear continuity solution. Inside the aneurysm were atherosclerotic plaques and parieto-luminal thrombus. Microscopic evaluation confirmed the lesions observed macroscopically and characterized the type of atherosclerotic plaques ("IV" and "VI" - *American Heart Association)*. Toxicology results were negative for alcohol, licit/illicit drugs, pesticides. Death was declared natural, sudden, unexpected, due to rupture and fistulisation to the duodenum of a thrombosed atherosclerotic aneurysm of the abdominal aorta, with massive intra-intestinal bleeding.
Conclusion: *Primary Aorto-duodenal Fistula (PADF)* is a rare condition (incidence: 0.04%-0.07%), with abdominal aorta aneurysm as risk factor. Yet, PADF is severe, life-threatening, mostly due to acute, massive and hard-to-control haemorrhage. Without treatment, 80%-100% are fatal, eventually suddenly and unexpectedly. The outcome is so dismal, that even with intervention, perioperative mortality ranges 18%-63%. Complete Medico-Legal postmortem examination (including anatomo-pathological and toxicological studies) are of major relevance, to disclose the cause of unpredicted deaths, as well as to clarify post-surgical in-hospital deaths.

E-PS-03-016
Morphological changes of coronary capillaries in different stages of cardiopulmonary bypass
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Background & Objectives: Complex cardiac surgery may require long-term cardiopulmonary bypass (CB), which can be complicated with heart failure. The study is aimed at studying the features of coronary hemocapillaries damage at different stages of the CB.
Methods: At different stages of CB, myocardial fragments from 4 patients with ischemic heart disease and left ventricle valves failure were taken from papillary muscles to be removed during mitral valve replacement. Morphological changes of capillaries were assessed by light and electron microscopy.
Results: In the first 30 minutes after the introduction of the cardioplegic solution, the most characteristic change of the capillaries were microclasmocytosis and electronically transparent lumens.
After 60 minutes of CB, the surface of the endothelial cells became smoother, an increased number of micropinocytotic vesicles was noted. The gaps were losing their electron transparency. The fragments of cellular detritus were found in swelled interstitium.
After 120 minutes of CB, endothelial cells retained their transport function mostly in small areas near the adjacent cardiomyocytes. The thickness of the endothelial layer was minimal. In the intercellular space, the severity of oedema and amount of cellular detritus were growing. The walls of the capillaries were becoming electron dense with extremely thinned layer of endothelium.
At the point of 185 minutes of CB, the tendency to dilate capillaries, as well as thinning of their walls, was progressing. Capillaries, postcapillaries, and venules had a balloon-like appearance, the thinned layer of the endothelium was very electron dense. The capillaries with signs of irreversible changes were noted.
Conclusion: 1. The duration of CB directly correlates with the severity of microvascular damage.
2. When CB lasts for more than 120 minutes, a critical impairment of endothelial function occurs, which can contribute to the postoperative complications.
3. There is need to develop measures to minimize endothelial damage, in particular by optimizing the CB duration.

E-PS-03-017
Medial degeneration in dissected thoracic aortas: meta-analysis
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Background & Objectives: Systematic review on dissected aortic cases analysed according to the criteria from the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology consensus statement was performed to analyse histopathological features in media aortic layer and feasibility of consensus in everyday practice.
Methods: The Pubmed serach resulted in 174 articles out of which ten articles met inclusion criteria for extraction of the data. Data on all histopathological features presence and grading listed in the Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology consensus statement were collected in Microsoft Excel and further analysed with Open Meta-Analyst program.
Results: A total of 871 cases out of 10 studies were analysed. The pooled prevalence of cases diagnosed with moderate overall medial degeneration as moderate among 264 cases of dissection from 5 studies was 47.1% (95% CI from 32.1 to 62.1%, I^2 was 85.34%). Out of all cases of dissection, 46.3% (95% CI from 28.7 to 63.9%, I^2 was 72.44%.) reported overall MEMA as moderate. Interlamellar MEMA was severe in most dissected cases (38.6% (95% CI from -4.5 to 81.6%), I^2 was 98.13%). Translamellar MEMA was moderate in the majority of analysed cases (46.6% (95% CI from 15.2 to 78.1%), I^2 was 94.97%).
Conclusion: The Society for Cardiovascular Pathology and the Association for European Cardiovascular Pathology consensus statement is a practical toolkit for assessment of thoracic dissected aorta samples in everyday practice. Nevertheless, its rigorous application is limited to several centres and the majority of users do not apply the consensus in its extent.

Funding: VTR funding from Fimlab Laboratories, Tampere Tuberculosis Foundation, Foundation of the Finnish Anti-Tuberculosis Association

E-PS-03-018
Patterns of fibrosis in secondary dilative cardiomyopathy
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Background & Objectives: Secondary dilative cardiomyopathy (S-DCM) is defined by non-familial heart dilation associated with severe left ventricular systolic dysfunction. Myocardial fibrosis is known as the remodelling of extracellular matrix, which leads to increased myocardial stiffness.
Methods: In this retrospective study we included 48 adult patients with postmortem examinations in which, the main morphologically diagnosis was S-DCM and were compared with a control group of 12 patients with non-dilative heart conditions. This study was conducted over four years in a regional emergency clinical hospital.
Results: The pattern of fibrosis in S-DCM may vary, from focal to stellate, diffuse or even scar-like.

Advanced stages of fibrosis have a pro-arrhythmogenic role in these patients because the isolation and exclusion of cardiac fibres by bundles of collagen fibres framed the appearance of so-called "myocyte micronodules", with both clinical and functional implications. These patients underwent severe arrhythmic events as a result of contractility impairment. Several of these sub-endocardial nodules presented with a central area of fibrosis, resembling a scar; this was a result of micro-infarction rather than apoptosis.
Transmural interstitial fibrous scars developed through intricate pathophysiological mechanisms, and the amount of collagen determined was over 4 times higher in S-DCM cohort compared the control group.
The special character of interstitial myocardial fibrosis is highlighted, with the individual fibre dissection which ultimately leads to the diminishing of the vascular nutritional supply necessary for each cardiac cell.
Conclusion: Myocardial fibrosis is an important constituent in the development and progression of S-DCM. Even though magnetic resonance is nowadays a gold standard for the assessment of cardiac fibrosis patterns, histology can help in establishing the cornerstone for single-cell sequencing in identifying the subpopulation of fibroblasts expression.

E-PS-03-019

Hyperacute cardiac allograft rejection with successful early retransplantation by bridging ECMO

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Background & Objectives: Hyperacute cardiac allograft rejection starting on the first day or even during transplantation leads to high mortality (approximately 70%). The rejection reaction depends on the presence of antibodies in the recipient and may result from previous hyperimmunization after blood transfusion [1-2].
Methods: Presentation of a rare case of hyperacute cardiac allograft rejection with successful early retransplantation by bridging extracorporeal membrane oxygenation (ECMO).
Results: Hyperacute cardiac allograft rejection was confirmed by examination of the explanted heart. Abundant intramuscular haemorrhages, linear deposits of complement protein C4d in the vessel walls and intravascular margination of CD68+ cells confirmed hyperacute rejection.
Conclusion: Bridging circulatory support using continuous ECMO allowed for successful early retransplantation of the hyperacute rejected organ, so this method can be used in such rare cases. The patient remains under the care of Silesian Centre for Heart Diseases in Zabrze.
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E-PS-04 E-Posters Cytopathology

E-PS-04-001

Incidence and outcomes of thyroid nodules with Atypia of Undetermined Significance (AUS) cytology in a tertiary government hospital: a ten-year review (2013 to 2022)

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Background & Objectives: Thyroid cancer is ranked as the ninth most common malignancy in the Philippines. Fine needle aspiration biopsy is the initial diagnostic of choice because it is noninvasive and cost-effective. Aspirates are diagnosed using the Bethesda System, one category of which is Atypia of Undetermined Significance (AUS) which poses a confusion among clinicians due to being a noncommittal diagnosis. This study aims to describe the frequency and outcomes of AUS and the reasons in choosing this category during a 10-year period in the Philippine General Hospital (PGH) and UP College of Medicine Pathology Research Laboratory (UPCM-PRL).
Methods: A records review was conducted using the available medical documents in PGH and UPCM-PRL.
Results: The percentage of Category III cases is 4.23% which is within the recommended standard of less than 7%. The quantity of repeat biopsies (15.38% in PGH, 18.64% in PRL) of Category III is small, and the most frequent diagnosis for benign cases is Thyroid Follicular Nodular Disease. For the malignant category, Papillary carcinoma, conventional/classic subtype occupies the top spot. The risk of malignancy (ROM) is very high (66.7% in PGH, 73.9% in PRL, 68.9% combined) although this is limited by the database available. The top basis of pathologists for choosing Category III remains to be "focal/mild atypia" that is not further elaborated in the histopathology reports.
Conclusion: A more accurate rate of biopsies and risk of malignancy can be achieved by having a larger database that includes registries outside the institution to follow the patients who receive management outside PGH. The application of the newly released 3rd edition of the Bethesda System for Reporting Thyroid Cytopathology in 2023 is also advised to give a better description of the atypia that can be observed in AUS cases.

E-PS-04-002

Unexpected guests on cytologic evaluation of anal Pap tests

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Background & Objectives: Anal Papanicolaou (Pap) tests are primarily used for detecting squamous intraepithelial lesions and carcinoma. However, the presence of intestinal amoebas is an incidental finding that is not well documented in medical literature. Intestinal amoebas can be transmitted via ingestion of amoebic cysts through contaminated water and food, or via sexual contact. Invasive amoebiasis such as Entamoeba histolytica can cause different clinical symptoms, while other species can be nonpathogenic. Morphologically, they can be indistinguishable. Despite this, there's no consensus on reporting these findings.
Methods: As a result of a incidental finding of scattered amoebic cysts in an anal pap test of a male who was diagnosed with human papillomavirus (HPV) years ago, the cytopathologists at our centre prospectively searched during a six month period for amoebas on cytologic evaluation of ThinPrep® slides. In all cases, quantitative PCR of high-risk HPV (HR-HPV) was performed. For clinical data and follow-up, the patients' medical records were reviewed.
Results: Three cases of amoebic cysts on anal pap tests were found, all belonged to HIV positive males, being the average patient age 47 years old. None exhibited intraepithelial lesions or malignancy, though two had HR-HPV positive results. Revising clinical data, one patient had autolimited diarrhoea, while the others were asymptomatic. *Blastocystis hominis* was detected by PCR in one asymptomatic patient.
Conclusion: Although anal Pap tests are primarily used for detecting dysplasia and carcinoma, recognizing amoebic cysts can provide

clinical benefits. Cytology alone cannot differentiate between different species of amoebas, however, it is important to recognize them and be able to differentiate them from other entities such as pollen, inflammatory cells, or other entities such as flagellate. Thanks to cytological identification of these cysts, microbiological examination and clinical follow-up could be achieved, despite the lack of standardized reporting guidelines.

E-PS-04-003

EUS-guided FNA findings of gastrointestinal subepithelial lesions

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Background & Objectives: Subepithelial lesions (SEL) of gastrointestinal track are difficult to diagnose using imaging alone. Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is an effective and safe tissue sampling technique. In this study it was aimed to investigate the cytopathological and demographic features of SELs diagnosed with EUS-FNA.
Methods: This retrospective study examined 18 consecutive SELs cases that sampled by EUS-FNA and histopathologically proven. Demographic data such as age, gender, size, location obtained from pathology report. If ancillary studies were performed, they were noted.
Results: The average age of the patients was 61.7±11.0 (range 28-73). 8 of the cases were female and 10 were male. 14 cases were diagnosed with Gastrointestinal stromal tumour (GIST), 2 cases with leiomyoma, 1 case with Schwannoma, and 1 case with lipoma with sizes of 16-36 mm (median 25 mm). The most common location is stomach-corpus (n:9), followed by stomach-fundus (n:4), duodenum (n:3), stomach-antrum (n:2). Immunohistochemistry (IHC) was used for differential diagnosis in 18 (94.7%) of the cases. The most frequently used markers were CD117 and CD34 (n: 18). CD117 was positive in 85.7% of GIST cases and CD34 was positive in 78.5%. DOG1 was positive in 100% (9/9), SMA was positive in 55.5% (5/9) of GISTs, immunohistochemically. While S100 positivity was observed in schwannoma case, Desmin were positive in leiomyoma cases (n:2).
Conclusion: EUS-FNA is a very useful diagnostic method not only for the diagnosis of pancreatic masses but also for SELs located in the gastrointestinal tract. In sufficient samples, a clear diagnosis can be made with appropriate cytopathological examination and ancillary studies, such as IHC.

E-PS-04-004

Evaluation of p53 and IMP-3 in Pancreatic Adenocarcinomas(PDAC) Diagnosed by Endoscopic ultrasound-guided fine-needle aspiration(EUS-FNA)

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Background & Objectives: Endoscopic ultrasound-guided fine-needle aspiration(EUS–FNA) is a safe and effective technique that can be used to diagnose pancreatic tumours, with a pooled sensitivity of 85%–92% and specificity of 96%–98%. Pancreatic ductal adenocarcinoma(PDAC) is one of the most aggressive malignant tumours, with a 5-year survival rate of only 4%.In our study, we aimed to investigate the diagnostic significance of p53 and IMP-3 expression in PDAC diagnosed by EUS-FNA.
Methods: A total of 79 cases diagnosed as PDAC(case group) and 10 cases that Negative for malignancy(control group) were included in the study. The demographic data of the patients were obtained from the electronic data system of the hospital.p53 and IMP-3 expressions were evaluated using immunohistochemical analysis.
Results: The median age of the patients was found to be 69 years. The sex distribution, 49 cases(62.8%) compared to 30 female cases(37.2%). In the analysis of pancreatic biopsy cases, the diagnostic value of the immunohistochemical markers IMP3 and p53 was assessed. The sensitivity of IMP3 positivity was calculated as 76.7%, while its specificity was 100%. p53 null mutant pattern-characterized by complete absence of p53 staining—was observed in 34.2% of the cases, aligning with a calculated sensitivity of 34% and specificity of 100%. IMP-3(+) and p53(+) co-expression was seen in 50.6% of the Case group(40 cases), but in 0% of the control group($p<0.01$).
Conclusion: While IMP-3 can be used as a positive marker, p53 positivity is significant, but its negativity(null-mutant pattern) is also meaningful. The combination of both IMP-3 and p53 expressions proved valuable in improving diagnostic accuracy in suspected malignant cases**.** These findings support the potential of using p53 and IMP-3 as diagnostic tools in EUS-FNA samples for PDAC, offering significant insights into tumour biology and aiding clinical decision-making.

E-PS-04-005

Cytological diagnosis of Langerhans cell histiocytosis: case report series

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Background & Objectives: Langerhans cell histiocytosis (LCH) is a rare disease, caused by clonal neoplasm of bone marrow-derived myeloid dendritic cells, predominantly affecting paediatric patients. The prognosis varies depending on the stage at presentation, ranging from spontaneous remission to life-threatening complications. Due to its rarity, the diagnosis of LCH can be challenging and often delayed. A precise cytological diagnosis, in conjunction with appropriate clinical evaluation, imaging studies and immunostaining, can reduce the need for unnecessary and invasive biopsies, facilitate a more rapid diagnosis and guide appropriate patient management.
Methods: We report three cases of LCH and one case of Langerhans cell sarcoma (LCS) diagnosed using fine-needle aspiration biopsy (FNAB). Two cases involved paediatric patients: a 26-day-old female neonate with congenital LCH (biopsy performed for diagnostic confirmation) and a 16-year-old male with a temporal skin lesion. Other two cases were adult: a 41-year-old female with a painful, indurated skin lesion on the forehead and a 65-year-old male presenting with cervical lymphadenopathy.
Results: All patients underwent FNAB. In three cases, the diagnosis of LCH was established—one based on cytomorphology and two with the aid of immunocytochemistry (CD1a+, Langerin+). In one patient, a diagnosis of "malignant tumour, cytologically and immunophenotypically consistent with LCS" was made (CD1a+, Langerin-/+, CD100+, CD68 PGM-/+, CD68 KP1+). Biopsy was performed and histopathological confirmation was obtained in one LCH case and the case of LCS. In the other two LCH cases where a biopsy was not performed, clinical presentation was consistent with the cytopathological findings.
Conclusion: Given the potential for life-threatening complications in LCH, timely and accurate diagnosis is essential. In our experience cytological evaluation, particularly in conjunction with immunocytochemistry, can facilitate the early diagnosis of LCH in the appropriate clinical setting, thereby expediting patient management.

E-PS-04-006

Bethesda IV thyroid nodules: malignancy rate and risk factor analysis

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Background & Objectives: The Bethesda IV cytological category represents a diagnostic gray zone in the classification of thyroid nodules. Lesions in this category exhibit a range of potential outcomes, from benign to malignant, making it challenging to predict malignancy. This study aims to assess the malignancy rate in Bethesda IV thyroid nodules at our institution and to identify associated risk factors.
Methods: A retrospective review of fine needle aspiration (FNA) cytology reports from our institution over a 3-year period (2021-2023) was conducted. All cases diagnosed as Bethesda IV according to the Bethesda System for Reporting Thyroid Cytopathology were included. Histological diagnosis, considered as the gold standard, was used for comparison. We also examined potential risk factors associated with malignant behaviour.
Results: A total of 452 FNA samples were analysed. Of these, 64 cases (14.2%) were classified as Bethesda IV. Histopathological follow-up was available for 34 cases. Among these, 27 cases (79.4%) were benign, including 15 cases of follicular adenoma, 9 cases of multinodular goiter, and 3 cases of lymphocytic thyroiditis. The remaining 7 cases (20.6%) were malignant, with 3 cases of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) and 4 cases of classic papillary thyroid carcinoma. No significant association was found between age, gender or ultrasonography characteristics and malignancy risk (p=0.8, 0.2 and 0.5 respectively).
Conclusion: Bethesda IV thyroid nodules exhibit a heterogeneous risk of malignancy, highlighting the need for careful evaluation. The malignancy rates in this study fall within the threshold suggested by the Bethesda consensus for Bethesda Category IV. NIFTP can be challenging on cytology, sharing cytomorphological characteristics with follicular neoplasms and having nuclear features that can range from mildly atypical to unequivocally suggestive of papillary carcinoma. Further studies are warranted to refine predictive factors for Bethesda IV nodules on larger samples.

E-PS-04-007

Diagnostic value of nipple discharge cytology: reassessment of initially insufficient samples in a single-centre experience

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Background & Objectives: Nipple discharge cytology is a commonly used diagnostic tool in evaluating patients with breast discharge; however, its sensitivity remains limited. This study aims to assess its diagnostic performance by comparing cytologic findings with histopathological outcomes and evaluating the effect of re-sampling by trained pathology staff on initially insufficient specimens. We particularly focus on the impact of repeat sampling in reducing the rate of insufficient cytology results.
Methods: A total of 438 nipple discharge cytology samples evaluated between 2011 and 2025 at Haydarpasa Numune Training and Research Hospital were retrospectively analysed. Cytological diagnoses were categorized as benign (n=341), atypical (n=26), malignant (n=12), or insufficient (initially n=76). A subset of 20 cases with initially insufficient cytology results, prepared externally, was recalled for repeat sampling by the pathology department. Histopathological follow-up was available in 80 cases. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated based on cases with definitive benign or malignant cases.
Results: Among the 80 cases with histopathology, there were 9 true positives, 1 false positive, 38 true negatives, and 8 false negatives. Sensitivity was 52.9%, specificity 97.4%, PPV 90.0%, NPV 82.6%, and accuracy 83.9%. Malignancy was identified in 61.5% of atypical cases and 18.2% of insufficient cases. Remarkably, 17 out of 20 initially insufficient cases (85%) became diagnostically adequate following repeat sampling by the pathology department, which reduced the number of insufficient cases from 76 to 59.
Conclusion: Although nipple discharge cytology demonstrates high specificity, its limited sensitivity may lead to missed diagnoses. Atypical and insufficient samples carry a considerable risk of malignancy and require further evaluation. Notably, re-sampling by trained pathology staff significantly improved the diagnostic adequacy, with a remarkable reduction in the number of insufficient specimens. These findings emphasize the importance of repeat sampling and multidisciplinary collaboration in improving diagnostic accuracy.

E-PS-04-008

***Strongyloides stercoralis* hyperinfection: a case report**

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Background & Objectives: Strongyloidiasis is a parasitosis caused by the intestinal nematode *Strongyloides stercoralis*, which can manifest from asymptomatic to severe forms in immunocompromised patients. Microscopically, the form we diagnosed is the rhabditiform larvae, measuring approximately 250–300 µm, showing a blunt anterior end, corresponding to the buccal cavity, and a pointed posterior end, coinciding with the anus. These larvae exhibit orangophilic characteristics in cytological extensions processed with the Papanicolaou technique. This case illustrates a clinical case of severe hyperinfestation, highlighting the clinical presentation, cytological and histological findings, and associated complications.
Methods: The case involves a 63-year-old male patient with a medical history of heart failure, Charcot-Marie-Tooth neuropathy type I, chronic obstructive pulmonary disease (COPD), smoking, and alcoholism. He presented with progressive dyspnoea on minimal exertion, productive cough, wheezing, and abdominal pain. Thoracic computed tomography (CT) revealed bilateral pulmonary collapse, pleural effusion, and cavitated pulmonary nodules. Abdominopelvic CT demonstrated jejunal intestinal obstruction with free peritoneal fluid.
An extensive jejunal resection was performed due to intestinal mural necrosis. He subsequently developed abdominal septic shock (positive *Enterococcus faecium* cultures) and respiratory sepsis, prompting fibrobronchoscopy with biopsies, bronchial aspirates (BAS), and bronchoalveolar lavage (BAL).
Results: Cytological evaluation of BAS and BAL revealed abundant mixed inflammation, necrotic material, and numerous elongated, orangophilic rhabditiform larvae, morphologically consistent with *Strongyloides stercoralis*. Bronchial and intestinal biopsies confirmed parasitic infestation.
Clinically, the patient progressed to severe hyperinfestation syndrome complicated by abdominal septic shock (*Enterococcus faecium*), bacteraemia (*Pseudomonas aeruginosa*), systemic sepsis resulting from intestinal bacterial translocation (*Enterococcus faecium* and *Enterococcus faecalis*), as well as gastrointestinal haemorrhage due to refractory intestinal ulcers. Ultimately, the patient succumbed to multi-organ failure.

Conclusion: Hyperinfection with *Strongyloides stercoralis* constitutes a severe clinical condition with significant septic complications, particularly among immunocompromised patients. Early clinical suspicion and timely cytological and histological diagnosis are crucial to improve therapeutic management and reduce mortality.

E-PS-04-009

Two for the price of one effusion: a case report of the cytological diagnosis and biomarker profiling of concurrent breast and lung adenocarcinoma

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Background & Objectives: Diagnosing concurrent primary malignancies within a single pleural effusion is exceedingly rare. Due to their overlapping cytomorphologic features, distinguishing coexisting malignancies in effusion cytology is challenging but has critical implications for diagnosis and treatment.
Methods: We describe the case of a 60-year-old woman with a remote history of breast cancer who presented with progressive dyspnea and large right-sided and small left-sided pleural effusions. Initial cytological analysis of the right-sided pleural fluid at an outside institution yielded a diagnosis of metastatic lung adenocarcinoma. However, evaluation of additional effusion cytology specimens from the left-side revealed two morphologically distinct tumour cell populations, raising suspicion for a second malignancy.
Results: Immunohistochemistry confirmed the presence of both metastatic lung adenocarcinoma (TTF1+, Napsin-A+, GATA3 -, ER-) and metastatic breast adenocarcinoma (GATA3 +, ER+, TTF1-, Napsin-A-). Biomarker analysis was successfully performed for both malignancies, revealing an ER+/PR-/HER2- profile for the breast adenocarcinoma. Meanwhile, the lung adenocarcinoma was negative for any targetable gene mutations (e.g. EGFR, ALK, ROS1 and others) but exhibited a Tumour Proportion Score of 1-49% for PD-L1, suggesting possible benefit from immunotherapy in combination with chemotherapy.
Conclusion: This case underscores the importance of meticulous cytomorphological assessment in effusion cytology, particularly when evaluating specimens with subtle heterogeneity. While pleural effusion metastases typically correlate with a known primary malignancy, the possibility of a second primary tumour should be considered in complex oncologic cases. Furthermore, cytological specimens provide valuable biomarker information for treatment planning, emphasizing the role of immunohistochemistry, in situ hybridization, and next-generation sequencing in precision oncology. To our knowledge, this is the first reported case of concurrent metastatic breast and lung adenocarcinoma diagnosed within a single pleural effusion specimen with successful biomarker analysis. This case highlights the diagnostic and therapeutic value of effusion cytology in detecting and characterizing multiple malignancies.

E-PS-04-010

Awareness of the spectrum of presentation of aspergillosis

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Background & Objectives: Aspergillus species are filamentous fungi capable of causing a broad spectrum of infections in humans, primarily infecting the lungs but also involving the sinuses, skin, eye and CNS. Forms of Pulmonary aspergillosis include allergic bronchopulmonary aspergillosis, saprophytic aspergilloma and invasive aspergillus pneumonia, necrotizing tracheobronchitis and necrotizing granulomatous inflammation. Human host reaction depends on immunologic status, underlying lung structure and nature of exposure. We present three different clinical cases of aspergillosis at our hospital, highlighting the diverse manifestations and diagnostic approaches.
Methods: We reviewed the clinical presentations, laboratory investigations, imaging studies and cytohistopathological findings of three patients diagnosed with aspergillosis. Key diagnostic features, risk factors and treatment outcomes were analysed. Bronchoscopy, sputum culture, cytological evaluation and imaging modalities were utilized for diagnosis.
Results: Case 1: A 77 year old male with intermittent haemoptysis was diagnosed with unsuspected aspergillus fumigatus infection after cytological analysis revealed a rare fungal hypha amidst inflammatory cells.
Case 2: A 67 year old female with bronchiectasis and mucus plugging had undiagnosed abundant aspergillus organisms confirmed through cytology and culture.
Case 3: A 60 year old female with a history of septic shock after laparotomy for benign disease developed pulmonary and cerebral aspergillomas and necrotizing tracheobronchitis. Despite treatment with amphotericin, the patient succumbed to the infection.
Conclusion: Aspergillosis presents with a diverse spectrum of clinical manifestations. A high index of clinical suspicion is required for timely intervention. The role of the pathologist in early detection is crucial. Antifungal therapy remains the mainstay of treatment but severe and invasive forms continue to pose significant morbidity and mortality.

E-PS-04-011

Artificial intelligence in the evaluation of urine sediment cytology

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Background & Objectives: To develop and test an IT tool for assessing urine sediment cytology.
Methods: To train artificial intelligence (AI), scans of slides assessed by experts and the result according to the Paris Classification (PC) for assessing urine cytology were used. Slides were made using the liquid cytology method, stained according to Papanicolaou. The IT tools used were Computer Vision Annotation Tool CVAT (a tool for labelling images and video files) and Digital Slide Archive DSA (a platform providing storage, management, visualization and annotation of image data sets). In addition to the main parameter of N/C assessment, an attempt was made to algorithmically determine other parameters of cell images. Traditional methods of feature extraction were used (colour histograms, textures or shape features). Due to the small number of available slides, additional synthetic images for training AI were generated. We used slides assigned to one of two target classes: HGUC (High Grade Urothelial Carcinoma) and suspected HG cancer (SHGUC). A method for validating the results was developed. To verify the system's operation, samples that did not participate in model training were randomly selected and the results of the AI algorithms were presented. A team of three independent cytopathologists was appointed. They verified the model predictions - confirmed or changed the category of cells marked as positive (HGUC, SHGUC), and made a final diagnosis. The experts' work was aimed at assessing the results of the algorithms.
Results: The result of the work is an application that allows the cytopathologists to view the sample scan, predictive markings (labels), edit them and add new ones. On this basis, the doctor issues a final diagnosis - confirms the initial diagnosis of the system or changes it, issuing his own.

Conclusion: The developed application is an useful auxiliary tool in the process of assessing urine sediment cytology.

Funding: National Centre for Research and Development: project no. POIR.01.01.01-00-0279/22

E-PS-04-012

Bethesda III thyroid cytopathology - un unpopular but necessary category. Cases 2020-2024 revisited

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Background & Objectives: The BIII category refined in the new edition of the TBSRTC (2022), allows for easy reclassification of previously diagnosed BIIIs. Our study focused on reviewing the frequency and types of BIII cases over a five-year period (2020-2024) comparing a faculty postgraduate training centre site with two diagnostic laboratories staffed by the same senior pathologist consulting also the training centre cases.
Methods: All FNABs classified as BIII were reviewed and subtyped. Clinical endocrinologists provided follow-up in cases where histopathological examination was not performed. An analysis of preanalytical and analytical factors influencing incidence was performed. Didactically most beneficial cases were included into a postgraduate workshop.
Results: The overall incidence of BIII in the period was 4.6 % (196 cases out of 4263 diagnoses; females 84%) for both compared groups, higher at the faculty workplace 6.1 % (84 cases out of 1370 diagnoses) compared to the private laboratory 3.9 % (112 cases out of 2893 diagnoses). The subtype distribution was BIIIo 58.6%, BIIIn 28.6%, combined BIIIn/o 12.9%. Biopsy was performed in 41 patients (20,9 %), 16 biopsy diagnoses were malignant (ROM 8.2%).
The higher incidence of BIIIs in a training centre with less experienced evaluating cytopathologists leads to a higher incidence even with regular consultation of BIII cases by an experienced consultant compared to laboratories with primary evaluation by a single experienced cytopathologist.
Conclusion: Strict application of diagnostic criteria for individual BIII subtypes and close interdisciplinary communication are tools for maintaining the sensitivity of thyroid FNAB and keeping the incidence of BIII within the range corresponding to the actual limits of the diagnosed sample.

Funding: Supported by Ministry of Health, Czech Republic – conceptual development of research organization 00064165, General University Hospital in Prague

E-PS-04-013

Evaluation of high-fluorescence cells parameter as a screening tool for malignant effusion screening using automated haematology analyser

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Background & Objectives: Effusion cytology plays a crucial role in the diagnostic and prognostic aspects of cancer management, particularly in the advanced stages of the disease. Cell counts by automated haematology analyser are now emerging as a preferred method over the conventional manual cell counting methods in all Body Fluids (BF). This study aimed to evaluate the high-fluorescence (HF)-BF parameter generated by an automated blood cell counter and correlate it with the final microscopic cytological assessment.
Methods: Effusion cytology plays a crucial role in the diagnostic and prognostic aspects of cancer management, particularly in the advanced stages of the disease. Cell counts by automated haematology analyser are now emerging as a preferred method over the conventional manual cell counting methods in all BFs. This study aimed to evaluate the HF-BF parameter generated by an automated blood cell counter and correlate it with the final microscopic cytological assessment.
Results: A total of 604 samples consisting of 43.79% ascitic fluids (AF), 50% pleural fluids (PF), 5.86% peritoneal fluid, and 0.33% pericardial fluid were included in the study. Of all the samples with corresponding cytopathology, malignant cells were found in 59 samples. The HF-BF%/100 WBCs (85.6 ± 347.79) for malignant BF samples were found to be significantly higher than the non-malignant samples (18.9 ± 106.54) (p-<0.01), while HF-BF# (#-absolute counts)was higher in malignant BF compared to non-malignant (24.21 ± 41.78 Vs 20.26 ± 91.55), however it was not significant (p=0.81).

Conclusion: The HF-BF parameter offers potential utility in identifying malignant samples; however, it should not be relied upon exclusively. A more meticulous microscopic examination is warranted when HF-BF% or counts exceed the laboratory's established thresholds. A comprehensive, large-scale validation study of the HF-BF parameter in BF mode is necessary to establish definitive standards for evaluating critical effusions.

E-PS-04-014

3D visualization & assessment with digital Papanicolaou stain on cell block samples

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Background & Objectives: Cell blocks, formed by embedding cytological specimens in paraffin blocks, preserve tissue architecture in addition to the features of individual cell/cell cluster. Drawing information from the surrounding tissue architecture, combined with visualization of nuclear morphology, can lead to an increased diagnostic specificity. Crucially, cell blocks are compatible with all ancillary and molecular tests.
However, cell block is sectioned with 4 um and sanctions are stained with H&E which makes difficult to distinguish cell boundaries or the separation between the nucleus and cytoplasm that are often useful to discriminate between malignant and benign and determine tumour sub-types.
While H&E stain is useful for examining tissue structure, Papanicolaou (Pap) staining is to focus on cell morphology. Cytologists are familiar to see Pap staining for cell features more than H&E stain. Therefore, we have developed Digital Pap stain on H&E slides and 3D visualization and assessment tools to support diagnostic process on cell blocks.
Methods: Eight pleural effusion cases (adenocarcinoma, squamous cell carcinoma, and malignant mesothelioma) were used. 4 µm H&E stain sections were scanned with 11 layers. (40 × mode: 0.23 µm/pixel, 11 layers 1 um pitch. Hamamatsu Nano Zoomer S60 Digital slide scanner C13210-01).
In-house Digital Pap stain algorithm was run on all cases. Digital Pap stained WSIs and H&E WSIs were then reconstructed in 3D using commercial 3D imaging application.
Results: The 3D Papanicolaou images allowed cells to be observed in three dimensions. Detailed features of the nucleus and cytoplasm, which were not visible in the 2D H&E images, became apparent.

Conclusion: 3D Visualization & Assessment with Digital Papanicolaou stain on Cell Blocks could support pathologists and cytologists during the diagnostic process, such as differentiating between "Adenocarcinoma vs SCC vs malignant mesothelioma", assessing tumour sub type can, and enabling appropriate treatment and drug administration.

E-PS-04-015

The effectiveness of Milan classification in salivary gland fine needle aspiration cytology evaluation

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Background & Objectives: The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) is a system that aims to standardize salivary gland fine needle aspiration cytology (FNAC) reports between cytopathologs. MSRSGC classifies cytologies into 6 different categories. Each category specifies the risk of malignancy and how it should be managed. This study aimed to determine the utility of the Milan Reporting System (MRS) for salivary gland FNAC.
Methods: Salivary gland FNAC specimens prepared with Thin Prep liquid-based cytology method that were accessed from the archive system of the Pathology Deparment of Gaziantep University Medical Faculty between 2010 and 2024 were retrospectively evaluated and reclassified according to the Milan classification system. Comparison with parotidectomy reports was used to evaluate the effectiveness of the Milan reporting system and malignancy and neoplasm risk for each category.
Results: A total of 722 FNAC and 409 excision specimens were evaluated. Of the total cytologies, 3% were classified as nondiagnostic (ND), 14.7% as nonneoplastic (NN), 13.4% as atypia of undetermined significance (AUS), 41.4% as benign, 5.7% as salivary gland neoplasm of uncertain malignant potential (SUMP), 5.7% as suspicious for malignancy, and 31% as malignant. At histopathologic follow-up, ROM (risk of malignancy) ratios for each category were 13.3%, 16.6%, 24%, 7.7%, 24.2%, 90%, 100%. The Milan classification was 92.93% accurate for malignant neoplasia/benign lesion differentiation, and 91.18% for non-neoplastic lesion/neoplasia.
Conclusion: Our study confirms that MRS helps establish a common language among cytopathologists when interpreting salivary gland FNAC, though the ROM is high in intermediate categories. To detection of malignant neoplasms or non-neoplastic lesions, MRS has a high specificity and accuracy, but a low sensitivity.

E-PS-04-016

Enhancing diagnostic precision: the utility of carbonic anhydrase IX and alpha-inhibin immunoperoxidase staining in fine-needle aspiration cell blocks for accurate diagnosis of pancreatic serous cystadenoma

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Background & Objectives: Pancreatic serous cystadenoma (pSCA) presents a diagnostic challenge in fine-needle aspiration (FNA) specimens due to limited cellularity. While molecular testing of cystic fluid can aid in diagnosis, its availability remains limited. Several immunohistochemical markers, including inhibin, CA-IX, and Glut-1, have been studied in histologic specimens, but their utility in cytologic diagnosis is still debated, representing a gap in current diagnostic strategies. In this study, we assessed the staining patterns of three markers—Inhibin, CA-IX, and CEA—in pSCA, cystic mucinous neoplasms, and contaminating gastrointestinal epithelial cells.
Methods: We identified the following pancreatic FNA cases: 1) Cell block is contributory with more than 20 epithelial cells; 2) Ten confirmed pSCA cases; 3) Five cases each of pancreatic mucinous cysts and gastrointestinal contaminants. Immunoperoxidase staining for pan-keratin, CEA, CAIX, and alpha-inhibin was conducted on cytologic cell blocks following standard protocols in our clinic's immunohistochemical laboratory.
Results: 1. Inhibin were positive in the epithelial cells of all the pSCA cases and negative in contaminated gastrointestinal and other mucinous epithelial cells (Figure 1).
2. CA-IX staining is non-specific for pSCA, and could be positive in both neoplastic mucinous epithelial cells and contaminated gastrointestinal epithelial cells (Figure 2).
3. CEA was negative in pSCA but focally positive in gastrointestinal epithelial cells.
Conclusion: 1. A combination of immunostaining markers, including inhibin, CA-IX, and CEA, demonstrates high specificity for diagnosing pSCA on FNA cell block preparations.
2. In the appropriate clinical and radiological context, this panel of markers serves as a supportive tool for the accurate diagnosis of pSCA, and thus potentially improving diagnostic precision and patient management.

E-PS-04-017

Fallopian tube fimbrial carcinoma presenting as a solitary huge omental mass – clinical and cytodiagnostic pitfalls

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Background & Objectives: It was recently suggested that a significant majority of so-called ovarian and peritoneal high-grade serous carcinomas (HGSCs) arise from a precursor lesion known as serous tubal intraepithelial carcinoma (STIC) of the fallopian tube, regardless of the tumour's primary location.
Methods: A 74-year-old Japanese woman with an abnormality detected by endometrial screening cytology three years earlier, presented to our hospital. MRI revealed a 53 mm omental mass, but no other suspicious lesions. Based on pathological examinations of the resected specimens, we ultimately diagnosed HGSC with STIC originating from the fimbria of the fallopian tube, which formed a bulky disseminated omental mass.
Results: On cytological smears, mononuclear or multinucleated, large atypical epithelial cells were sporadically observed, mainly forming small clusters, in the background of endometrial tissues with neither proliferative changes nor atypia. The atypical cells exhibited a high nuclear/cytoplasmic ratio and possessed polygonal, foamy cytoplasm and hyperchromatic nuclei with irregularities in size and shape (Papanicolaou classification: class IIIb). Similar atypical cells were also seen in small numbers in cervical smears. Endometrial biopsy and curettage were performed, but no atypical cells were detected, and CT, MRI, and F-18-FDGPET/CT showed no abnormalities. At subsequent follow-up, nine endometrial cytological examinations and two endometrial biopsies were performed, none of which showed abnormalities.
Conclusion: If atypical epithelial cells with the possibility of an extrauterine primary are incidentally found on endometrial cytology, but no abnormalities are identified by diagnostic modalities, periodic (every six or 12 months) imaging examinations can be recommended, considering the potential for these lesions to originate from the fimbria of the

fallopian tube. In our current case, fibrous encapsulation of the omental seeding focus might, fortunately, have prevented further contiguous spread as well as wider dissemination.

Funding: JSPS KAKENHI Grants (Nos. 21K06910 and 23K11869), the National Hospital Organization (NHO) Grant (H29-NHO-01), and Joint Research Support Grants based on the Comprehensive Agreement between Saitama University and Saitama Medical University (21-J-14, 22-J-01, 23-J-08 and 24-J-2)

E-PS-04-018

Second look ultrasound (US)/fine needle aspiration (FNA) in the breast oncology field - cytopathological analyses

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Background & Objectives: The significance of second look ultrasound (US)/fine needle aspiration (FNA) has recently been drawing attention in the breast oncology field, while vacuum-assisted biopsy is frequently used as an intervention from the viewpoint of research on biomarkers, genomic medicine, and so on. Technologically, 2nd look US/FNA means that a lesion not detectable by the first US might be identified by other modalities such as magnetic resonance imaging and mammography, and re-US followed by FNA cytology would then be performed to evaluate the lesion. This study aimed to clarify the characteristics of mammary lesions detected by 2nd look US/FNA.
Methods: From among the 248 breast cancer cases undergoing surgery at our hospital during the period from January 2019 to March 2021, 13 specimens obtained from 10 cases (4%) undergoing 2nd look US/FNA were cytopathologically analysed.
Results: The patient ages ranged from 41 to 82 (mean 63.2) years, and the puncture site was ipsilateral in 7, contralateral in 2, and bilateral in 1 case. Clinical imaging findings were 6 masses, 4 cystic lesions, 1 low echoic area, 1 duct dilation, and 1 unknown. The cytodiagnostic classification was 'adequate' in 10 samples. Specifically, 5 were "benign", 1 "suspicious of malignancy", and 4 "malignant". The other three samples were 'insufficient' or 'inadequate'. Based on subsequent verification with surgically-resected specimens, all 5 lesions cytologically suggesting malignancy corresponded to ductal carcinoma *in situ*, and 3 of these (60%) were the solid papillary/neuroendocrine variant.
Conclusion: Cytodiagnoses were appropriately made in this investigation, and the utility of 2nd look US/FNA was accordingly verified. The histological cancer subtype was often neuroendocrine (solid papillary), and these tumours tend to occur multicentrically in the background of neuroendocrine cell hyperplasia (*J Clin Pathol*, 2012. *Pathology*, 2018), supporting our current research results.

Funding: JSPS KAKENHI Grants (Nos. 21K06910 and 23K11869), the National Hospital Organization (NHO) Grant (H29-NHO-01), and Joint Research Support Grants based on the Comprehensive Agreement between Saitama University and Saitama Medical University (21-J-14, 22-J-01, 23-J-08 and 24-J-2)

E-PS-04-021

Fine Needle Aspiration (FNA) biopsy from lung metastasis of myxopapillary ependymom

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Background & Objectives: Myxopapillary ependymoma (MPE) is a rare central nervous system tumour, particularly seen in children and young adults. Our patient is a 34-year-old female who presents with complaints of lower back pain and a palpable mass. A firm, fixated mass is palpated during the digital rectal examination. The patient has a surgical history from 3 years ago, but the pathological diagnosis is unknown. MRI imaging shows a 36x20 mm mass located in the midline distal to the coccyx. Upon surgical excision, multiple nodular lesions with smooth, well-defined capsules are observed macroscopically.
Methods: Histopathological examination of the specimen reveals papillary structures characterized by columnar cells located around fibrovascular cores, along with abundant myxoid material. The myxoid material stains positive with Alcian Blue. The immunohistochemistry (IHC) panel of the tumour shows GFAP:+, S100:+, EMA:-, CK(AE1/AE3):- staining. The Ki67 index is found to be 10%. The case is reported as MPE. The patient, who is clinically monitored, experiences a recurrence in the retrorectal region within subcutaneous tissue 4 years later. The tumour has similar IHC results to the previous material, with a Ki67 index of 23% and mitosis of 11/10 HPF. The case is reported as anaplastic transformation of MPE, classified as WHO Grade III.
Results: The patient, who has been clinically monitored, underwent a Chest CT scan 3 years later, which revealed multiple subpleural nodules in the right lung, the largest being 25x20 mm at the basal segment of the lower lobe. An FNA biopsy was performed on the lesion. The cytology material showed a tumour composed of cells with radial arrangement around vascular lumens, exhibiting a monotonous granular chromatin structure, with poorly defined cytoplasmic borders.
Conclusion: In the differential diagnosis, neuroendocrine tumours, including carcinoid tumours, were considered, and after performing IHC, the case was reported as metastasis from MPE.

E-PS-04-022

Cytology-histology correlation in epithelioid angiomyolipoma: diagnostic pitfalls in intraoperative imprint cytology

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Background & Objectives: Epithelioid angiomyolipoma (EAML) is a rare renal mesenchymal tumour that can closely mimic renal cell carcinoma (RCC) in radiologic and cytologic evaluations. While computed tomography (CT) imaging is often diagnostic for conventional angiomyolipoma due to its fat content, tumours with minimal adipose tissue present a diagnostic challenge. Imprint cytology may be inconclusive or misinterpreted, underscoring the importance of histopathologic confirmation and immunophenotyping.
Methods: A 73-year-old male underwent evaluation for an incidental solid, renal lesion (2.6 cm) in the left interpolar region, classified as an intermediate-probability RCC (group 3, CCLS scoring) based on MRI characteristics. Patient underwent a total nephrectomy and an imprint cytology was performed prior to formalin fixation and a histopathological and immunohistochemical correlation was made.
Results: Imprint cytology revealed an hypercellular smear with hematic background, sheets of round to plump spindle cells with indistinct cell borders, sometimes with displaced eccentric nuclei with a voluminous, frothy cytoplasm and occasional nuclear pseudoinclusions. Histopathological examination of the resected tumour (2.9 × 1.9 cm) demonstrated a proliferation of epithelioid cells with abundant cytoplasm, interspersed blood vessels, fascicles of smooth muscle, and occasional mature adipose tissue. Immunohistochemical staining confirmed positivity for actin and caldesmon, HMB45 and MelanA. The absence of a clear adipose component in the imprint cytology

contributed to initial diagnostic uncertainty, highlighting the difficulty of diagnosing EAML when fat is scarce.
Conclusion: EAML with minimal fat content can be a diagnostic pitfall in both radiology and cytology. Intraoperative imprint cytology, while useful for rapid assessment, may be inconclusive without adipose tissue, leading to potential misclassification as RCC or sarcomatoid tumours. This case underscores the need for histologic confirmation and immunophenotyping to achieve accurate diagnosis, avoiding unnecessary overtreatment.

E-PS-04-023
HPV infection and prevalence in a Colombian cohort of patients with cervical cytology abnormalities
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Background & Objectives: Cervical cytology (CC) plays a crucial role in detecting HPV-related abnormalities. The integration of molecular testing for High risk HPV (HR-HPV) genotyping improves the screening strategies and complements cytological assessments, providing valuable insights into the progression and prevention of cervical lesions. Vaccination programs aim to reduce HPV prevalence and associated lesions; therefore, correlating vaccination status, cytological findings, and genotype distribution is essential to refining public health strategies.
Methods: This descriptive study analysed 7645 CC samples collected during 2019, that were reported according to the Bethesda system. Positivity was defined as atypical squamous cells of undetermined significance (ASCUS and above). Diagnoses were categorized into low-grade lesions LGL (ASCUS and LSIL) and high-grade lesions HGL (HSIL, glandular atypia and adenocarcinoma). Demographic data, vaccination status, HPV genotyping, and vaccination status underwent statistical analysis.
Results: A total of 334 positive samples (4.3%) were identified and categorized as LGL n=272 (3.5%) , and HGL n=62 (0.8%). HPV-genotyping was positive for HR-HPV in 263 cases (78%), 221 cases from LGL (84%) and 42 cases from HGL (25,9%). HPV 16 and 52 were the most frequent genotypes (20 and 15 patients) .Vaccination information was available only for 14 patients, among this 5 were not vaccinated and 9 were vaccinated, HR-HPV was found on 5/9 of vaccinated patients (serotypes 26,82,30 and 59). Multiple infection (more than one HPV genotype) was found in 42 patients (12,5%)
Conclusion: This study underscores the importance of HPV molecular testing in confirming high-risk genotypes. Although the sample is limited findings indicate a significant prevalence of HPV-related abnormalities with HR-HPV genotypes present in both vaccinated and unvaccinated individuals. In our population multiple-infection is lower than reported in the literature. Despite small representation of vaccinated population in our sample, HR-HPV genotype persistence warrants further research in vaccine efficacy and genotype coverage.

E-PS-04-024
A polarising issue - turnaround times for synovial fluid cytology
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Background & Objectives: Synovial fluid analysis is the gold standard test for crystal arthropathies. The Royal College of Pathologists (RCPath) recommends a 7-10 day turnaround time (TAT) for cytopathology, and the Irish National Histopathology Quality Improvement Programme advises a similar TAT. There is some ambiguity in terms of expected TAT for synovial fluid - neither guideline mentions a specific TAT, though of note, the RCPath bone and soft tissue pathway does recommend analysis within 12-48 hours. We assessed TAT for these samples in Galway University Hospital, a tertiary hospital with a weekday cytology service.
Methods: Cytology cases tissue coded for crystals, and SNOMED coded gout or pseudogout between July 2023 and January 2024 were reviewed. Evaluated variables included: patient demographics, sampling date and location, date received into laboratory, report authorisation date. Request forms were also reviewed for date received in microbiology prior to receipt in cytology.
Results: Eighty samples were included in the analysis. 57.5% of samples were from inpatients. TAT within the laboratory was 98.75% within 48 hours, with one outlier reported within 72 hours during a public holiday period. The clinical TAT from joint aspiration to authorised report ranged from <24 hours to 6 days, with an average of 60 hours. Longer delays were seen prior to check in for samples taken Friday-Sunday or on public holidays. 51.25% of specimens were not analysed within 12-48 hours. There was no statistically significant difference between inpatient and outpatient TAT.
Conclusion: Though the recommended laboratory TAT was achieved, delays were identified in the overall turnaround, particularly on samples taken on non-working days. These delays may have clinical implications in terms of treatment decisions and length of stay. Potential solutions include a limited weekend cytology service or provisional wet prep reporting by clinicians. A need for greater clarity on TAT for specific cytology specimens has also been identified.

E-PS-04-025
PHOX2B is a reliable marker for diagnosing neuroblastoma in fine needle aspiration material
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Background & Objectives: Neuroblastoma (NB) is the most common solid extra cranial tumour in children, responsible for around 7 % of childhood cancer cases and 15 % of child cancer mortality. These tumours arise from primitive neural crest cells, most commonly in the adrenal medulla and sympathetic chain ganglia. For diagnosis, fine needle aspiration cytology (FNAC) can be preferred over core needle biopsies for its lower complication rate and quicker route to diagnosis. However, since neuroblastomas belong to the small round blue cell tumour (SRBCT) group they can sometimes be difficult to distinguish from other tumours in this group cytomorphologically without ancillary immunocytochemical staining. PHOX2B is a marker for differentiation of sympathetic and autonomic neurons and has been found effective in differentiating NB from other SRBCT on histologic material.
In this study, we aim to evaluate the sensitivity and specificity of the immunocytochemical marker PHOX2B in differentiating neuroblastomas from other small round blue cell tumours in fine-needle aspirated cytologic material.
Methods: A total of 43 cases of NB and other SRBCT were collected from the archives of the Department of Pathology and Cancer Diagnostics at Karolinska University Hospital between the years 2016 and 2023. All samples either already had been or were stained immunocytochemically (ICC) with PHOX2B, and histologic material from the same patient and tumour was stained with PHOX2B as control. All cases were reviewed by a panel of senior cytopathologists. Nuclear staining of PHOX2B in >5 % of tumour cells was considered positive.
Results: We found a sensitivity of 80 % and a specificity of 100 % on ICC of PHOX2B in diagnosing NB and differentiating it from other SRBCT when used on FNAC material.

Conclusion: We are proposing the use of PHOX2B as a reliable marker to diagnosing and differentiating neuroblastoma among other SRBCTs in FNAC as well as in histologic tissue samples.

E-PS-04-026

Identification of oxidized regenerated cellulose (surgicel) in transbronchial/transthoracic fine needle aspiration of pseudotumoral lesions following pulmonary lobectomy: a case series

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Background & Objectives: Topical hemostatic agents like oxidized regenerated cellulose (e.g., Surgicel) are commonly used during surgical operations. These substances are usually reabsorbed within two weeks at the surgical site; however, incomplete absorption can occasionally lead to foreign body reactions that mimic neoplastic recurrence. Imaging studies may not provide accurate diagnoses in such cases. This study aims to emphasize the role of fine needle aspiration (FNA) in diagnosing these changes in patients with suspected recurrence after lung cancer surgery.
Methods: Fine needle aspiration, either transbronchial or transthoracic, was performed in three patients with imaging findings suspicious for malignancy recurrence following pulmonary lobectomy, and cytological samples were evaluated at the Pathology Department of Hacettepe University.
Results: The clinical details and cytological findings of the three cases were as follows:
Patient 1: A 71-year-old female who had undergone right upper lobectomy for lung adenocarcinoma. Fifteen months after surgery, imaging revealed soft tissue thickening at the distal right main bronchus.
Patient 2: A 68-year-old male with right upper lobectomy for high-grade adenocarcinoma with mediastinal lymph node metastases. Four months post-surgery, PET-CT displayed FDG uptake in the right lower paratracheal and subcarinal regions.
Patient 3: A 55-year-old female who had left lower lobectomy for colloid adenocarcinoma. Three months postoperatively, FDG uptake was observed in an extrapleural mass.
In all cases, FNA revealed the presence of inorganic, elongated, quadrangular foreign body material, exhibiting birefringence under polarized light, in a dense proteinaceous background—findings consistent with oxidized regenerated cellulose (Surgicel). Notably, one case also showed a foreign body giant cell reaction.
Conclusion: FNA is a rapid and minimally invasive technique for identifying oxidized regenerated cellulose causing pseudotumoral reactions. Familiarity with its cytomorphological features is essential for accurate diagnosis and appropriate patient management.

E-PS-04-027

A comprehensive study of alveolar soft tissue sarcoma: five cases with cytology, immunocytochemistry and molecular alterations

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Background & Objectives: Alveolar soft part sarcoma (ASPS) is a rare tumour of uncertain origin with predilection for the lower extremities. It has an indolent course and often the patient has already metastases when the disease is discovered. ASPS has a specific translocation between the transcription factor TFE3 in Xp11.2 and ASPSCR1/ASPL in chromosome 17. This translocation can be detected by immunocytochemistry with an antibody against TFE3 , FISH or PCR. Here we describe five cases in a period of 12 years from the archives of our institution and compare with publish cases related to cytologic diagnosis of ASPS and importance of immunocytochemistry.
Methods: A total of five cases diagnosed as ASPS between 2012 and 2024 were retrieved from the archives of the Department of Pathology and Clinical Cytology of Karolinska University Hospital, Stockholm, Sweden. Cytologic and histologic material were reviewed by two cytopathologists. Molecular analys were performed in all five cases. Immunocytochemistry for TFE3 was performed in two cases.
Results: All five cases showed typical cytologic features for ASPS. Cellular smears with dominance of bare nuclei and prominent nucleoli. Aggregates of tumour cells were also present, with light fine granulated cytoplasma, with one case showing vacuolated cytoplasm. A granulated material was present in the background. All cases showed TFE3::ASPSCR1 translocation on PCR. Two cases were positive for TFE in immunocytochemistry. Two of our cases were in the lower extremities and two patients had lung metastasis at diagnosis. These features are in accordance with previous published cases of ASPS. Medium age is 38 years, which is a bit higher that expected for ASPS.
Conclusion: ASPS is a rare tumour that must be remembered in young patients with soft tissue tumours. The typical cytomorphology can be wrongly mistaken as carcinoma. Immunocytochemistry is useful for the diagnosis but confirmation with PCR should be mandatory.

E-PS-04-028

Challenges in anal cytology for screening high-grade squamous neoplasia and above lesions in high-risk populations: a single institution's experience over the past three years

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Background & Objectives: Anal high-grade squamous intraepithelial lesions (HSIL) are precursors to anal squamous cell carcinoma, and screening with anal cytology in high-risk populations, such as HIV-positive patients, is recommended. Anal cytology is used alongside digital rectal examination and high-resolution anoscopy. However, the sensitivity of anal pap cytology has historically been low, and its specificity is variable. The aim of this study is to evaluate the correlation between anal cytology and follow-up biopsy results in high-risk patients (HIV-positive), focusing on improving the detection of HSIL.
Methods: Retrospective cohort study conducted at our institution reviewed anal cytology cases with follow-up biopsy results from January 1, 2022, to March 8, 2025, at a level three trauma centre.
Results: A total of 812 anal pap smears were analysed during the 3-year period, with 97 patients meeting the inclusion criteria. Of these, 91.8% (n=89) were classified as abnormal on cytology: 13.4% (n=13) had high-grade cytology (ASC-H/HSIL), 43.3% (n=42) had atypical cytology (ASC-US), and 35.1% (n=34) had low-grade cytology (LSIL). Follow-up biopsies revealed that 49.5% (n=48) were diagnosed with HSIL/AIN2-3, 2.1% (n=2) with squamous cell carcinoma, 47.4% (n=46) with LSIL/AIN1, and 1.0% (n=1) had negative results. Of the cases with high-grade cytology, 92.3% (n=12) had corresponding high-grade or worse histology. Among biopsy-proven high-grade lesions, 92% (n=46) had abnormal cytology: 30% (n=15) ASC-US, 38% (n=19) LSIL, and 24% (n=12) ASC-H/HSIL.
Conclusion: While the specificity of high-grade cytology was high (97.8%) and correlated well with high-grade histology, the sensitivity remains low. A significant portion of patients with high-grade histology and above had preceding low-grade or atypical cytology. Successful cytology sampling is crucial for improving sensitivity, and high-risk patients with any abnormal anal pap screening results should undergo further evaluation by high-resolution anoscopy.

E-PS-04-029

Cytology vs histology in lung cancer diagnosis: a concordance study

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Background & Objectives: Bronchial biopsies and cytological specimens (bronchial brushing, washing and aspiration) are frequently used in parallel to investigate suspected pulmonary neoplasms. While histology is often considered the reference method, cytology with cell-block preparation may also provide relevant diagnostic and molecular information. This study aimed to evaluate the concordance between histology and cytology in terms of malignancy and histological subtype.
Methods: We retrospectively analysed 40 diagnostic episodes in patients with clinical suspicion of lung neoplasm, each comprising both histological and cytological sampling. Cytological specimens were processed using the *cell block* technique, enabling improved cytomorphological assessment and ancillary studies. Each episode was considered independently, reflecting real-life clinical decision-making, including repeated procedures when required. Concordance between methods was evaluated using Cohen's kappa coefficient, and discordant cases were further analysed.
Results: Among the 40 diagnostic episodes with valid results, overall agreement regarding malignancy was 72.5%, with moderate concordance (Cohen's kappa = 0.44). Cytology identified malignancy with specific subtyping in 5 cases where histology was negative. Conversely, histology identified malignancy in 6 cases missed by cytology. Among discordant cases, cytology more frequently diagnosed adenocarcinoma, while histology showed a broader distribution across subtypes. Subtype concordance was evaluated in 9 episodes where both methods provided a specific diagnosis. A perfect agreement was observed in this subgroup (Cohen's kappa = 1.00), which included adenocarcinoma and squamous cell carcinoma.
Conclusion: Cytological assessment with cell-block processing shows high concordance with histology and may provide complementary or even superior diagnostic information in selected cases. Its role in the diagnostic work-up of lung cancer is particularly valuable when histological sampling is limited or inconclusive.

E-PS-04-030

A comprehensive review of sarcoma involvement in fluid cytology with focus on cytomorphology: a 10-year study at an Indian oncology centre

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Background & Objectives: Malignant effusions are some of the most common specimens evaluated in cytopathology. In comparison with carcinomas, sarcomas are rare, accounting for less than 1% of primary adult malignancies and the presence of sarcomas in effusion specimens evaluated by cytology is extremely rare. This study evaluates cytomorphology of sarcomas in fluids and determines characteristic features for identification and classification.
Description of clinico-pathological landscape in known cases of sarcomas, involving body fluid with emphasis on cytomorphologic details.
Methods: This study is based on a 10-year experience, conducted from January 2014 to February 2025, at a tertiary care oncology institute in India. It includes cases identified as positive for sarcoma involvement through fluid cytology, encompassing pleural, ascitic, and cerebrospinal fluid specimens.
Results: A total of 30 fluid samples/cases were studied, including 6 CSF, 5 ascitic, and 19 pleural fluid. The case spectrum included 11 cases of Ewing Sarcoma, 5 of rhabdomyosarcoma, 4 cases of osteosarcoma, 3 of synovial sarcoma, 2 of malignant peripheral nerve sheath tumour, one case each of chondrosarcoma, leiomyosarcoma, angiosarcoma, extrarenal rhabdoid tumour and desmoplastic small round cell tumour.
Conclusion: Although metastasis of carcinomas of lung and liver occur with relative frequency, the presence of sarcomas in effusion specimens evaluated by cytology is extremely rare. Cytological evaluation of sarcomas in exfoliative cytology specimens are complicated by several factors. They are commonly hypo cellular with altered cytomorphology. The cells tend to round up in fluids and lack tissue arrangement or vascular, stromal pattern as seen in histopathology and fine needle aspiration specimens. This study highlights on the evaluation of fluids for sarcomatous exfoliation with focus on cytomorphology.

E-PS-04-031

Outcome of Bethesda III-V categories thyroid nodules: single institution experience

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Background & Objectives: Fine Needle Aspiration Biopsy (FNAB) is a widely used diagnostic technique for thyroid nodules. The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) significantly enhances its diagnostic accuracy. The aim of this study is to analyse Bethesda category III, IV and V nodules with emphasis on the final histological diagnosis.
Methods: We retrospectively analysed FNAB diagnosed in our department between January 2005 and December 2023 retrieved from our files (12,670 samples). All thyroid aspiration specimens were stained with haematoxylin and eosin (HE). All cases received a microscopic description and diagnosis including a category comparable to BSRTC. We reclassified all cases using BSRTC 3rd edition.
Results: 565 samples (4.5%) from 508 patients were diagnosed as Bethesda III (139; 27.4%), IV (257; 50.6%), or V (112; 22.0%). Samples were representative in 93%, of limited adequacy in 7%. 71.2% of Bethesda III nodules underwent follow up FNAB (median within 6.4 months), of these, 43.9% were downgraded to Bethesda II, 20.2% remained in Bethesda III-V, 4.3% were inadequate and 2.9% were upgraded to Bethesda VI and histologically confirmed as malignant. 28.8% were lost to follow-up. 73.5% of Bethesda IV nodules underwent surgery (median within 3.4 months), of these 13.6% were malignant, and 56.8% benign. 2.3% received repeat FNAB and were again classified as Bethesda IV, 27.2% were lost to follow-up. 78.6% of Bethesda V nodules underwent surgery (median within 1.9 months), of these were 50.0% malignant and 28.6% benign; 17.0% were lost to follow-up. The frequency of malignancy between the 3 cytological groups was statistically significant ($p<0.001$; chi^2 test).
Conclusion: The study confirms the diagnostic variation across Bethesda categories III - V with respect to underlying histology and endorses the importance of consistent follow-up and optimized patient management. The use of liquid-based cytology would facilitate molecular reflex testing in challenging cases.

E-PS-04-033

Morphological findings in cytology based on HPV types

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Background & Objectives: HPV typing has gained importance since the causality relationship between cervical cancer and HPV was determined. The aim of our study is to determine the predictive value of

cytological findings and high-risk HPV type association in cases with PAP smear test and positive high-risk HPV test.
Methods: A total of 490 cases with a positive PAP smear and a single high-risk HPV subtype evaluated between January 2021 and December 2022 in the Department of Medical Pathology of Health Sciences University Haydarpaşa Numune Training and Research Hospital were included in the study. Molecular high-risk HPV subtypes detected by Real Time PCR were obtained from pathology reports. Liquid-based cytology slides were examined microscopically for classical coilocytes, perinuclear halo, multinucleation, nuclear hyperchromasia, nuclear membrane irregularity, naked nucleus, atypical cell pattern, dyskeratosis, parakeratosis, squamous metaplasia and inflammation. The relationship between high-risk HPV subtypes and cytomorphologic findings was evaluated.
Results: There was a statistically significant correlation between the presence of classical coilocytes on liquid-based cytology and positive detection of other high-risk HPV types ($p<0.001$). A statistically significant correlation was found between nuclear hyperchromasia and nuclear membrane irregularity and HPV16 positive detection ($p<0.47$, $p<0.17$, respectively). No statistically significant correlation was found between high-risk HPV types and the presence of perinuclear halo, multinucleation, naked nucleus, atypical cell pattern, dyskeratosis, parakeratosis, squamous metaplasia and inflammation.
Conclusion: In cases where access to HPV testing is limited for various reasons, cytomorphologic findings may be helpful for HPV subtyping.

E-PS-04-034
The impact of COVID-19 on cervical cytology services in the Free State, South Africa
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Background & Objectives: Cervical cancer is a major global health issue, with the highest rates in low- and middle-income countries. Screening methods such as Papanicolaou (Pap) smears and human papilloma virus (HPV) testing are critical for early detection and treatment. The COVID-19 pandemic disrupted cervical cancer screening services worldwide, raising concerns about an increase in undiagnosed cases. The aim of this study was to investigate the impact of the COVID-19 lockdown on cervical cytology screening in the Free State Province of South Africa.
Methods: In this retrospective, descriptive study, data from the National Health Laboratory Service (NHLS) electronic database spanning from 25 September 2019, to 5 October 2022, were analysed to compare screening rates six months before, during and six months after the pandemic.
Results: This study found a significant decline in cervical screening rates during the pandemic, with regional disparities within the Free State province. The average daily specimen collection rate in the Free State declined by 52.1% during the peak of the pandemic. A slight decrease in the adequacy rates of cervical cytology samples were noted during the lockdown. Differences in the daily rates of premalignant, malignant and normal diagnoses were identified however, these were not statistically significant. A moderate negative correlation was found between the number of positive COVID-19 tests and the number of Pap smears conducted.
Conclusion: The pandemic markedly affected cervical cancer screening rates, which could have long-term public health implications. These results emphasise the need for adaptable screening strategies and resilient healthcare systems to maintain essential preventive and diagnostic services during global health crises.

E-PS-04-035
Application of ROSE (rapid on-site evaluation) in the study of pulmonary nodules by CT (computerized tomography): preliminary analysis in 49 patients
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Background & Objectives: Rapid on-site evaluation (ROSE) in endoscopic and imaging procedures has been proven useful in obtaining suitable specimens for cytologic or histologic diagnosis. We evaluated the effectiveness of ROSE on specimen adequacy and diagnostic accuracy in pulmonary hard-to-reach nodules, by CT (computerized tomography).
Methods: Forty-nine patients underwent CT-guided biopsy for suspicious pulmonary image with ROSE by cytologic imprint. A diagnosis of negative, representative non-conclusive (RNC), atypia, suspicious of malignancy (SOM) or insufficient was made. For insufficient, three samples or any clinical contraindication were demanded. When a diagnosis of atypia or SOM was made, an extra sample for molecular study was obtained, and for atypia suspicious of lymphoproliferative disease (LPD), material for flow cytometry analysis was separated. ROSE diagnoses were compared with final diagnoses.
Results: We collected 15(30,6%) negative, 7(14,3%) RNC, 9(18,4%) atypia, 17(34,7%) SOM and 1(2%) insufficient ROSE diagnoses. A unique sample for on-site diagnosis was needed in all cases, except for the insufficient. Final definitive diagnosis was made in 95,9% of the cases: 19 negative (14 of ROSE negative and 5 of ROSE RNC); 28 malignant (25 carcinomas and 3 LPD) included all ROSE SOM and atypia and 2 of ROSE RNC. Two definitive diagnoses were insufficient (the ROSE case and one ROSE negative). Correlation with ROSE diagnosis was observed in 46 cases. For atypia cases, 5 were suspicious of LPD, with confirmed diagnosis in three (the remaining two corresponded to small cell carcinoma). No false positive ROSE diagnoses were collected. The diagnostic sensitivity was 80% with a specificity of 100%, concluding a PPV (positive predictive value) of 100% with a NPV (negative predictive value) of 74%.
Conclusion: Our results indicate that ROSE exhibits high diagnostic accuracy when applied in the study of pulmonary hard-to-reach nodules by CT and it optimises the specimen adequacy, avoiding rescheduling the patient.

E-PS-04-036
Bronchial aspirate surprise: cytological diagnosis of amyloidosis!
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Background & Objectives: Amyloidosis encompasses a group of disorders characterized by extracellular deposition of misfolded proteins (amyloid), leading to progressive organ damage. Definitive diagnosis traditionally relies on invasive biopsies for histopathological identification of amyloid deposits. Congo red staining, with its characteristic apple-green birefringence under polarized light, remains the gold standard for confirmation. Minimally invasive cytological specimens, such as bronchial aspirates, present a promising diagnostic alternative but require further systematic validation. This case study aims to: (1) demonstrate the utility of cytological specimens in diagnosing amyloidosis, (2) highlight the role of Congo red staining in differentiating amyloid from mimicking entities in bronchial samples, and (3) emphasize that amyloidosis may be rarely observed in cytology.

Methods: A 51-year-old woman with Sjögren's syndrome presented with dyspnea and cough. Thoracic CT revealed bilateral nodular lesions, central consolidations, bronchiectasis, and a 4 cm thin-walled cavitary lesion in the left lower lobe. Suspecting granulomatous/fungal infection or malignancy, fiberoptic bronchoscopy was performed. Aspirated material was processed using the ThinPrep method for cytology: smears were Papanicolaou-stained, and cell blocks were prepared with haematoxylin-eosin. Congo red staining was performed, and slides were examined under polarized light microscopy to confirm amyloid deposition.
Results: Cytological smears revealed bronchial epithelial cells, histiocytes, and lymphocytes. Cell block analysis identified eosinophilic amorphous material admixed with histiocytes and epithelial cells. Congo red staining demonstrated red-orange positivity under light microscopy, with characteristic apple-green birefringence under polarized light, confirming amyloid. The findings distinguished amyloid from differentials such as mucus, alveolar proteinosis, fibrin, and corpora amylacea.
Conclusion: This case underscores the diagnostic efficacy of Congo red staining in cytological specimens obtained via minimally invasive bronchoscopy. It highlights the critical role of histochemical methods in differentiating amyloid from morphologically similar entities in pulmonary samples. Integrating Congo red into cytopathology workflows enhances diagnostic precision, reducing reliance on invasive biopsies in suspected amyloidosis cases.

E-PS-04-037
Indeterminate thyroid follicular nodule of the Italian classification: other morphological features could drive the risk of malignancy?
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Background & Objectives: The "Italian consensus for the classification and reporting of thyroid cytology" (ICCRTC), proposed to split the "indeterminate" category (TIR3) in two subcategories with different risk of malignancy: TIR3A and TIR3B. TIR3B nodules frequently undergo surgery even if at final histology only a part (hypothetically 30%) is malignant. This study aim is to identify potential cytological features associated with malignancy in a series of TIR3B nodules.
Methods: We retrospectively evaluated 142 patients who underwent thyroid FNA at the University Hospital of Pisa from 2017 to 2019, and received a cytological diagnosis of TIR3B. Overall, 147 TIR3B nodules were revised. For each nodule, the following features were evaluated: architecture (microfollicular, trabecular, cluster or single cells), the presence and type of colloid, cellularity, follicular cells characteristics (size, elongated form, eosinophilic cytoplasm, nuclear size, chromatin type, presence of nuclear grooves and presence of nucleoli) and background composition (blood, macrophages, lymphocytes, necrosis). According to histology, patients were divided into thyroid cancer (TC) or benign nodules. Chi-square test were used to compare groups, while ROC curves were used to determine the diagnostic performance.
Results: Among the 147 TIR3B nodules, at final histology only 60 (40,8%) were benign and 87 (59,2%) were TC (including PTC, FTC, PDTC and NIFT-P). We found that predictors of thyroid cancer are: elongated cells (p-value: 0,01) and nuclear grooves (p-value: 0,03). Elongated cells had a specificity of 0,80, a sensitivity of 0,41, an accuracy of 0,57, PPV of 0,75 and NPV of 0,48. Nuclear grooves had a specificity of 0,27, a sensitivity of 0,88, an accuracy of 0,63, the PPV of 0,64 and the NPV of 0,62.
Conclusion: Cytological features, such as elongated follicular cells and nuclear grooves, could be very important in TIR3B risk stratification. Further analysis should be carried on to confirm the data.

E-PS-04-038
Anaplastic thyroid carcinoma cytopathology – the good, the bad, and the ugly: a case report
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Background & Objectives: Anaplastic Thyroid Carcinoma (ATC) is a rare but highly aggressive malignancy with a poor prognosis. Cytological diagnosis is crucial for early intervention, but it remains challenging because of its overlapping characteristics with other thyroid neoplasms. We present a case of ATC with unique cytomorphological features, emphasizing the associated diagnostic challenges and conducting an extensive literature review highlighting the wide cytomorphological spectrum seen in association with this aggressive tumour.
Methods: Herin, we present a rapidly enlarged thyroid mass in a 61-year-old patient with a fine needle aspiration reported provisionally as unsatisfactory. Case was reviewed at our specialised Head and Neck unit and a diagnosis of ATC was suspected as very spare highly atypical cells with bizarre nuclei were detected and were thought to be degenerate at first sight. Subsequent biopsy confirmed the diagnosis, and the tumour was deemed non-resectable clinically and radiologically.
Results: This case including the detailed literature review have emphasized on the cytological spectrum of ATC—the "good" (high cellularity facilitating diagnosis), the "bad" (sparsely cellular aspirates due to extensive fibrosis, tumour cells mixed with extrathyroidal tissue due to rapid tumour infiltration and overlapping features with other tumours), and the "ugly" (necrotic smears and morphologically features of squamous cell carcinoma, spindled cell neoplasm, and multinucleated giant cell-like tumours posing diagnostic challenges).
Conclusion: Given the wide cytological spectrum of this tumour, the lack of supportive diagnostic ancillary testing such as immunocytochemistry, and the challenge of obtaining a meaningful molecular profile due to the limited number of cells in the aspirates, it is crucial to familiarize oneself with the atypical and rare cell morphology seen in association with this tumour. This will help prevent misinterpretation and ensure timely clinical intervention.

E-PS-05 E-Posters Dermatopathology

E-PS-05-001
A highly aggressive giant malignant chondroid syringoma of the occipital scalp with rapid tumour recurrence and progression to lymph node and pulmonary metastasis
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Background & Objectives: Malignant chondroid syringoma (MCS) is a rare cutaneous adnexal tumour characterized by its potential for local recurrence and distant metastasis, with only 52 cases reported in published literature to date. It most frequently arises on the trunk and extremities, with involvement of the head and neck being exceptionally uncommon. The median tumour size is approximately 4 cm, and lesions exceeding 5 cm have been associated with increased risk of metastasis and mortality.
Methods: We report a rare and clinically striking case of giant MCS arising on the occipital scalp of a 38-year-old woman who presented with a 15.0 × 10.0 × 10.0 cm ulcerated, exophytic mass that had

remained indolent for ten years before undergoing rapid growth over a two-month period. Wide local excision with partial-thickness skin grafting was performed, yielding negative surgical margins.
Results: However, within six weeks, the patient developed local recurrence followed by rapidly progressive, multilevel, bilateral cervical lymphadenopathy, and subsequent pulmonary metastases.
Conclusion: This case highlights a particularly aggressive clinical course of MCS and illustrates the tumour's capacity for sudden transformation and rapid progression, even after prolonged latency. It underscores the importance of maintaining a high index of suspicion for aggressive transformation in longstanding lesions and reinforces the need for early diagnosis and timely surgical intervention. Additionally, this report contributes to the limited literature on MCS and supports the goal of pursuing a formal subclassification of these lesions into low-grade and high-grade variants to facilitate more consistent prognostication and standardized management approaches.

E-PS-05-002
Basal cell carcinoma invading the humerus: a case report
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Background & Objectives: Basal cell carcinoma (BCC) is a common skin cancer, but its invasion into the bone is exceedingly rare. This report highlights a case of BCC with unusual osseous involvement.
Methods: A 72-year-old woman, known with schizophrenia, was hospitalized for progressive right arm and shoulder pain. She related that the pain was progreesively aggravated in the last 7 years. CT-scan revealed an ill-defined mass with soft tissue and bone invasion, osteolysis, and a pathologic humeral fracture. Surgical management included right arm disarticulation, glenoid fossa resection, and partial clavicle removal. The surgical specimen was send for histopathological assesment.
Results: The macroscopic examination revealed a large nodular tumour with extensive ulceration and direct bone invasion. Histopathologic analysis showed proliferation of basaloid cells, arranged in nests, with peripheral palisading, cleft-like spaces, necrotic foci and loose myxoid stroma. Immunohistochemical profile of tumour cells showed positivity for BerEp4, while CK7, EMA and CEA were negative, supporting the diagnosis of BCC with bone invasion. The patient is still alive at five months after surgery.
Conclusion: Although BCC is a slowly growing tumour, in neglected cases it can have aggressive potential with invasion of deep soft tissues and bone. Early recognition and prompt intervention remain of paramount importance in optimizing patient outcome and preventing further progression.

E-PS-05-003
Pathological spectrum and epidemiological trends of skin adnexal tumours: a 6-year retrospective study
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Background & Objectives: Skin adnexal tumours (SATs) are rare tumours with a wide spectrum of differentiation, making them a diagnostic challenge. We conducted the first 6-year retrospective study in Algeria to review and shed the light on the most common SATs in the local population.
Methods: We reviewed 146 cases of SATs that we got over a 6-year period (January 2019-December 2024). All relevant data have been collected.
Results: Our study found a prevalence of 0.34%, and a slight male predominance, with a sex ratio of 1.18:1, consistent with findings reported in multiple studies.
An evaluation of clinicopathological features highlighted a predominance of tumours located in the head-and-neck region (69.86%) due to the rich distribution of skin appendages with high sun exposure.
SATs are a wide group that arise from multipotent stem cells into follicular, sebaceous, eccrine and apocrine tumours, with a considerable morphological overlap between individual entities, making histopathology the gold standard for diagnosis. Histopathological analysis of our cohort demonstrated eccrine/apocrine differentiation in 81 cases (55.48%), followed by follicular then sebaceous differentiation, with pilomatricoma being the predominant SAT, and sebaceous carcinoma as the most frequent malignant tumour.
Several studies, such as ours, showed that malignant tumours are rare compared to benign counterparts (7.53% vs. 92.47%). However, they are more aggressive with high potential of metastasis, making accurate diagnosis essential for appropriate therapeutic management. Benign SATs can be a falsely reassuring diagnosis as there may be genetic diagnoses associated with selected SATs, such as Muir-Torre/Lynch syndrome for sebaceous gland tumours, which underlines the importance of emerging molecular markers, genetic counselling and surveillance.
Conclusion: Our study largely aligns with the literature, proving that these tumours are rare, often in the head-and-neck region, and predominantly benign. Their precise diagnosis and correct treatment are crucial for optimal patient care.

E-PS-05-004
Hidradenoma featuring lymph node metastasis: a rare phenomenon
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Background & Objectives: Hidradenoma is considered a benign sweat gland tumour. While lymph node metastases are more common in malignant counterparts (hidradenocarcinoma), rare cases of lymph node involvement in so-called benign hidradenomas have been reported. We present a case of hidradenoma with lymph node metastasis.
Methods: A 59-year-old man with a history of previous metachronous gastric (tubular, intestinal-type, pT1a N0 R0) and colorectal (NOS, G2, pT4b N0 R0) adenocarcinomas, 5 and 4 years earlier, respectively, with no further evidence of progression; microinstability testing was negative. He presented with a nodular skin lesion (1.2 cm largest dimension) on the chest, which was excised. Three years later, he developed an enlarged axillary lymph node, which was also excised.
Results: Histopathology of the skin lesion revealed a well-circumscribed dermal solid-cystic neoplasm composed of bland clear (glycogen: PAS/PASD-), eosinophilic, and focally mucinous cells with focal stromal sclerosis. The mitotic index was low (<1/mm²). No significant atypia, necrosis, lymphovascular, or perineural invasion was observed. Immunohistochemistry showed diffuse and strong p40 and p63 expression, ductal differentiation (CEA and EMA), and absence of myoepithelial markers (SMA and S100), confirming hidradenoma. Three years later, histopathology revealed an axillary lymph node with identical neoplastic features, indicating metastasis. Next-generation sequencing (primary tumour and lymph node metastasis) identified a CRCT1::MAML2 fusion gene. No recurrence was observed after one year of follow-up.

Conclusion: We still dispute the aetiology and never reported neoplasm association after excluding known cancer-predisposing syndromes (e.g., Lynch/Muir Torre). Nevertheless, our case highlights the rarely reported lymph node metastasis in tumours with benign hidradenoma features, adding evidence to the exceptional "benign metastasis" phenomenon. Although the long-term prognosis remains unclear, current evidence suggests that surgical excision is the therapeutic modality of choice and extended follow-up may be more suitable than adjuvant treatments, given the seemingly favourable clinical outcomes.

E-PS-05-005

10 year histopathological review of adnexal tumours of the skin in Accra, Ghana

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Background & Objectives: Adnexal tumours of the skin are a wide range of skin neoplasms which arise from the sebaceous glands, hair follicles and sweat glands. Due to the rarity of these neoplasms, there are very limited studies on them in sub- Saharan Africa. This report aims to review the histopathological pattern of adnexal tumours of the skin diagnosed in the Department of Pathology of the Korle Bu Teaching Hospital in Accra, Ghana.
Methods: A retrospective analysis of histopathology records in the Department of Pathology of the Korle Bu Teaching Hospital in Accra, Ghana was conducted. Data was collected over a 10 year period, from 2015- 2024 and analysed using STATA 14.
Results: A total of 69 cases were reported in the period, accounting for 4.7% of the total number of skin lesions reported in the same period. The male-to-female ratio was 1:1.4. The patient ages ranged from 7 months to 90 years with the commonly affected age group being 60-69 years. The head and neck region was the most commonly occurring site, accounting for 63.3%. The sweat gland derived tumours were the most frequently diagnosed, making up 47.8% of reported cases, then follicular derived tumours, accounting for 27.5% and lastly the sebaceous gland tumours, making up 24.6%. Most of the reported cases were benign (95.7%). Chondroid syringoma was the most frequent benign tumour (15.9%), while eccrine porocarcinoma was the most common malignant tumour (66.7%).
Conclusion: Most adnexal tumours of the skin in our setting were benign, with the commonest tumours being of sweat gland origin. The tumours were most frequently located in the head and neck region. This study contributes valuable regional data on the histopathology of adnexal tumours and highlights the need for further research in this area for prognostic and clinical significance.

E-PS-05-006

Unveiling the complexity of cutaneous collision tumours: a rare triad of squamous cell carcinoma, basal cell carcinoma and melanocytic nevus

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Background & Objectives: Cutaneous collision tumours (CCT) are rare entities defined as two or more neoplasms that arise in close proximity to each other yet separated by a tumour-free zone. Although the exact pathogenesis remains unclear, it is believed that neoplastic heterogeneity and paracrine effects on the tumour's nearby epithelial and stromal elements play important roles.
Methods: We report the case of an 81-year-old male patient presenting with an ulcered nodular lesion on the nasal area, measuring 9x7mm. Subsequently, the patient underwent surgical excision. The resected specimen was submitted and further processed in our Pathology Department. Tissue paraffin-embedded sections were stained using routine Haematoxylin-Eosin, and complementary immunohistochemical reactions were performed.
Results: Microscopic examination revealed two distinct malignant cell populations separated by a clear transition zone. A squamous-cell carcinoma (SCC) was noted, characterized by plaques of atypical keratinocytes with abundant eosinophilic cytoplasm, marked nuclear pleomorphism, and focal keratin-pearl formation, which exhibited positivity for EMA. A second malignant proliferation was present less than 1 mm from SCC and was composed of basaloid cells with large hyperchromatic nuclei, peripheral palisading, and peritumoral retraction artifacts. The atypical basaloid cells were positive for BCL-2 and Androgen-Receptor. Additionally, a third neoplastic lesion, a melanocytic nevus, was identified nearby SCC. All surgical margins showed residual tumour cells.
Conclusion: Non-melanoma skin cancers (NMSCs) mostly arise on sun-damaged skin, with a particular predominance for head and neck region. CCT is an umbrella term that encompass a wide range of lesions including benign-benign, benign-malignant or malignant-malignant neoplasms. The most frequent CCT occurs between basal-cell carcinoma and a melanocytic nevus. Thus, the association of two distinct NMSCs within the same lesion is particularly rare, it may indicate a more aggressive behaviour. CCT are unique but well documented entities that usually pose diagnostic challenges to both clinicians and dermatopathologists.

E-PS-05-007

Basal cell carcinoma with a mysterious guest: dermal granuloma surrounding uninvited Demodex mites

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Background & Objectives: This article presents the case of a 74-year-old male patient previously diagnosed with basal cell carcinoma on the zygomatic region of the face, with a dermal granulomatous foreign body inflammatory reaction suggestive for *Demodex* mites. As studies within the current existing literature suggest a possible correlation between demodicosis and basal cell carcinoma, we present a case of demodicosis gravis in order to raise awareness to a rare histopathological variant.
Methods: After the initial basal cell carcinoma diagnosis, the patient was admitted to the General Surgery Department of Emergency City Hospital in Timisoara, Romania. A surgical excisional skin biopsy was performed with a subsequent histopathological examination using morphological Haematoxylin–Eosin (HE) staining. Microscopic examination revealed incomplete surgical resection margins. Considering the incomplete histological margins, the patient was once again referred to the General Surgery Department of Emergency City Hospital in Timisoara, Romania for further surgical treatment. On this occasion, three excisional skin biopsies were performed on the remaining scar tissue and processed in the manner previously described.
Results: After staining with Haematoxylin–Eosin, microscopic examination of the skin fragments revealed a dermal granulomatous reaction with multinucleated foreign body giant cells surrounding suture material, as well as multinucleated foreign body giant cells, epithelioid cells

and lymphocytes surrounding microorganisms suggestive for *Demodex* spp. Dermal granulomas with phagocytized mite remnants in foreign body giant cells indicate a distinctive variant of demodicosis gravis. No further cancerous cells were identified.
Conclusion: Within the current existing literature, demodicosis is linked to various dermatoses and a possible correlation between demodicosis and basal cell carcinoma is also under inquiry. We present this case of demodicosis gravis in order to improve awareness to a distinctive histopathological variant with dermal granulomatous inflammatory reaction in a patient previously diagnosed with basal cell carcinoma.

E-PS-05-008
An unusual manifestation of extranodal Rosai-Dorfman disease
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Background & Objectives: Rosai-Dorfman disease (RDD) is a histiocytic disorder of uncertain aetiology. Though initially described as a lymph node disease, extranodal lesions can be the only manifestation, 10% of cases featuring soft tissue involvement. Multicentric and recurrent disease is exceedingly uncommon. The following case report features an unusual RDD presentation with recurrence.
Methods: We report a case of a 56-year-old man, which showed a loosely delineated subcutaneous occipitocervical mass, measuring 34/81/56 mm, with mobile superjacent skin on clinical examination and involvement of subjacent muscle without bone invasion on computed tomography. Surgical excision was performed. One month later, the patient showed on clinical examination a thoracic cutaneous nodular mass (13/11/7 mm), which was excised.
Results: Histopathology showed in the first (subcutaneous) sample a loosely distributed reactive histiocyte population without atypia, with epithelioid histiocytes with vesicular nuclei, foamy macrophages, some of them with intracytoplasmic lymphocytes (emperipolesis), rare multinucleated giant cells, associated with brisk inflammatory infiltrate. The histiocytic proliferation extended in the peripheral adipose and muscle tissue, without involvement of the lymph node structures. Histopathology showed in the second (cutaneous) sample a nodular, loosely delineated histiocytic proliferation without atypia in the deep dermis, which consisted of foamy macrophages, some with emperipolesis, epithelioid histiocytes, plasma cells, eosinophils, and neutrophils. Immunohistochemistry showed CD68+, CD163+ and SOX10- histiocytic proliferation, frequent S100+ macrophages, and Ki67+ in 15-20% of the lymphoplasmacytic infiltrate.
Conclusion: The samples' histopathology and immunophenotype revealed extranodal soft tissue RDD with cutaneous recurrence. The timeframe between the two lesions' debut was short (five months), but the first clinical and computed tomography examination did not objectify thoracic or other locations anomalies. Considering these findings, multicentric RDD was not a viable hypothesis. The only accurate conclusion pertains to soft tissue RDD recurrence, which is exceedingly rare and, according to our knowledge, with no other literature report of a cutaneous recurrence.

E-PS-05-009
Juvenile Scleroderma: diagnostic challenges and insights in a series case study
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Background & Objectives: Juvenile scleroderma represents the third most frequent rheumatic condition in childhood, with an incidence rate of 0.34-0.9 cases every 100,000 children per year, age ≤16 years. JLS has a poorer outcome than LS, with high morbidity due to major disfigurement and functional impairment, while mortality is extremely rare. Histopathologic changes reflect stages of the localized skin disease but are limited by sampling bias, and repeated biopsies are inconvenient and discouraged. Regardless, they can be useful in cases with atypical skin presentation.
Methods: In our archive, we discovered 2 cases in the last 10 years of JLS with different clinical presentations: one presented a 1-year-old atrophic and sclerotic white area, while the second presented a 4-month-old pink patch lesion on the thigh that was slowly spreading to the leg. In both cases, a biopsy was performed for differential diagnosis. The samples, upon arrival, were fixed in formalin, processed, embedded in paraffin, and a traditional slide stained with haematoxylin and eosin was prepared.
Results: The slides showed fibrosis and sclerosis of the reticular and papillary dermis with a mild lympho-histiocytic inflammatory infiltrate with fibroblasts both peri-adnexal and perivascular, and with collagen cords sometimes invading the adipose tissue. The histologic presentation confirmed the diagnosis of JLS in an intermediate phase in both cases.
Conclusion: JLS is a broad disease and, in some cases, a very severe disorder that can become highly disabling. Most JLS patients who receive timely and appropriate treatment have a favourable prognosis, with most achieving remission on treatment. Early diagnosis is crucial, and even if a biopsy is not needed in most cases, when the clinical presentation and history are not decisive, histologic analysis and dialogue between the clinical team and pathology can be the best option for prompt diagnosis and treatment.

E-PS-05-010
Recurrent eccrine spiradenoma with malignant transformation: a diagnostic pitfall
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Background & Objectives: Eccrine spiradenoma is a rare benign adnexal tumour, but malignant transformation (spiradenocarcinoma) poses significant diagnostic challenges due to overlapping histological features. We report a case of recurrent spiradenoma with malignant progression, emphasizing clinicopathological correlation.
Methods: A 48-year-old female presented with a 5-year history of a recurrent anteromedial right leg mass. Initial biopsy revealed cystic eccrine spiradenoma. Following recurrence, complete excision was performed. Comprehensive pathological evaluation included macroscopic examination, histopathological analysis with haematoxylin and eosin staining, and immunohistochemical studies (SMA, S100, CK7, CK18, Ki67). Diagnostic assessment incorporated WHO criteria for malignant transformation.
Results: Macroscopic evaluation identified two well-circumscribed subcutaneous nodules (2.2 cm and 1.5 cm) showing cystic degeneration and haemorrhagic changes. Histopathological examination demonstrated characteristic benign spiradenoma components juxtaposed with malignant transformation foci featuring tumour necrosis, nuclear atypia, and increased mitotic activity (7 mitoses per 10 high-power fields). Immunohistochemistry confirmed myoepithelial differentiation (SMA+, S100+) and epithelial origin (CK7+, CK18+), with a Ki67 proliferation index of 10% in malignant areas. Notably, the tumour extended to within 1 mm of the deep surgical margin.
Conclusion: This case illustrates several important aspects of spiradenocarcinoma diagnosis. First, the transition from benign to malignant features was abrupt, with distinct areas showing necrosis and increased

mitotic activity. The immunohistochemical profile, particularly the elevated Ki67 index in malignant foci, supported the diagnosis of transformation. Recent studies suggest that molecular markers such as p53 and MYB may provide additional diagnostic value in challenging cases, though these were not assessed in our patient. In conclusion, recurrent spiradenomas require thorough pathological evaluation to exclude malignant transformation. The combination of careful histological examination and targeted immunohistochemistry can facilitate accurate diagnosis. This case contributes to the growing literature on diagnostic criteria for this rare malignancy and highlights the need for long-term follow-up in such patients.

E-PS-05-011

Clinical and histopathological evaluation of urticaria pigmentosa: a retrospective study

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Background & Objectives: Urticaria Pigmentosa (UP) is the most common form of cutaneous mastocytosis, characterized by excessive mast cell accumulation in the skin. It primarily affects infants and young children but can also present in adults, sometimes with systemic involvement. This study aims to evaluate the clinical and histopathological characteristics of UP, emphasizing differential diagnosis and systemic associations.
Methods: A retrospective cohort study was conducted to assess the clinical and demographic characteristics of patients diagnosed with UP in our department between 2015 and 2025. Medical records were reviewed, and demographic, clinical, and histopathological data were collected.
Results: A total of 34 patients (17 males, 17 females) were included, with 80% (n=27) in the paediatric age group and 7 adults. Organ involvement was observed in 7 patients (20%), including 5 paediatric cases. Histopathological analysis revealed characteristic mast cell infiltrates in the dermis, confirmed by tryptase and CD117 immunohistochemistry. Our findings indicate a higher prevalence of systemic involvement in paediatric patients, suggesting a need for careful monitoring in this age group.
Conclusion: Our findings align with recent studies emphasizing that paediatric mastocytosis often presents with a higher likelihood of organ infiltration compared to adult-onset cases. The literature highlights that mutations in the **KIT** gene, particularly **KIT D816V**, play a crucial role in mast cell proliferation and disease progression. Additionally, elevated serum tryptase levels and persistent skin lesions have been correlated with an increased risk of systemic mastocytosis.
Given the chronic nature of the disease, long-term follow-up is essential, particularly in paediatric cases where disease progression may be unpredictable. Current guidelines recommend a multidisciplinary approach, including dermatological, haematological, and genetic evaluations, to ensure accurate diagnosis and timely management. Further studies are warranted to explore novel therapeutic targets and improve patient outcomes.

E-PS-05-012

Cutaneous metastatic lobular carcinoma: a pitfall diagnosis

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Background & Objectives: Invasive lobular carcinoma (ILC) is a distinctive subtype of breast cancer that possesses unique clinical and pathological characteristics, such as its propensity to metastasize to atypical sites, although skin involvement remains relatively uncommon. When such cases arise, they often exhibit histological ambiguity due to a "single-file" pattern of cell infiltration, which can complicate detection during a biopsy and may lead to misdiagnosis as other dermatological conditions.
Methods: A sixty-eight-year-old female, with a history of invasive lobular carcinoma diagnosed in 2021 was admitted to the hospital for excision of a subcutaneous mass located in the presternal area. This mass had developed over a six-month period and was removed for aesthetic reasons. After the surgical excision, the specimen was sent to the Pathology department of Mureș County Clinical Hospital for further examination.
Results: On section, the received skin flap showed an imprecisely demarcated white area measuring 5x3mm. At microscopy, on usual stain we initially observed an abundant proliferation of collagen fiber bundles with irregular patterns resembling a pseudocicatriceal asppearance. However, after extensive examination, a single focus of tumoral growth was identified, consisting of a few small, discohesive cells with a characteristic “Indian file” arrangement. The tumour cells displayed eosinophillic cytoplasm with nuclear pleomorphism and were positive for CTK AE1/AE3, GATA3, ER and PR immunomarkers and negative for E-Cadherin. Based on morphology, immunohistochemistry and the pacient’s history, a diagnosis of cutaneous ILC metastasis was established.
Conclusion: Diagnosing skin metastasis of ILC presents significant challenges for pathologists due to its rare occurrence, atypical presentation, and unique growth pattern characterized by diffuse infiltration rather than discrete masses. As metastatic skin involvement can indicate advanced disease and impact treatment decisions, awareness remains critical. Future directions should focus on developing standardized diagnostic protocols and enhancing molecular profiling to differentiate ILC metastases from other dermatological conditions.

E-PS-05-013

Epithelioid melanoma of the breast in a male patient: a rare occurrence

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Background & Objectives: Malignant melanoma is an aggressive neoplasm of melanocytes, primarily affecting the skin. Breast involvement is rare, particularly in male patients. When metastatic to the breast, it may present as a palpable mass or remain asymptomatic. Prognostic factors such as tumour thickness, depth of invasion, and tumour-infiltrating lymphocytes (TILs) play a crucial role in assessing metastatic potential and survival..We present the case of a 76 year-old man with an epithelioid melanoma of the breast.
Methods: A 76-year-old Caucasian male presented with a palpable, ulcerated mass in his right breast, evolving over six months. Initial evaluation included a detailed history, physical examination, and surgical resection of the breast lesion. Morphologic and immunohistochemical analysis was performed on the resected tissue, with staining for S100 and HMB45.
Results: On gross examination, the dark brown-coloured skin lesion, was ulcerated and measured 7 cm in its greatest dimension. On serial sections, the lesion infiltrated the breast parenchyma. On microscopic examination, an atypical melanocytic proliferation with heavy pigmentation and skin ulceration was observed. The tumour cells stained positive for S100 protein and HMB-45. Brisk TILs were identified.
Conclusion: Epithelioid malignant melanoma metastatic to the male breast is an exceptionally rare occurrence. Immunohistochemistry is crucial for diagnosis and prognosis, guiding both local and systemic treatment decisions. In such cases, optimal management includes wide tumour resection with axillary lymph node dissection, followed by

adjuvant systemic therapy. Case reports are essential for sharing diagnostic strategies and informing appropriate management approaches for such uncommon presentations.

E-PS-05-014

Rare and unusual locations of melanoma: a retrospective study

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Background & Objectives: Melanoma is a highly aggressive malignancy that primarily affects the skin but can also arise in mucosal and visceral locations. These uncommon presentations pose diagnostic challenges due to their rarity and potential for misdiagnosis. Mucosal and visceral melanomas tend to have worse prognoses compared to cutaneous melanomas due to late detection, aggressive histological features, and resistance to conventional therapies. This study aims to analyse melanomas in rare anatomical sites, highlighting clinicopathological features and the role of immunohistochemistry in diagnosis.
Methods: We retrospectively reviewed cases of melanoma diagnosed at the Clinical Hospital Colentina, Bucharest, between 2009 and 2025. From all diagnosed cases, we selected those with the most unusual locations. The study included nine patients (seven males, two females) aged between 57 and 80 years. The identified sites were the small intestine, rectum, anal canal, palatal mucosa, urinary bladder, ocular, vulva, and penis. Histopathological examination and immunohistochemical analysis were performed, utilizing markers such as HMB45, Melan A, PRAME, and AE1/AE3. Clinically, all cases were initially diagnosed as tumours, except for the vulvar melanoma, which was correctly identified as melanoma before histopathological confirmation.
Results: The cases showed morphological and immunohistochemical variability, predominantly epithelioid, with large tumour cells, abundant cytoplasm, vesicular nuclei, and prominent nucleoli. High mitotic activity and deep tissue invasion were observed, indicative of aggressive biological behaviour. Melanomas of the anal canal and small intestine were diagnosed at an advanced stage due to nonspecific symptoms, whereas intraocular and mucosal melanomas showed rapid progression despite early detection.
Conclusion: Melanomas in rare locations pose significant diagnostic and therapeutic challenges. Immunohistochemistry is crucial for accurate diagnosis, especially in tumours mimicking other malignancies. Early recognition, molecular testing, and a multidisciplinary approach are essential for improved outcomes.

E-PS-05-015

A rare tumour of skin: microcystic adnexal carcinoma - combined solid and eccrine epitheliomatous variants

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Background & Objectives: We present a rare variant of microcystic adnexal carcinoma (MAC) on the scalp from a 66-year-old male patient.
Methods: Histological examination, including Haematoxylin and Eosin (H&E) staining, and immunohistochemical analysis (EMA, CEA, p40, SOX10, CK7, CK20, AR, and Adipophilin), were used to confirm the tumour's origin.
Results: H&E staining revealed a biphasic tumour in a sun-damaged skin. The superficial part of the tumour consisted of solid aggregates of neoplastic cells with nuclear atypia and mitotic figures. The deep part consisted of round ductal structures with bland cytology. The superficial part was positive for EMA and p40, while the luminal cells of the deep part were positive for EMA, CEA and p40. The morphological and immunophenotypical profile suggests a variation on the theme of microcystic adnexal carcinoma - combined solid and eccrine epitheliomatous variants. The alternative diagnosis would be squamous cell carcinoma with underlying syringoma, but the cytology is not obviously that of squamous cell carcinoma.
Conclusion: The solid variant of MAC is a rare skin tumour that usually occurs on the scalp. To our knowledge, this case is the first report of the combined solid and eccrine epitheliomatous variant of MAC. The risk of recurrence is very high in this tumour and Mohs micrographic surgery is the treatment of choice.

E-PS-05-016

Bleeding ulcerated pigmented nodule on the back: a case report

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Background & Objectives: Pigmented lesions encompass a wide spectrum of benign and malignant melanocytic and non-melanocytic tumours. One of the latter is malignant melanocytic matricoma, an exceedingly rare adnexal neoplasm, that may mimic melanoma.
Methods: An 88-year-old female presented with an occasionally bleeding pigmented nodule on her back, that had been present for an unknown period of time. It was removed by simple surgical excision. Grossly, the lesion was a well-circumscribed, variably pigmented, ulcerated nodular mass.
Results: Histopathological examination revealed an asymmetrical nodular tumour composed of a mitotically active malignant epithelial component with obvious squamous differentiation and patchy matrical keratinization, intimately admixed with pigmented and dendritic melanocytes without significant nuclear atypia or mitotic activity. The neoplasm immunohistochemically showed the two lineages with appropriate markers. Additionally, there was both cytoplasmic and nuclear expression by beta-catenin. p53 was also strongly expressed. The combined CK AE1/AE3/Ki67 revealed brisk proliferative activity in the epithelial component, while nuclear immunoreactivity in the melanocytes was rare. The overall histologic features were consistent with malignant melanocytic matricoma. The immunohistochemistry results supported the diagnosis, and it was completed with next-generation sequencing (NGS) analysis, which revealed a mutation in the CTNNB1 gene.
Conclusion: Malignant melanocytic matricoma is a unique adnexal tumour. Despite the presence of architectural and cytological features of malignancy, the biological potential and the prognosis of malignant melanocytic matricoma is essentially unknown, with very few cases reported and limited clinical follow-up available. Further research is needed to better understand its biological behaviour and predict the clinical outcome.
Pathologists should be aware of this extremely rare entity when evaluating pigmented skin lesions to avoid misdiagnosis.

E-PS-05-017

Pleomorphic fibroma of he eyelid: a rare and unusual location of a benign entity

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Background & Objectives: The pleomorphic fibroma (PF) of skin was first described by Kamino et al. in 1989 as a slow-growing lesion and clinically indistinguishable from a polypoid skin tag. They show loosely arranged spindle cells with large pleomorphic nuclei

but lacking mitotic activity. Herein we present a case in an unusual location.
Methods: Seventy-three-year-old male presented with a 4 mm cystic lesion extending to the conjunctiva in the right lower eyelid. It had appeared 12 years ago and remained the same size throughout. After total excision, the lesion examined by using routine pathological methods.
Results: Macroscopic examination revealed a 4x3x3 mm, nodular, cream-white coloured mass with on cut surface. On H&E; the lesion was polypoid in structure, with relatively well-circumscribed margins, and located immediately beneath the epidermis, extensively filling the dermis. It consisted of spindle cells with lightly swollen, oval nuclei, eosinophilic cytoplasm, and indistinct cytoplasmic borders, arranged in irregular bundles and storiform pattern within a fibrous stroma. There were also some multinucleated cells. Mitotic activity, significant inflammatory cell infiltration, epidermal involvement and ulceration were not observed. On immunohistochemical analysis the tumour cells were CD34 and Factor 13a positive. S100, STAT6, SOX10, CD68, CD163 were negative. The Ki67 proliferation index was 2-3%. Loss of Rb was detected.
Conclusion: PFs are rare, slow-growing tumours showing loosely arranged spindle cells with some large pleomorphic cells. They follow a benign clinical course. Diagnosis of PF requires few immunostains with typical expression CD34. However, it is important to consider that CD34 positivity can be seen in a couple of benign fibroblastic tumours. A PF located on the eyelid, which has been reported very rarely in this localization in the literature. This entity should be considered in any solitary slow-growing spindle cell tumours located even on an eyelid.

E-PS-05-018
Cylindroma arising after a human bite trauma: a case report
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Background & Objectives: Cylindroma is a rare benign adnexal tumour of eccrine or apocrine origin, typically located on the scalp and face. Although this condition is often associated with genetic mutations, particularly in the CYLD gene, trauma-induced cases have not been previously reported. This case presents the first instance of cylindroma developing following a human bite injury, suggesting that trauma might act as a potential trigger for tumour formation.
Methods: A 61-year-old female patient presented with a 3 × 3 cm mass on her right shoulder, beneath scar tissue from a previous human bite. The lesion was initially considered an epidermoid cyst or lipoma. The patient had a history of smoking, orthopedic knee surgery, and lipoma excision from the chest. The mass was excised without prior radiological evaluation.
Results: Histopathological examination revealed a solid, nodular mass composed of acinar structures with basaloid cell aggregates. Immunohistochemistry showed positive staining for CK7 and CK8, with a Ki-67 proliferative index of 8%. The diagnosis was confirmed as cylindroma.
Conclusion: This case describes the first reported occurrence of cylindroma arising after a human bite trauma. Although trauma is not commonly recognized as a causative factor, it may serve as a trigger for tumorigenesis in genetically predisposed individuals. Chronic inflammation and tissue remodelling following injury could contribute to tumour development. Cylindromas are usually slow-growing and have an excellent prognosis, with surgical excision being the standard treatment. Long-term monitoring is advised, especially in patients with multiple lesions or a genetic predisposition, such as Brooke–Spiegler Syndrome. This case represents the first documented instance of cylindroma arising after a human bite trauma in the literature. Further research is needed to establish a definitive association between trauma and cylindroma development.

E-PS-05-019
Histopathological assessment of fibrin sealants in burn injury treatment: insights from a rat model
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Background & Objectives: Burn injuries constitute a significant health issue globally, requiring skilled management by trained plastic surgeons, which however, are not always available, implementing a need for alternative effective treatment methods that non-expert healthcare providers could use. This experimental study aimed to assess the safety and effectiveness of a fibrin sealant (TISSEEL™) compared to traditional treatment with sulfadiazine for partial-thickness burns in a rat model.
Methods: Sprague-Dawley rats underwent partial thickness contact thermal burn wound, divided into three groups: control group (no treatment), silver sulfadiazine cream group and TISSEEL™ group.
Following animal sacrifice, a blinded histopathologic analysis was performed to assess the inflammatory response, healing, and tissue regeneration. Haematoxylin-eosin staining was used as it can distinguish dermal structures. Fibroblastic proliferation was observed through Vimentin staining, known as the most effective marker for identifying fibroblasts. Moreover, neovascularization observed through the use of CD-31, a crucial marker for endothelial cells.
Results: In total, 30 animals were included with a median weight of 236 ± 10 g. Animals in the TISSEEL™ group presented dominant collagen expression compared to animals in the control and silver sulfadiazine cream group ($p = 0.000$). Histopathologic analysis also demonstrated marked leukocyte infiltration ($p = 0.009$), increased neovascularization ($p = 0.000$) and higher fibroblast expression ($p = 0.002$) in the TISSEEL™ group compared to the other two groups
Conclusion: TISSEEL™ appears to be a safe and effective choice for treating partial-thickness burn injuries. Thus, TISSEEL™ could be used in clinical settings for the initial treatment of partial-thickness burn injuries.

E-PS-05-020
Desmoplastic cutaneous squamous cell carcinoma: a scar simulator
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Background & Objectives: Desmoplastic cutaneous squamous cell carcinomas (DCSCs) are rare neoplasms that usually affect the sun-exposed skin of older people.
Microscopically, they are characterised by atypical and inconspicuous epithelial cells associated with a prominent desmoplastic stroma. To broaden this clinicopathological spectrum, we present 2 cases of an unusual variant of desmoplastic SCC.
Methods: These are two male patients aged 85 and 93 years respectively. They present in periorbital region and scalp with 3 and 2.5 cm crusted plaques.
Results: Both cases are characterised by isolated atypical cells, thin cords and spindle cells. Occasionally the cytoplasm is dense, squamoid. The stroma is very extensive and desmoplastic. The stroma accounts for more than 70 % of the tumour area. One case showed a large ulcer. One case showed associated actinic keratosis. Perineural invasion was observed in both cases. The squamous nature of the tumour was confirmed by p63.
Conclusion: Desmoplastic squamous carcinoma is a very aggressive subtype with extensive local infiltration that must be distinguished from other epidermoid carcinomas.

Confirmation of the squamous nature by immunohistochemistry is essential.
It shows a high proportion of perineural invasion.
It is difficult to diagnose due to the low cellularity in a very large stroma, simulating a scar.

E-PS-05-021
Periscrotal apocrine carcinoma with extensive pagetoid spread and nodal metastasis
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Background & Objectives: Apocrine carcinoma is a rare and the axilla is the most commonly involved site. In particular, periscrotal occurrence is very rare and according to some reports, it is known to be accompanied by pagetoid spread.
Methods: The patient underwent three operations, and pathologic findings were observed in all of the periscrotal masses, scrotum skin, and inguinal lymph nodes.
Results: A 41-year-old male patient visited the hospital because of various masses around the scrotum. On physical examination, several verruciform masses were observed on the right side of the penis, and skin involvements were also suspected in the left side of scrotum. It is said that the mass grew gradually over the years. The sizes of submitted masses were 4.5x3.0cm, 5.5x4.0cm, and 5.0x1.5cm, respectively. Macroscopically, these masses showed a gravel-shaped surfaces. Histologically, a mass in the form of adenocarcinoma infiltrating the dermis was observed, and it was accompanied by extensive pagetoid spread looking similar to extramammary paget disase in most of the specimens. Dermal adenocarcinoma showed well-differentiated tubular form, and in some tubules decapitation secretions were also observed along with the abundant eosinophilic cytoplasm, leading to the estimation of the origin of apocrine glands. Immunohistochemical staining was positive for CEA, CK7, GCDFP-15, androgen receptor, and EMA. These findings were combined and diagnosed as apocrine carcinoma. Subsequently, part of the scrotum skin was further resected, and only extramammary paget disease-like findings were confirmed here. Radiologically, bilateral inguinal lymph node metastasis was suspected and surgery was performed, and metastatic carcinoma was histologically confirmed.
Conclusion: One report shows a pagetoid spread in about half of this carcinoma. In another report, apocrine carcinoma is cited as an example as the underlying disease of extramammary paget disease. This case is reported to be shared because it shows extensive pagetoid spread and nodal metastasis with apocrine carcinoma.

E-PS-05-022
A rare case of oseteocartiligious differentiation in metastatic melanoma
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Background & Objectives: Metastatic melanoma has been called the great mimic, and rightly so. Melanoma can exhibit a wide variety of histological patterns, which can confound diagnosis, and transdifferentiation of melanoma to a variety of sarcomatoid and carcinomatous phenotypes is described. We present a case of a rare variant of sarcomatoid metastatic melanoma post immunotherapy, with osteosarcomatous and chondrosarcomatous components.
Methods: n/a
Results: 51 year old male initially presented with acral melanoma of left little toe. A sentinel lymph node resection of the patient's left groin showed a single 0.5mm deposit of metastatic melanoma. A plan was made for 3 monthly ultrasound follow-up and he was commenced on anti-PD1 therapy (Pembrolizumab). Unfortunately, he re-presented the following year with groin swelling and underwent groin dissection. Five of twelve lymph nodes resected contained metastatic melanoma, along with three dermal in-transit metastases. No histological evidence of response to therapy was seen. The melanoma in the repeat resections showed extensive areas of sarcomatoid changes, with metaplastic chondrosarcoma and osteosarcoma present. These changes were not present in the primary tumour.
Sox-10 and HMB-45 immunohistochemistry (IHC) was positive in the areas of conventional melanoma, but expression was lost in the sarcomatoid areas. No BRAF or NRAS mutations were detected.
Conclusion: This is a case of malignant osteochondroid differentiation within metastatic melanoma. Osteochondroid differentiation is rarely observed in primary and metastatic melanomas, with most lesions arising in acral/subungual and mucosal locations, as in our case.
Transdifferentiation is a well-documented feature of melanoma, which can cause diagnostic difficulty and is often associated with loss of expression of melanocytic markers by immunohistochemisty. Awareness of this unusual morphology is essential to avoid misdiagnoses.
Of note, there was no evidence of treatment effect post-immunotherapy in this case. The role of immunotherapy in sarcomatoid melanoma may warrant further investigation.

E-PS-05-023
Modern aspects of melanoma diagnosis and treatment
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Background & Objectives: Melanoma of the nail apparatus is a variant of acral lentigo melanoma. This form of melanoma is not associated with exposure to sunlight. It is rare. In 0.7% - 3.5% of cases, the tumour is malignant. It occurs in all racial groups, predominantly in African-Americans and Asians. In particular: in the African population 75%, in China - 25% and in Japan - 10%.
Methods: We report a case of a old female in her 7^{th} decade of life referred to the clinic, purulent surgeon, phlegmon of the first toe of the left ankle. After removing the nail, during examination of the bed, melanoma was suspected, there was a black formation, a biopsy was taken. A digital PET/CT scan was performed. We actively sought clinical information, including medical and family history, to facilitate accurate diagnosis.
Results: H&E sections revealed fragments of stratified squamous epithelium, adjacent fibrous-connective tissue, excessive pigment, as well as proliferation of epithelioid unsaturated cells of round, large cells, nuclear hyperchromasia, dusty pigmented cytoplasm, which are presented diffusely and in the form of nests, mitotic figures. The tumour cells were positive for Melan A, S100, HMB45, Ki67 index was $\geq$ 50%. Examination of mutations in tumour tissue: BRAF - 50%: NRAS – 20%: KIT Mutational analysis 5%.
Conclusion: Acral lentiginous melanoma is rare, accounting for no more than 5% of all types of melanoma. This type of disease is characterized by the appearance of a malignant lesion on closed areas of the skin, under the nail plates, which excludes the usual effect of ultraviolet and ionizing radiation for the appearance of melanoma. Another difference between acrolentiginous melanoma and other forms of pathology is the absence of the influence of nevi. An unfavourable prognosis also depends on the high risk of metastases penetrating the internal organs at the initial stages.

E-PS-05-024
Integrating three-dimensional histopathology with bread loafing and orientation preservation without artificial coloring
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Background & Objectives: Basal cell carcinoma (BCC) is a common form of non-melanoma skin cancer (NMSC) that, despite its rare metastasis, can cause significant morbidity through tissue infiltration. Due to its proximity to critical anatomical structures, precise control of resection margins is essential. However, thorough margin examination in small excisions may compromise the central tumour assessment. We propose a novel method that combines three-dimensional (3D) histopathology with bread loafing to address this challenge and reduce the risk of recurrence.
Methods: In our technique, the specimen is first incised during macroscopic work-up for optimal dehydration, ensuring correct orientation. The excision is then divided during embedding with aligned cutting planes, and the spindle tips are centrally divided. The bread loafing step involves tilting the narrow cutting planes toward the lesion and folding the spindle tips outward for 3D margin assessment. Additionally, we propose preserving orientation without tissue coloring by leaving the sample intact during initial grossing, keeping suture markings, and avoiding dissection during macroscopy.
Results: While established techniques have certain limitations, our approach combines their strengths and mitigates their weaknesses. 3D processing supports margin control in narrow specimens but may overlook central tumour evaluation. Bread loafing facilitates central lesion assessment but doesn't fully capture lateral margins. Our combined method optimizes both, potentially reducing recurrence risk while sparing healthy tissue. Although based on theoretical estimations, follow-up studies comparing techniques are needed to confirm whether the increased tip coverage in our method leads to better clinical outcomes.
Conclusion: Having successfully integrated our technique into routine histology practice, the next step is to retrospectively evaluate its performance, which we are currently in the process of doing.

E-PS-05-025

The prognostic value of PRAME, P16 and Ki-67 for metastatic risk in early stage melanomas in the D-ESMEL study

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Background & Objectives: Cutaneous melanoma is an aggressive skin cancer with a high risk of metastasis. Despite early detection, many stage I and II patients remain at risk of recurrence, with a significant proportion experiencing relapse within five years. Traditional prognostic models rely on clinicopathological factors such as Breslow thickness and ulceration, but emerging molecular biomarkers may improve risk assessment. Preferentially Expressed Antigen in Melanoma (PRAME), Ki-67, and p16 have shown potential in refining melanoma prognostication. This study evaluates their prognostic value in predicting metastatic progression, aiming to enhance risk stratification and guide clinical decision-making.
Methods: Formalin-fixed paraffin-embedded tissue blocks from stage I/II melanoma cases were analysed using samples from the Dutch Early-Stage Melanoma Study (D-ESMEL), a population-based matched case-control study. Cases and controls were matched on key prognostic factors. Immunohistochemical staining was performed for PRAME, Ki-67, and p16. PRAME and P16 were assessed by a pathologist and resident, while Ki-67 positivity was detected using a specialized app. Paired analyses was used to explore the relationship between biomarker expression and melanoma progression.
Results: PRAME expression was higher in melanoma cases than controls, with dermal positivity and intensity increasing in metastatic cases (OR=1.82, 95% CI: 0.94–3.93, p=0.129; OR=1.43, 95% CI: 0.59–3.46, p=0.432), though neither was statistically significant. P16 expression was significantly lower in metastatic cases (p=0.012), and clonal loss was associated with increased metastatic risk (OR=2.05, 95% CI: 1.23–3.41, p=0.007). Ki-67 expression showed no significant difference but trended higher in metastasized cases (OR=1.023, 95% CI: 0.99–1.06, p=0.140).
Conclusion: P16, particularly clonal loss, is a significant prognostic marker for melanoma progression and metastatic risk. Further validation and clinical implementation of this biomarker is needed to improve risk stratification and guide clinical decision making in melanoma management. PRAME and Ki-67 did not demonstrate strong predictive value.

E-PS-05-026

Advanced nonscarring alopecia associated with longstanding dermatomyositis, calcinosis cutis and porokeratosis in an elderly female, masked by disease-modifying treatment: a case report and discussion

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Background & Objectives: A 70-year-old Caucasian female with a 30-year history of dermatomyositis (DM) associated with anti-NXP2 antibody, presented with a 4-year history of alopecia starting in the central/parietal scalp. She noticed hair falling in clumps following Methotrexate treatment. She was on Azathioprine, intravenous immunoglobulin (IVIG) and high dose Prednisolone. Examination showed shiny, smooth parietal and frontal scalp with scarring, mild erythema and scaling in the occiput. She had subcutaneous nodules and bilateral eczematous leg lesions, consistent with porokeratosis. She had history of muscle weakness, Whipple procedure for pancreatic intraductal papillary mucinous neoplasm, type 1 diabetes mellitus, dietary iron and zinc deficiency, hypertension and heart failure.
Methods: One scalp 4mm punch biopsy showed three terminal hair follicles, two vellus follicles and two stelae. The epidermis was intact. The other punch was tangentially embedded and showed three terminal hair follicles and seven stelae with one catagen follicle, and severe elastosis in the upper dermis. No significant or inflammation or fibrosis was noted. Alcian blue stain confirmed mucin deposition. The epidermis showed mild hyperkeratosis and the basal layer was intact. The skin nodules showed calcinosis cutis.
Results: Scalp involvement is present in around 12.8% of DM patients, about 30-40% of which have alopecia. DM alopecia is usually a diffuse nonscarring type, with vacuolar interface dermatitis, increased reticular dermal mucin and perivascular lymphocytes. Cases of alopecia areata and universalis have been reported in association with DM. Medications such as steroids, Cytotoxic drugs and IVIG are known to modify the inflammatory process, as in our patient.
Conclusion: We have presented a case of advanced nonscarring alopecia associated with longstanding dermatomyositis severe, showing dermal elastosis and absent basal epidermal vacuolar degeneration. Long term steroid and cytotoxic therapy may have masked the usual interface epidermal findings and it is important to correlate this with the clinical history to reach the correct diagnosis.

E-PS-05-027

Favre-Racouchot syndrome: case report

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Background & Objectives: Favre-Racouchot syndrome is a disease of elderly male that develops due to chronic sun exposure. It is also known

as nodular elastosis with cyst and comedones. The etiopathogenesis is not known but chronic sun exposure, smoking, radiation and physical agents are proposed predisposing factors.
Methods: We report a case of 70 year old male who presented with dark coloured raised lesions along with thickening of facial skin which was increasing progressively.
Results: Physical examination showed the presence of thickened inelastic skin along with deep furrows and wrinkles involving the entire face. Histopathological examination epidermis showed epidermal cyst formation containing laminated keratin and superficial dermis shows follicular infundibular plugging and large nodules filled with keratinous material.
Conclusion: We present an elderly male patient who was diagnosed to have Favre-Racouchot syndrome with typical distribution of the comedones on the face and years of heavy smoking history. Our patient's findings were quite demonstrative of Favre-Racouchot syndrome.

E-PS-05-028
Porokeratosis in skin biopsies: insights and challenges from the experience of university histopathology service
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Background & Objectives: Porokeratosis is a rare genodermatosis characterized by cornoid lamella on histopathology and an increased risk of malignant transformation, particularly in certain clinical forms, longstanding lesions, and immunosuppressed patients. This study examines the incidence and major characteristics of porokeratosis patients diagnosed at university.
Methods: We retrospectively analysed porokeratosis cases diagnosed at the Institute of Pathology, Faculty of Medicine, University of Belgrade in the period 2016-2024 and evaluated demographics, clinical presentation, and histopathological findings.
Results: Only 27 biopsies from 22 patients were diagnosed as porokeratosis in the examined period, with an annual incidence of $\leq$0.17% in skin biopsies. Porokeratosis was more common in women (68.2%) and older individuals (median age: 70 years, range: 18–86). Clinical misdiagnosis occurred in six patients (27.3%), often as skin tumours. Inflammatory skin diseases were a frequent differential diagnosis (27.3%). Lesions were mostly multiple and regionally restricted (50%), usually on legs, though some were disseminated (27.3%) or focal (on leg, face, chest, or back) (22.7%). Disseminated superficial actinic porokeratosis (DSAP) was the most frequent clinical form (68.1%), followed by porokeratosis of Mibelli (12.5%), with rarer forms (combination of DSAP and Mibelli forms, linear, follicular, palmoplantar) seen in single cases. The two youngest patients (age 18 and 19 years) presented with focal lesions on the face as Mibelli form. Neoplastic transformation was observed in five DSAP cases, with actinic keratosis more common than squamous cell carcinoma (4:1). Retrospective analysis found porokeratosis was suspected but not histologically confirmed in 15 additional patients. One patient diagnosed in 2008 was later found to have porokeratotic eccrine ostial and dermal duct nevus, an entity frequently debated as a form of porokeratosis.
Conclusion: Porokeratosis is exceptionally rare, even in a university setting. DSAP is the most common form, with a risk of neoplastic transformation, mainly into actinic keratosis, highlighting the need for accurate diagnosis.

Funding: This research was supported by the Ministry of Science, Technological Development and Innovation of the Republic of Serbia and the Faculty of Medicine, University of Belgrade, project No. 451-03-66/2024-03/200110

E-PS-05-029
Molecular profile of cutaneous melanomas in an Algerian population
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Background & Objectives: In Algeria, cutaneous melanoma remains rare and its molecular profile is poorly understood. This study aims to investigate the molecular profile of cutaneous melanoma in an Algerian population.
Methods: We analysed the molecular profile of 52 cutaneous melanomas. Immunohistochemistry (IHC) was performed in 30 patients using the Ventana VE1 antibody. Real time Polymerase Chain Reaction (RT-PCR) was conducted in 45 cases using the BRAF Threscreen Qiagen kit to detect the V600 allele. Next-generation sequencing (NGS) was performed in 7 patients using the Oncomine^{TM} Focus Panel (ThermoFisher).
Results: Our samples consisted of 41 primary tumours and 11 metastasis from 28 men and 24 women. The mean age was 51.82 years (range: 14-86 years). Histological types included: nodular melanoma NM (15 cases), acral lentiginous melanoma ALM (11 cases), superficial spreading melanoma SSM (11 cases), lentigo maligna melanoma LMM (1 case), unclassifiable melanoma (3 cases). 47 patients presented with locally advanced or metastatic disease. By IHC, 27 patients expressed BRAF. RT- PCR revealed BRAF mutations in 30 patients.
We assessed the concordance between IHC and RT-PCR in 30 patients; results were concordant in 25 cases; Chi2 test: $p < 0.0001$. NGS performed identified one case of BRAF mutation and one case of NRAS mutation. The molecular profile according to histological type: NM: 7 BRAF+; ALM: 6 BRAF+ and 1 NRAS+; SSM: 9 BRAF+, LMM: BRAF-, Unclassifiable melanoma: All BRAF+. Among the 11 metastasis, 6 presented with BRAF mutations.
Conclusion: This study represents the first molecular profiling of cutaneous melanomas in Algeria. Our findings demonstrate a high proportion of patients with locally advanced or metastatic disease at diagnosis. BRAF mutations were identified in 54.54% of ALM, which contrasts with findings in litterature. Statistical analysis revealed significant concordance between immunohistochemistry and RT-PCR results, supporting the utility of immunohistochemical assessment as a primary screening approach for BRAF V600E mutations.

E-PS-05-030
Metastatic porocarcinoma resolved with patient history and molecular analysis – a case report illustrating experience of a university consultation service
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Background & Objectives: Porocarcinoma is a rare malignant tumour of skin appendages with well-defined genetic features. Up to a third of cases metastasize mostly to regional lymph nodes. The main predictors of metastatic potential are increased mitotic activity (>8 per square millimetre) and high tumour thickness (over 7 mm). Here, we describe

the evolution of metastatic porocarcinoma in a patient and show the importance of patient history in the diagnostic process.
Methods: We described histopathological, immunohistochemical, and molecular features of primary and metastatic porocarcinoma.
Results: An axillary skin tumour in a 58-year-old woman was referred for a consultation from a regional hospital. It was composed of epithelioid solid nests occupying epidermis and dermis, with focal ductal formation and prominent mitotic activity (15 per square millimetre). The final diagnosis of porocarcinoma was based on the expression of CK7, p63, pCEA, and EMA, and on the rearrangement of *WWTR1* gene; no expression of NUT was identified. Tumour thickness was 5 mm (AJCC 8th Ed.; 7.5 mm AJCC 7th Ed.). After 16 months, patient was admitted at University Clinical Centre with tumours in axillary skin and pleura but with a history of cutaneous squamous cell carcinoma; the data on true nature of primary tumour was lost. Samples were received for a consultation, and on both sites, tumour cells with abundant, focally clear cytoplasm were organized in strands and glands. Immunohistochemical features could not exclude triple-negative breast carcinoma (CK7+, GATA3 + focally, GCDFP15+, TRPS1+, Mammaglobin-, ER-, PR-, HER-2-). Access to our digital archive revealed true nature of metastasis, and porocarcinoma metastases were confirmed with WWTR1 rearrangement using FISH in both samples.
Conclusion: Breast carcinoma represents the main diagnostic dilemma in the cases of metastatic porocarcinoma. Preservation of medical history and good clinical communication can prevent excessive use of immunohistochemistry; a simple WWTR1 FISH analysis is enough to confirm porocarcinoma metastasis.

Funding: This research was supported by the Ministry of Science, Technological Development and Innovation of the Republic of Serbia and the Faculty of Medicine, University of Belgrade, project No. 451-03-66/2024-03/200110

E-PS-05-031
Columella nasal isolated cutaneous sarcoidosis mimicking a cancer in phototype 1 caucasian patients: a rare presentation
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Background & Objectives: Sarcoidosis is a chronic inflammatory disorder that occur that occur in all age, sex ethnicity and race with peaks in the third and fourth decades followed by the sixth decades and a high incidence among black women. Although the lower respiratory tract is affected in 90% of cases head and neck location are very uncommon with a prevalence varying between 1 % and 6,5%. Cutaneous locations involving the face and neck are present in 25% to 35% of patients with systemic disease, but may also be isolated
Methods: A caucasian man in his 40s phototype 1 was referred for a firm and nonpainful papulonodular isolated nasal columella skin lesions no associated to endonasal pathology. The lesion was radically excised and columella reconstructed using flip over buccal mucosa flap.
Results: Histological examination showed the presence of granulomas noncaseating characterized by aggregates of epitheliod histiocytes with abundant eosinophilic cytoplasm without lymphocytes or inflammatory cells and absence of necrosis. Multinucleated giant cells were also present with asteroid bodies, eosinophilic starbust lesione, and Schaumann bodies, laminated cytoplasmatic calcification. Periodic acid Shiff, Grocott and Zielh stains were negative. The patient workup including thorax computed tomography, pulmonary function electrocardiogram and ophthalmologic examination were negative.
Conclusion: Sarcoidosis is a multiorgan disease with high levels of cutaneous involvement. Head and neck isolated cutaneous fist manifestation of disease is unusual. This can be challenging for a timely diagnosis to treat those a chronic and progressive disease. It is a diagnosis usually made following the evolving findings of both clinical and investigatory test. In cases of nasal papulonodular lesions the diagnosis remains doubtful and local biopsy is useful. However despite various medical treatments complete disappearance was never obtained.

E-PS-05-032
Botryomycosis in the leg of a farmer: unveiling diagnostic challenges
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Background & Objectives: Botryomycosis is a rare, chronic granulomatous bacterial infection primarily affecting the skin but can occasionally involve visceral organs. The main causative agent is *Staphylococcus aureus*, with less common involvement from other bacteria like *Pseudomonas spp.*, *Escherichia coli*, *Proteus spp.*, and *Streptococcus spp.* It is characterized by granule formation due to the pathogen's low virulence, an intermediate inoculum, and the host's immune status. The condition involves the Splendore-Hoeppli phenomenon, where antigen-antibody reactions cause granuloma formation. Botryomycosis can mimic neoplastic, fungal, or actinomycotic infections. Lesions usually appear as nodular, purulent masses that may develop fistulas. The cutaneous form has a better prognosis than the visceral form. Risk factors include cystic fibrosis, immune disorders, chronic granulomatous disease, diabetes, and HIV, making it a rare opportunistic infection.
Methods: This case report describes the diagnosis, clinical presentation, and management of a patient with botryomycosis, a rare chronic granulomatous bacterial infection. We present a detailed analysis of the clinical, microbiological, and histopathological findings associated with the condition, as well as the treatment approach.
Results: We report the case of a 66-year-old male with a six-month history of a mass in his left leg. Physical examination revealed a 3 cm resilient mass on the anterior thigh, initially suspected to be a lipomatous lesion, which was subsequently resected. Histopathological analysis revealed multiple fragments of skin and soft tissue with pronounced acute abscess formation. The abscesses contained moderate-sized bacterial colonies displaying the Splendore-Hoeppli phenomenon—granules encapsulated within an eosinophilic matrix, as seen in Gram-stained samples. Ziehl-Neelsen, PAS, and Gomori methenamine silver stains did not identify fungal microorganisms or mycobacteria.
Conclusion: Following prophylactic antibiotic therapy and surgical excision, the patient showed favourable progress, with complete resolution of the lesion. This case highlights the clinical challenges in identifying the lesion's nature and underscores the importance of accurate diagnosis.

E-PS-05-033
CR-1 expression of cutaneous melanoma tumour cells and correlation with histopathologic and prognostic parameters
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Background & Objectives: Melanoma is a malignant tumour that can be seen in any organ where melanocytes are found, especially in the skin, and has a poor prognosis in advanced stages. Our study aimed to investigate the immunohistochemical expression of CR-1, an oncofoetal protein, and its relationship with clinicopathological parameters in cutaneous melanoma cases.

Methods: Cutaneous melanoma cases diagnosed at Istanbul Cerrahpaşa University-Cerrahpaşa Medical Faculty Hospital between January 2016 and January 2023 were scanned from the system. Immunohistochemical CR-1 stain was applied to all cases and the results were compared with clinicopathological parameters.
Results: 78 cutaneous melanoma cases diagnosed between January 2016 and January 2023 were included in the study. CR-1 expression was observed in melanoma cells in 9% (n=7) of the cases. Although statisticaly insignificant, CR-1 positive tumours were mostly located on the intermittantly sun exposed skin (57.1%; n=4), pT4 (71.4%; n=5), without regression (71.4%; n=5), low density of tumour infiltrating lymphocytes (71.4%; n=5), and wtBRAF p.V600 tumours (85.7%; n=6). While the average survival was 16.5±11.6 months in CR-1 positive cases and 39.4±3.9 months in CR-1 negative cases, this result was not found to be statistically significant.
Conclusion: CR-1 is a candidate protein for targeted therapy because it is an oncofoetal protein and its expression is shown to be increased in malignancies while its expression is low/absent in normal adult tissues. In this study, immunohistochemical expression of CR-1 expression was investigated in cutaneous melanoma cases and it was found to be not associated with clinicopathological parameters.

E-PS-05-034
Lichen Sclerosus mimicking clinical atrophic variant of mycosis fungoides in persistent 2-year evolution dermatosis: a case report
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Background & Objectives: Lichen sclerosus (LS) is a chronic skin condition predominantly located in the anogenital area, although 15-20% of cases may present in the extragenital form.
The latter is a challening diagnosis due to clinical overlap with other dermatoses, including cutaneous T-cell lymphoma.
Methods: A 45 year-old woman presents a persistent and progressive dermatosis, with approximately 2 years of evolution. Clinically, it shows a cephalo-caudal distribution, consisting of erythematous-brown reticulated spots, with occasional confluence and bright surface.
No associated symptoms were described. Several biopsies were performed during this period without a definitive diagnosis.
Results: Mixed connective tissue disorder and atrophic variant of mycosis fungoides were the main clinical differential diagnosis. However, histopathological examination revealed a slightly atrophic epidermis with foci of acanthosis. The papillary dermis is partially occupied by a band of hyaline, sclerotic tissue, with some dilated capillaries. In the reticular dermis, there is a perivascular and interstitial inflammatory infiltrate, predominantly composed by lymphocytes and histiocytes.
The immunohistochemical study confirms the predominance of T cells in the infiltrate as shown by CD3, which also highlights mild exocytosis between the basal keratinocytes of the epidermis. CD20 reveals few B cells, exclusively in the dermal infiltrate.
Conclusion: Lichen Sclerosus was the final diagnosis, even with this unusual clinical presentation. Despite the mild exocytosis, there were not histopathological findings that could confirm the suspicion of mycosis fungoides.
The aetiology of LS remains unclear, however, some Borrelia species have been detected in lesional skin. This can also lead to controversial association with morphea, as the diagnosis of LS has also been reported in patients with coexisting autoimmunediseases.
Therefore, clinical and histopathological correlation remain essential for the correct diagnosis.

E-PS-05-035
PRP and hyaluronic acid in treatment of vulval lichen sclerosus et atrophicus – a case report
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Background & Objectives: Lichen sclerosus et atrophicus (LSA) is a rare condition whose incidence in genital area is 1.5% to 2.5%.
Methods: A 62-year-old female patient complained of itching and pricking in the vulva area. After the initial biopsy and diagnosis of LSA, the indicated therapy is a combination of injections of platelet-rich plasma (PRP) and 1 ml of hyaluronic acid given once a month for a period of 3 months, and after three months (6 months from the first therapy) a control biopsy is performed. Initial and control biopsies were histologically processed using haematoxylin and eosin (HE), Mallory's and Orcein staining.
Results: Before treatment, perianal sclerotic-atrophic plaques were present, while the vulva had circular, erythematous and mildly atrophic plaques. Histopathological examination of initial biopsy showed hyalinization of the papillary dermis with vacuolar alteration of epidermis basal cells. Also, fragmented collagen fibres are observed, as well as the lack of elastic fibres and blood vessels in the papillary dermis. After treatment, we observed a pale erythema around the vulva, while perianally erythematous plaques with lesser degree of atrophy were predominant. On the control biopsy the absence of hyalinization of the papillary dermis and vacuolar alteration of epidermal basal cells were observed. Collagen fibres are arranged in a honeycomb pattern, while elastic fibres and blood vessels appear in the papillary dermis.
Conclusion: Therapy with a combination of PRP and hyaluronic acid after only 6 months led to a significant reduction of both macroscopically and pathohistologically verified changes.

E-PS-05-036
Sarcomatoid carcinoma associated with a poroid neoplasm (Sarcomatoid porocarcinoma): an extraordinary case report
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Background & Objectives: Primary cutaneous sarcomatoid carcinomas are rare tumours, mostly arising in association with basal cell carcinoma or squamous cell carcinoma. Adnexal associations are exceedingly rare, with only nine cases reported in the English literature. We present a case of cutaneous sarcomatoid carcinoma arising in association with a poroma.
Methods: An 89-year-old female who presented for evaluation of a pink, exophytic, polypoid and ulcerated tumour measuring 4 x 4 x 3 cm located on skin surface of the left lower leg. The patient underwent an excisional biopsy, and the specimen was submitted for histopathological evaluation.
Results: Microscopic examination revealed an ulcerated polypoid tumour composed predominantly of a high-grade spindle cell proliferation arranged in fascicles with focal myxoid changes. At the periphery of the lesion, the epidermis and superficial dermis exhibited a proliferation of small, ovoid, and monotonous poroid cells with areas of ductal differentiation. In several areas, the poroid component merged with the high-grade spindle cell component. The mitotic rate was 10 mitoses per 10 high-power fields. No lymphovascular invasion or necrosis was observed.

Immunohistochemical analysis demonstrated diffuse positivity for cytokeratin AE1/AE3, CK5/6, and p63 in both the high-grade spindle cell and poroid components, supporting an epithelial origin. CEA was positive in the ductal areas of the poroid component. These findings confirmed the diagnosis of sarcomatoid porocarcinoma.
Conclusion: Porocarcinoma is a rare malignant adnexal tumour, and sarcomatoid transformation within these neoplasms is exceptionally uncommon. This case highlights the importance of recognizing this entity and contributes to the limited pool of reported cases in the English literature.

E-PS-05-037
Mycobacterium Chelonae on a skin biopsy associated with peritoneal dialysis catheter - case report and review of the literature
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Background & Objectives: Cutaneous infections by Mycobacterium Chelonae present heterogeneously, including papules, pustules, and deep lesions. It commonly affects immuno-compromised patients. Histopathological findings show granulomatous inflammation depending on immune status and vacuoles. They are frequently associated with trauma and medical procedures, including catheter use.
Methods: A biopsy was performed and processed for histological examination using H&E staining, along with specific histochemical techniques such as Ziehl-Neelsen for mycobacteria, PAS and methenamine silver for fungi. Additionally, microbiological cultures were conducted to isolate microorganisms. These methods allowed for both histological evaluation and identification of the infectious aetiology. Furthermore, we performed a review of the literature.
Results: A 75-year-old man who was taking immunosuppressant drugs including corticosteroids presented with a painful ulcerated nodule with suppuration in the area of the dialysis catheter with an evolution of 5 months. The patient had been treated with several antibiotics with only partial resolution. A sample was sent to microbiology. Histological examination revealed in the deep dermis a mixed inflammatory reaction with neutrophils and abscessed areas, histiocytes, some of them foamy, steatonecrosis and cicatricial fibrosis. Extracellular vacuoles were seen in the dermis with filamentous structures forming clumps within the spaces. The Ziehl-Neelsen stained the filamentous structures, being consistent with mycobacteria. PAS and methenamine silver stains were positive. The culture was positive for Mycobacterium chelonae.
Conclusion: This case emphasizes the importance of recognizing the histopathological features of Mycobacterium Chelonae, a rare cause of cutaneous infections, especially in immuno-compromised patients. A mixed inflammatory reaction, especially with extracellular vacuoles, provides crucial diagnostic clues. The Ziehl-Neelsen stain and microbiological cultures are essential for confirming mycobacterial aetiology. Early diagnosis and appropriate treatment are vital for improving outcomes, particularly in patients with underlying conditions or recent medical procedures, such as catheter placement.

E-PS-05-038
Primary cutaneous apocrine carcinoma of the foot carrying *WWTR1::ANKUB1 f*usion: two exceptional findings
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Background & Objectives: Primary cutaneous apocrine carcinoma (PCAC) is a rare malignant adnexal neoplasm arising from apocrine sweat glands, characterized by definitive features of apocrine differentiation, in absence of distinctive histopathological features seen in other apocrine well-defined tumours. To date, knowledge about its histogenesis, molecular biology and clinical aspects is scarce and needs further investigation.
Methods: Clinical history of the patient was retrieved. Tissue samples were formalin-fixed and paraffin-embedded, then haematoxylin-eosin and immunohistochemical staining were performed. RNA-based NGS was employed for molecular evaluation.
Results: A 68-year-old male presented with a slowly enlarging nodule of 1.5 cm, located on the second digit of the right foot. Surgical excision was performed. Histologically, the tumour was made up of highly atypical cells with round to oval large nuclei, abundant granular eosinophilic cytoplasm, and decapitation secretion, arranged in tubules and solid sheets. Mitotic activity was brisk. Neoplastic cells were positive for CK7, GCDFP-15, ER and AR, while HER2 was negative. RNA-based NGS revealed *WWTR1::ANKUB1* gene fusion. Further clinical workup excluded the possibility of a metastasis.
Conclusion: We report a rare case of PCAC with two unusual features: foot location and *WWTR1::ANKUB1* gene fusion. The anatomical site is very uncommon for PCAC, which usually presents in the axillary or head-neck area. Moreover, the reported fusion has never been described in PCAC, thus representing a novel genomic finding. *WWTR1* gene rearrangement has been occasionally reported in poromas, exerting an oncogenic role through the disruption of Hippo pathway/YAP-signalling (Sekine et al., 2019). *WWTR1* encodes a proto-oncogene whose activity is normally suppressed by the Hippo pathway *via* phosphorylation at a serine residue in the C-terminal region, which prevents its nuclear translocation. As a consequence of the fusion, the loss of this regulatory domain may allow the constitutive nuclear localization of the chimeric protein, thereby promoting transcription of genes involved in cellular proliferation and survival.

E-PS-05-039
Clinicopathologic features of enfortumab vedotin–induced cutaneous toxicity: a case series and review of the literature
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Background & Objectives: Enfortumab vedotin (EV) is an anti-Nectin-4– monomethyl auristatin E (MMAE) antibody–drug conjugate which has significantly improved progression-free and overall survival for patients with advanced urothelial carcinoma. While cutaneous adverse events have been recognized in nearly half of patients receiving EV, the histopathology of EV-induced cutaneous toxicity (EVICT) remains incompletely characterized. We sought to provide a comprehensive understanding of EVICT by integrating clinical and histopathologic features and correlating with a detailed review of the literature in the largest series of biopsy-proven EVICT.
Methods: Retrospective review of hospital records identified 10 patients who developed cutaneous eruptions during EV therapy, from whom thirteen skin biopsies were obtained during the course of care. Clinical presentations and histopathologic features were studied for each case. A literature review was conducted to identify all published, biopsy-confirmed cases of EVICT through March 2025.
Results: Fewer than 30 cases of biopsy-confirmed EVICT have been published. In our cohort, patients typically presented with diffuse, erythematous, maculopapular eruptions, though a subset exhibited lichenoid or eczematous features. Pruritus was common (>80%), and mucosal involvement was rare (1 case). Histopathologically, 10 of 13 specimens (77%) exhibited vacuolar interface dermatitis with basal cell damage and dyskeratotic keratinocytes. The remaining specimens showed a lichenoid interface pattern with a band-like lymphocytic infiltrate at the dermoepidermal junction, and 2 demonstrated

focal full-thickness epidermal necrosis. All cases featured superficial perivascular lymphocytic inflammation (with eosinophils in roughly half of the cases). In 11 of 13 (85%) specimens, abnormal keratinocyte mitoses (including ring-shaped and "starburst" forms) were identified.
Conclusion: EV-induced cutaneous eruptions exhibit a consistent pattern of interface dermatitis with significant keratinocyte injury, highlighted by distinctive ring mitoses, consistent with MMAE inhibition of microtubule polymerization. This study represents the largest series of EVICT correlating clinical and histopathologic findings. Recognizing these features is crucial for accurate diagnosis and management.

E-PS-05-040

Correlation between ex vivo fusion confocal microscopy and conventional haematoxylin-eosin for the diagnosis of cutaneous squamous cell carcinoma

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Background & Objectives: Cutaneous squamous cell carcinoma (cSCC) is a highly prevalent skin cancer, second only to basal cell carcinoma, originating from the keratinocytes of the epidermal spinous layer. Although histological examination remains the gold standard, some cases present diagnostic challenges. Ex vivo fusion confocal microscopy (eFuCM) integrates reflectance and fluorescence signals via an advanced algorithm to produce high-resolution, real-time digital Haematoxylin-eosin (H&E) like images, comparables to conventional histology. This study aimed to evaluate the diagnostic performance of eFuCM for cSCC and to assess its concordance with conventional H&E histology.
Methods: A total of 59 fresh lesions suspicious for cSCC were biopsied and analysed using the VivaScope 2500 (MAVIG Gmgh, Munich) from January to May 2019. Digital images obtained by eFuCM were evaluated by two dermatopathologists with no previous experience in this technology. Diagnostic performance metrics, including sensitivity, specificity, positive predictive value, and negative predictive value, were calculated alongside Cohen's kappa to determine concordance with conventional H&E histology.
Results: The study included 59 cSCC lesions from 51 patients and 7 benign/premalignant lesions from 16 patients. For cSCC diagnosis, eFuCM achieved a sensitivity of 91%, specificity of 85%, positive predictive value of 95%, and negative predictive value of 75%, with a substantial concordance (κ=0.733; $p<0.001$) compared to H&E. Regarding invasive staging, sensitivity was 88%, specificity 94%, positive predictive value 92%, and negative predictive value 91%, with almost perfect concordance (κ=0.839; $p<0.001$). Histological features such as desmoplasia and mitosis showed high specificity (93% and 92%, respectively).
Conclusion: Ex vivo fusion confocal microscopy with digital H&E offers reliable diagnostic accuracy for cSCC and its invasive features, producing images comparable to conventional H&E. The good diagnostic concordance achieved by dermatopathologists without prior eFuCM training supports its potential use as a rapid alternative in urgent cSCC diagnostics.

E-PS-05-041

Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T cell lymphoma (AECTCL): a case report

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Background & Objectives: AECTCL is a rare cutaneous lymphoma characterized by proliferation of epidermotropic CD8+ cytotoxic T cells, aggressive clinical behaviour, and poor prognosis. In WHO classification (5th edition) is recognized as a distinct entity. Represents <1% of cutaneous T cell lymphomas (CTCL). Most patients are adults, presenting localized/disseminated eruptive papules-nodules showing central ulceration-necrosis or superficial hyperkeratosis. Progresses rapidly (weeks-months) with propensity to disseminate to visceral sites, lymph nodes are often spared.
Methods: A 57-year-old man was admitted to hospital for multiple cutaneous lesions in different evolution stages that appeared one week ago. He presented body disseminated lesions not affecting face, palms and soles. Initially were maculo-papular, later ulcerated with raised edges, and necrotic background, others were hyperkeratotic. In addition unquantified weight loss over months with no other symptoms. Oncologic PET/CT showed multiple hypermetabolic cutaneous thickening, bilateral axillary and inguinal hypermetabolic lymphadenopathy and a hypermetabolic focus in the cavum associated with a left IIb adenopathy suggestive of malignancy.
A 10 cm diameter scapular skin lesion was biopsied.
Results: A 0.9x0.4x0.4 cm cutaneous punch is received. Microscopically epidermis showed pronounced rete ridges, abundant lymphocytic infiltrate with marked epidermotropism, spongiosis and reactive changes. Lymphocytes were atypical, with coarse chromatin and frequent mitoses, forming microabscesses. In dermis an inflammatory infiltrate with similar characteristics. It does not affect deep dermis or subcutaneous tissue and is accompanied by adnexal structures destruction. The IHC studies showed intraepidermal tumour lymphocytes: CD8+;CD3+;CD7+;CD5+;focal TIA1+;diffuse CD56+; CD45RO-; CD2-; CD4-; CD30-;TCR beta -; TCR delta -; TOX-; high Ki67.
A TCRG rearrangement study on fresh sample showed presence of T lymphocytes with monoclonal rearrangement.
A FISH study on deparaffinized tissue sections showed JAK2 monosomy 75%.
Conclusion: Diagnosis of $CD8^+$ AECTCL is based upon combination of clinical, histopathologic, and immunophenotypic findings. Since several types of primary CTCLs express $CD8^+$ T cell phenotype, careful clinicopathologic correlation is key.

E-PS-05-042

Two studies confirm superior diagnostic accuracy of molecular PCR over dermatopathology for differential diagnosis of psoriasis and eczema

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Background & Objectives: Targeted treatments for non-communicable chronic inflammatory skin diseases offer significant potential for effective therapy. However, therapeutic success requires an accurate diagnosis, which is challenging due to overlapping clinical and histological features. We aimed at assessing the diagnostic accuracy of the molecular classifier (MC), a novel test designed to assist in the differential diagnosis of psoriasis and eczema.

Methods: In two studies, FFPE samples (n_1=54 and n_2=94) from suspected psoriasis and/or eczema cases were evaluated by 3 and 4 independent dermatopathologists, respectively. MC was performed using the fully automated qPCR system (PsorX©, Dermagnostix, Germany). Diagnostic performance of PsorX© was compared to the reference diagnosis which in study 1 was based on suspected clinical diagnose and histopathology while in study 2 it was based on clinical presentation and course of disease supported by photo documentation, histopathology, blood parameters, and treatment response. Inter-examiner variability in histopathology was assessed using Cohen's and Fleiss' Kappa tests.
Results: There was only moderate diagnostic agreement among dermatopathologists (Fleiss Kappa = 0.22 in study 1 and 0.45 in study 2) in distinguishing eczema from psoriasis. Compared to the respective reference diagnosis, the performance of PsorX© was as follows: sensitivity 85.0% (study 1) and 90.7% (study 2); specificity 87.1% (study 1) and 86.3% (study 2); and accuracy 85.8% (study 1) and 88.3% (study 2). In comparison, histopathological analysis showed a mean sensitivity of 89.7% (75.9-100%, study 1) and 72.0% (62.5-86.0%, study 2), specificity of 61.3% (44.0-92.0%, study 1) and 86.7% (79.5-92.2%, study 2) and accuracy of 76.5% (70.4-83.3%, study 1) and 79.7% (71.4-89.4%, study 2) compared to the respective reference diagnosis.
Conclusion: High interrater variability in histopathology highlights the challenge of distinguishing between psoriasis from eczema, despite expert assessment. This underscores the need for reliable, objective diagnostics like PsorX, which enable precise examiner-independent diagnoses and improve clinical decision-making.

E-PS-05-043
Recurrent skin tumour with mixed features of microcystic adnexal carcinoma, squamous cell carcinoma, and basal cell carcinoma in a renal transplant recipient; a very rare case report
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Background & Objectives: Microcystic adnexal carcinoma (MAC) is a rare malignant sweat gland tumour with central face predilection. Perineural invasion (PNI) is present in around 80% of cases. Risk factors include UV radiation, immunosuppression, and previous radiotherapy. Herein we report a case with each of these risk factors and a rare triple mixed tumour morphology.
Methods: A 69-year-old Caucasian male renal transplant recipient (RTR) presented with a clinical squamous cell carcinoma (SCC) on the right cheek. He had been immunosuppressed for 7 years. The primary lesion was treated by wide local excision (WLE) and reported as a pT3 high-risk SCC. He underwent adjuvant radiotherapy with 45Gy in 10 fractions and was started on Acitretin. At 16 months follow-up there was clinical evidence of tumour recurrence reported as MAC on biopsy and subsequently treated by Mohs surgery.
Results: The primary lesion was a 27mm SCC of no specific type, expressing moderate and poorly differentiated areas and a superficial focal basal cell carcinoma-like area 3.5mm from nearest margin, with deep PNI, 1mm from margin. The clinically recurrent 15mm lesion was within the scar. Diagnostic punch biopsy showed MAC. Mohs surgery was completed requiring 4 stages to excise an ulcerated tumour invading deeply into the facial musculature and parotid duct, with widespread PNI. The recurrent tumour had mixed features of MAC and moderately-differentiated SCC, both expressing strong CK5 immunohistochemistry. There was extensive ductal differentiation in the deeper component comprising small/elongated microacini lined by single cell layers, highlighted widely by EMA and focally by CK7, CK19, Cam5.2 and CEA.
Conclusion: Few cases of MAC have ever been reported in transplant recipients. Post-transplant SCC can show divergent differentiation. Two confirmed cases of MAC in RTRs were locally aggressive requiring extensive surgical resection due to bone invasion. More studies are required to confirm the optimal approach for management to minimise recurrence/metastatic risk.

E-PS-05-044
Carcinoma Erysipeloides: a rare entity
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Background & Objectives: Carcinoma erysipeloides (CE) is an uncommon type of cutaneous metastasis in which malignant cells spread to the skin via superficial dermal lymphatic vessels. The lesions present as ill-circumscribed erythematous plaques resembling cellulitis or erysipelas. Although it is most commonly seen in breast cancer, it can also occur in melanoma, lung, ovarian, colonic and pancreatic carcinomas.
Methods: A 42-year-old woman suffering from red cutaneous lesions on her right chest skin applied to Dermatology Clinic. In her physical examination, there were many ill-defined erythematous macules and plaques resembling cellulitis or erysipelas on her right chest and breast skin. There was no evident crusting or scaling. She had left mastectomy surgery 3 years ago because of breast carcinoma. A punch biopsy with formaldehyde fixation and a fresh punch biopsy for immunofluorescence examination were sent to the Pathology Laboratory.
Results: In the microscopic evaluation of the formaldehyde fixed, paraffine embedded biopsy, under the orthokeratotic and acanthotic epidermis, there were many atypical cells with pleomorphic, hyperchromatic nuclei, large eosinophilic cytoplasm filling the dermal lymphatics. These cells expressed GATA3, oestrogen receptors (ER), progesterone receptors (PR), Keratin7 and they were not stained positive with p40, Keratin20, CD34, Vimentin immunohistochemically. Dermal extravascular invasion of these cells was not present. Inflammatory cells were present in the dermis.
No Immunoglobulin, Compleman and Fibrinogen accumulation was detected in the direct immunofluorescence application to the fresh biopsy.
The lesion was diagnosed as CE.
Conclusion: CE manifests clinically as a fixed erythematous patch or plaque resembling cellulitis or erysipelas without fever. The inflamed area may show a distinct raised periphery and oedema secondary to lymphatic obstruction.
Malignant cells predominantly locate within the dermal lymphatic vessels and malignant thrombi-induced lymphatic obstructions cause the erysipeloid induration.
CE is associated with a poor prognosis and the average life expectancy is 2 years from the diagnosis of CE.

E-PS-05-045
The impact of BRAF mutational status on survival in our group of patients with advance melanoma
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Background & Objectives: Melanoma accounts for less than 2% of all cancers worldwide but is responsible for 80% of skin cancer-related deaths. Among the various genetic alterations in melanoma, BRAF and NRAS mutations are among the most common. While multiple studies have confirmed the involvement of BRAF in melanoma, its role as a prognostic marker remains debated. However,

the BRAF V600E mutation is clinically significant, as its presence determines eligibility for targeted therapy with BRAF inhibitors. This retrospective study aimed to correlate BRAF mutation status with the clinicopathological characteristics of primary skin melanoma, assess the impact of BRAF-mutated versus BRAF wild-type melanoma on disease progression and overall survival, and to evaluate the influence of BRAF inhibitor therapy on survival outcomes.
Methods: A total of 152 patients with advanced melanoma along with available clinical data were included in this study. BRAF mutational status was determined by allele specific real-time PCR between 2013 and 2020 at the Clinical Hospital Centre Rijeka.
Results: Of the 152 patients, 80 (52%) had BRAF-mutated melanoma, which showed a slight predilection for the trunk. Histologically, nodular melanoma was the most commonly associated subtype. No significant difference was observed in terms of disease progression and overall survival between BRAF-mutated and BRAF wild-type patients. However, in patients with BRAF-mutated melanomas, those who received BRAF inhibitors exhibited improved survival outcomes in advanced disease stages.
Conclusion: Overall, this study shows that BRAF inhibition therapy is a proper way for combating melanomas with distant metastases, at least until new and more efficient form of therapy is discovered.

E-PS-05-046
Epithelial hyperplasia with serrated appearance and other reactive changes of eccrine glands
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Background & Objectives: The existing literature contains a paucity of studies that specifically investigate reactive changes in the eccrine glands. To the best of our knowledge, the occurrence of epithelial hyperplasia within the eccrine unit has not been previously documented. The objective of this study was to ascertain the prevalence of various reactive changes observed in eccrine glands and the accompanying entities.
Methods: During a 6-month period, a total of 2215 skin samples from 2190 patients were examined during routine examination. Epithelial hyperplasia was defined as the presence of at least three cell layers in the eccrine duct and four or more cell layers in the coil.
Results: Epithelial hyperplasia of eccrine coil (cEH) was detected in 19 cases and manifested as serrated appearance, epithelial bridges or slit-like irregular fenestrations. The lower extremity was the most affected area. Epithelial hyperplasia of the eccrine ductus (dEH) was identified in 14 cases and was frequently associated with marked desmoplasia or dermal fibroblastic proliferation.
Clear cell change in eccrine coil (cCCC) was observed in 39 cases and was not associated with diabetes mellitus. Clear cell change of the basal epithelium of the eccrine sweat duct (CCCBESD) was found in 25 cases and was frequently observed in biopsies sampled from the face and trunk. Syringofibroadenomatous hyperplasia (SFAH) was observed in 20 cases.
Conclusion: cEH is typically detected in glands exhibiting a serrated appearance. It was suggested that cEH and dEH may be caused by conditions that impede sweat excretion, such as thick keratin layer, sclerotic/desmoplastic changes. SFAH, cCCC and CCCBED are observed with greater frequency than expected and in various pathologies, some of which are not documented in the literature. This study represents the most extensive series reported in the literature examining the association between reactive eccrine gland changes and various parameters.

E-PS-05-047
Syringocystadenoma papilliferum arising on background sebaceoma: a case report
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Background & Objectives: Syringocystadenoma papilliferum (SCAP) is a rare benign adnexal tumour that typically arises in the context of other skin conditions, particularly in individuals with basal cell nevus syndrome. SCAP presents as a papule or plaque on the skin and is characterized by the proliferation of sweat gland ductal epithelium. Sebaceoma, a tumour of the sebaceous gland, is also a rare, benign neoplasm, often associated with nevoid basal cell carcinoma syndrome (Gorlin-Goltz syndrome). We present a rare case of SCAP arising on a background of sebaceoma, highlighting the importance of recognizing this unusual histopathological finding. The patient, a 56-year-old male, presented with a solitary, asymptomatic lesion on the scalp that had been growing for several years. Histopathological examination revealed the presence of both SCAP and sebaceoma, with the SCAP component showing the characteristic cystic structures and papilliferous projections, while the sebaceoma component exhibited sebaceous differentiation and characteristic features of basal cell nevi. This case underscores the importance of considering multiple adnexal tumours in the differential diagnosis of cutaneous lesions and emphasizes the need for thorough histopathological evaluation.
Methods: N/A
Results: Histopathological examination plays a crucial role in the diagnosis of such rare associations. The identification of both SCAP and sebaceoma components in a single lesion requires careful consideration of their respective features and immunohistochemical markers.
Conclusion: This case demonstrates the rare occurrence of SCAP arising on a background sebaceoma, emphasizing the need for thorough histopathological evaluation when diagnosing adnexal tumours. The presence of both SCAP and sebaceoma in the same lesion underscores the importance of considering multiple adnexal tumours in the differential diagnosis, particularly in patients with genetic predispositions such as basal cell nevus syndrome. Further research is needed to better understand the pathogenesis and potential genetic underpinnings of such rare tumour associations.

E-PS-05-048
Spindle cell variant of epithelioid fibrous histiocytoma with aneurysmal changes: a case report
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Background & Objectives: Epithelioid fibrous histiocytoma is a rare mesenchymal neoplasm with cutaneous ALK rearrangement. The spindle cell variant has recently been described. However, intralesional diffuse bleeding (aneurysmal change) has not been reported to date.
Methods: We report on a case of Epithelioid Fibrous Histiocytoma, Spindle Cell Variant (EFH-SP-v) with Aneurysmal Changes, diagnosed in dermatopathology department of University of Health Sciences, Istanbul Training and Research Hospital.
Results: An 18-year-old woman presented with a 1 cm painless purple papule located on the anterior aspect of the right thigh with a halo formation on the periphery. The lesion was excised with the prediagnoses of haemangioma, angiokeratoma and melanoma. Microscopic

examination revealed a tumoral formation consisting of spindle cells with large cytoplasm, and bland uniform oval shaped nucleus, forming short bundles crossing each other, located in a smoothly circumscribed-rounded area in the superficial and mid dermis. Aneurysmal areas containing pools of erythrocytes were observed in the centre of the tumour. In immunohistochemical study, tumour cells expressed ALK (clone D5F3) and Factor XIIIa, while epithelial, smooth muscle, melanocytic and vascular markers were negative. These findings were consistent with the diagnosis of Epithelioid Fibrous Histiocytoma, spindle cell variant (EFH-SP-v).
Conclusion: In the differential diagnosis of EFH-SP-v, there are ALK-expressing and ALK-negative mimics. ALK-expressing mimics include some Spitz lesions, inflammatory myofibroblastic tumour, "ALK-rearranged CD34-positive spindle cell neoplasms resembling dermatofibrosarcoma protuberans". Although considered as a differential diagnosis, there is a morphologic spectrum between Epithelioid Fibrous Histiocytoma and "Superficial ALK-Rearranged Myxoid Spindle Cell Neoplasm". Cutaneous Syncytial Myoepithelioma, Cellular Neurothekeoma, Reticulohistiocytoma may show morphologic similarities with EFH-SP-v, although they do not express ALK.
In order to arrive at an accurate diagnosis, it is imperative to integrate morphologic, immunophenotypic and, in select cases, molecular data. It is also crucial to bear in mind EFH-SP-v.

E-PS-05-049
Porocarcinoma of the scalp a rare cutaneous cancer: a case report
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Background & Objectives: Eccrine porocarcinoma is a malignant tumour of eccrine sweat glands, it represents 0.005% of malignant skin epithelial tumours.
The first case was described by Pinkus and Mehregan in 1963 as "epidermotropic eccrine carcinoma".
Methods: We reported the case of a 61 years (3)old woman, who had a skin mass of the right parieto-occipital scalp measuring 6 cm in long axis, largely ulcerated, evolving for 5 months, she had a surgical excision.
Results: ***Macroscopic examination:*** we received a 9x7cm skin sample with an ulcerated lesion of 6x6cm and 5cm thick, The tumour was polypoid, granular and heterogenous coloured with necrotic and haemorrhagic changes.
The microscopic examination : reveals an infiltrating carcinomatous proliferation connected to the epidermis and extended to the reticular dermis, associated to foci of benign eccrine poroma.
An immunohistochemical study was carried out, revealing a positivity of the cells to the anti CD117, EMA and ER antibodies.
Discusson: Porocarcinoma is a very rare tumour. It most often occurs in the elderly, the age at diagnosis being between 60 and 80 years. Tumour size varies widely from < 1 cm to 10 cm. It commonly affects the lower limbs followed by the trunk. Rare locations such as the scalp have been reported in the literature. Ours is similar to that of *Masamatti and Al*, observed in a woman and occurring in the right parieto-occipital region. Most frequently porocarcinoma occurs on a pre-existing poroma as in our case.
Conclusion: Porocarcinoma is an aggressive and rare skin cancer. Surgery is the main modality of treatment.

E-PS-05-050
Mycosis fungoides in Algeria: a 3-year retrospective study
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Background & Objectives: Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma (CTCL) , with an incidence of 2 to 4 cases per 1,000,000 individuals, and well-documented epidemiological patterns.[1] However, data from North Africa remain scarce. This study presents the first Algerian analysis of MF, examining its prevalence, sex distribution, histological subtypes, and immunophenotypic characteristics.
Methods: This retrospective study reviewed 20 cases of MF that we got in the Pathology department of the University Hospital of Constantine-Algeria, over a period of 3 years (February 2022 to February 2025). All relevant data such as sex, histological aspect and immunophenotypes were collected and reviewed.
Results: Among the 42,382 pathological specimens received during the study period, MF accounted for 20 cases (0.04%). The study cohort included 10 male and 10 female patients, yielding a sex ratio of 1:1.
Histopathological analysis highlighted a marked predominance of classic MF, comprising 15 cases (75%) followed by 3 cases of folliculotropic variant MF (15%), and only 2 granulomatous MF cases (10%).
Immunohistochemical analysis found a typical CD4+ phenotype in 16 cases of MF, while 4 cases (20%) exhibited a CD8+ cytotoxic phenotype.
Conclusion: Our study provides the first Algerian data on mycosis fungoides, revealing a balanced sex distribution and a higher-than-expected prevalence of CD8+ cases. These findings challenge established epidemiological patterns and emphasize the need for further research to understand MF's characteristics in North African populations.

E-PS-05-051
Clear-cell atypical fibroxanthoma: a rare subtype in a 25-year case analysis
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Background & Objectives: Atypical fibroxanthoma (AFX) is a rare, low-grade malignant neoplasm of dermal fibroblastic-histiocytic origin, primarily affecting sun-exposed skin in elderly individuals. Its histopathological variability and similarities with other skin tumours make diagnosis challenging. This study reviews AFX cases diagnosed at Hospital Universitario La Paz (HULP) over 25 years, focusing on a rare clear-cell subtype case to assess epidemiological, clinical, and histopathological characteristics and highlight diagnostic challenges.
Methods: A retrospective review was conducted on all AFX cases diagnosed at HULP between 2000 and 2024. Data were extracted from pathology reports, including patient demographics (sex, age), lesion location, initial clinical diagnosis, histopathological findings, immunohistochemistry (IHC) profiles, and revision diagnoses. Cases were analysed to determine patterns in diagnosis and misclassification rates.
Results: Over 25 years, 85 AFX cases were identified. The mean age was 78.76 years, with a median of 80. Of these, 66 were male and 19 were female. The most common location was the scalp, followed by the ear, forehead, and cheek. The predominant clinical suspicion was basal cell carcinoma or squamous cell carcinoma, with only four cases correctly identified as AFX before histopathological evaluation. The spindle-cell subtype was the most frequent histological variant, while the clear-cell variant appeared in just one case, highlighting its exceptional rarity and the diagnostic challenges associated with it. This case underscores the importance of considering other differential diagnoses, such as clear cell renal cell carcinoma, to avoid misclassification.

Conclusion: AFX remains a diagnostic challenge due to its clinical and histopathological overlap with other neoplasms, particularly when uncommon histological subtypes are present. A thorough histopathological evaluation, supported by IHC (positive staining for CD10 and vimentin, and negative for keratins, S100, and CD34), is essential for accurate diagnosis and to avoid misclassification. Increased awareness and recognition of AFX features can improve diagnostic accuracy and patient management.

E-PS-05-052

Unna's papillomatous nevi with nuclear atypia trap for young pathologists

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Background & Objectives: Unna's papillomatous nevi are exophytic intradermal or compound melanocytic proliferations, whose dimensions are often larger than 1 cm, rarely described in the literature. Additional signs of regression and senescence can be a trap for young pathologists.
Methods: We present a case of a papillomatous Unna's nevi from the neck of a 39 year women, which persisted for about ten years, until just before the excision when signs of discomfort appeared in the patient. A skin excision measuring 0.8x0.7x0.1 cm, with a papillomatous brownish lesion measuring 2.3x1.x1.3 cm present on the surface, was submitted to our department. The material was serially dissected and completely embedded for microscopic analysis, and the sections were stained with haematoxylin and eosin, and additionally one of them was stained with Alcian blue - PAS.
Results: Microscopic analysis showed a compound nevus with prominent papillomatous proliferated epidermis, presence of intraepidermal keratin cysts, and hyperkeratosis on the surface. Prominent blood vessels, stromal oedema, periadnexal growth, pseudotubular and pseudolacunar structures, and signs of neuritization were found. However, the presence of nuclear atypia was puzzling, but we termed senescent, because no mitoses were found. Stromal mucin deposits and corneal Malessezia furfur have been seen on the special stain.
Conclusion: Large size од papillomatous nevi, nuclear atypia, and signs of natural regression can be confusing in the routine work of general young pathologists. So, excluding the presence of mitoses on a series of sections, on basic staining, may be the only way to exclude nevoid melanoma, where the use of artificial intelligence can save a lot of time.

E-PS-05-053

Spotlight on Spitz: unravelling the spectrum of Spitz tumours in a Romanian county hospital

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Background & Objectives: Spitz nevus was firstly described by Sophie Spitz as the „benign nevus of childhood" in 1947 and further transformed in the category of Spitz tumours. Spitz tumours are represented by the Spitz nevi, Spitz melanocytoma, Atypical Spitz tumour and Spitz melanoma. The objective of our study was to emphasize the epidemiological and histopathological characteristics of Spitz nevi and atypical Spitz tumours in a county hospital in Romania.
Methods: A retrospective study was performed based on the histopathological diagnosis of Spitz nevi or Atypical Spitz Tumour (AST), including 10 cases of Spitz tumours which were diagnosed in the Clinical Pathology Department of the Mures Clinical County Hospital, Romania, between 2018-2024. The tissue samples were received from either the General Surgery or Plastic Surgery ward from patients diagnosed with a skin tumoral proliferation.
Results: Out of 10 Spitz tumours the highest incidence of 30%(n=3) were diagnosed in 2022, with a mean age of 20.2 years-old (maximum 40 years-old). Grossing revelled plane or elevated lesions on the tegument, with different localizations (arm, calf, forearm, thorax) and variations of colour from white-grey to brown. Histopathological, 100% (n=10) of cases presented fusiform cells, in combination with 70%(n=7) with epithelioid and rhomboid cells. 10%(n=1) of cases showed cytological atypia, 30%(n=3) presented pagetoid migration and 20%(n=2) presented mitoses. Immunohistochemically, the tumoral cells where positive for S100 in 70%(n=7) cases, for SOX10 in 30%, melanA in 40%(n=4) and Ki67 was under 5% in 100%(n=10) cases. The final histopathological diagnostic was Spitz nevus in 90% cases (intradermic or compound) and ATS in 10%(n=1) cases.
Conclusion: Even though Spitz tumours are rare, they represent a challenge in diagnosis especially when the age is higher, with different histopathological appearance, but with a high importance of differentiation between benign and malignant with direct impact on the prognostic of the patient.

E-PS-05-054

Paediatric spiradenoma with adenomyoepithelial hyperplasia and high mitotic activity: a diagnostic challenge in the benign-malignant spectrum

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Background & Objectives: Spiradenoma is typically a benign adnexal tumour seen in adults, with a predilection for the head and neck. In paediatric patients, this tumour is exceedingly rare. The concurrent presence of adenomyoepithelial hyperplasia and a high mitotic rate further complicates the differentiation between a benign process and potential malignant transformation. This case report presents a 12-year-old male with an unusual toe lesion, highlighting the diagnostic dilemma posed by overlapping histopathological features.
Methods: A 12-year-old male presented with a progressively enlarging nodular lesion on the dorsum of the toe, which had been subject to repeated trauma. An excisional biopsy was performed on a 2.5 cm firm, cream-brown nodule, resulting in the achievement of clear surgical margins. The specimen underwent comprehensive histopathological evaluation, with special emphasis on p63 immunohistochemistry and assessment of the Ki-67 proliferation index.
Results: Microscopic analysis revealed solid nests and glandular structures composed of dual cell populations, including ductal and myoepithelial elements. Myoepithelial differentiation was confirmed by strong p63 positivity. Despite the absence of significant cytologic atypia, necrosis, or infiltrative growth, an elevated mitotic rate (5 mitoses/HPF) and a high Ki-67 index (%70) were observed.
Conclusion: This case emphasizes the diagnostic challenge encountered in paediatric spiradenomas exhibiting adenomyoepithelial hyperplasia and high mitotic activity. The overlap between benign and malignant features necessitates cautious interpretation and underscores the importance of meticulous histopathological evaluation. Moreover, to

the best of our knowledge, such a paediatric case with these specific histopathological features has not been previously reported in the literature. Long-term clinical follow-up is imperative to monitor for any signs of progression, and further studies are required to clarify the prognostic implications of these atypical features.

E-PS-05-055

Folliculotropic mycosis fungoides: about 4 cases

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Background & Objectives: Folliculotropic mycosis fungoides (FMF) is a particular subtype of mycosis fungoides (MF), characterized by invasion of hair follicles, sebaceous glands, and/or sweat glands by atypical T-cells.
Methods: A retrospective descriptive study of all cases with histological diagnosis of FMF between January 2005 and December 2024.
Results: During the study period, 4.8% of cases of MF attended our institute were folliculotropic (4/84). Three patients were male and one was female. The age at the time of diagnosis ranged between 7 to 78 years. FMF presented as ill-defined plaques with follicular papules (n=3,75%), nodular lesions (n=2, 50%), and patchy-plaque alopecia affecting the scalp (n=3, 75%) or the eyebrows (n=1, 25%). The majority of patients had lesions in the limbs (100%), followed by the trunk (75%) and the scalp (50%). The skin biopsies of all FMF patients showed perifollicular or intrafollicular infiltration with atypical T cells. Follicular mucinosis was not noted in any case. Large cell transformation was observed in one case (25%). Lymph node metastasis was present in one case. Three patients showed early-stage (stage IA–IIA) and one showed advanced-stage (IVA–IVB) disease at the time of diagnosis. All patients survived after a follow-up period of 2 years. The treatments used were topical corticosteroids, UVB therapy, and retinoids.
Conclusion: FMF represents 4.8% in our study which is a lower frequency than reported in other series (10%). It can affect the paediatric population and accounts for 3 to 36% of all paediatric MF. The head and neck are usually reported to be the predilection site of the lesions, unlike our patients. It is commonly believed that FMF has a more aggressive clinical course than classical MF.

E-PS-05-056

Primary cutaneous Ewing sarcoma of the distal fifth finger: a rare paediatric presentation

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Background & Objectives: Ewing sarcoma is the second most common paediatric malignant bone tumour, primarily occurring in long bones. Nevertheless, extraskeletal locations are uncommon, with primary cutaneous Ewing sarcoma being exceedingly rare.
Methods: We report the case of a previously healthy 12-year-old boy who presented with a cutaneous lesion on the palmar aspect of the fifth digit of his left hand. The lesion had been present for several months and had recently exhibited accelerated growth. Clinically, a pyogenic granuloma was suspected and the lesion was ressected. The specimen was submitted to our department for histopathological evaluation.
Results: Macroscopic examination revealed multiple irregular tan to white fragments, the largest measuring 2.1 cm. Microscopic analysis demonstrated skin infiltrated by a high-grade neoplasm composed of uniform, small round blue cells exhibiting mild nuclear irregularity and scant cytoplasm, arranged in a solid architectural pattern. No bone was identified. Immunohistochemistry showed positivity for CD99 (diffuse and membranous), NKX2.2 (multifocal) and CAM5.2 (focal). There was also unusual immunoreactivity for S100, SATB2 and p63, that promped challenging differential diagnosis. No immunoreactivity was observed for TLE1, WT1, SOX10, SMA, Desmin, Myogenin, MyoD1, CD45, HMB45, CD34, or ERG. Fluorescence in situ hybridisation (FISH) revealed rearrangement of the EWSR1 gene and no rearrangement of SS18. Next-generation sequencing (NGS) identified a EWSR1-FLI1 fusion (QIAseq RNA Fusion XP Sarcoma Panel). A diagnosis of Ewing sarcoma was established.
Conclusion: Cutaneous Ewing sarcoma presents a diagnostic challenge in paediatric tumours, due to its rarity and unique histologic and clinical characteristics, besides relatively better prognosis compared with skeletal Ewing sarcoma. A high index of suspicion and comprehensive histopathological evaluation, in conjunction with cytogenetic and molecular studies, are essential for timely diagnosis and adequate management of these patients.

E-PS-05-057

A race against time: cutaneous angioinvasive mycosis in an immunocompromised patient – a diagnostic and therapeutic challenge

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Background & Objectives: Angioinvasive fungal infections are life-threatening complications in immunocompromised individuals, particularly in patients with hematologic malignancies and prolonged neutropenia. Fusarium spp. is an emerging opportunistic pathogen with intrinsic resistance to multiple antifungal agents and high mortality in disseminateddisease. Cutaneous involvement—often mimicking ecthyma gangrenosum or leukaemia cutis, is common and may delay accurate diagnosis and timely intervention.
We report the case of a 19-year-old female with refractory B-cell acute lymphoblastic leukaemia (ALL), currently undergoing third-line chemotherapy and presenting with prolonged neutropenia. During hospitalization, she developed respiratory symptoms with pulmonary masses unresponsive to broad-spectrum antibiotics. Physical examination revealed a necrotic cutaneous plaque on the thigh, measuring approximately 3 cm. An excisional biopsy and tissue cultures were performed. Initially suspected to be leukaemia cutis, histopathologic analysis revealed angioinvasive hyaline septate hyphae, raising suspicion for invasive fungal infection. Antifungal therapy was promptly initiated, resulting in favourable clinical response and avoiding surgical debridement. SubsequentGomori methenamine silver (GMS) staining confirmed fungal elements, and cultures identified Fusarium spp. Blood cultures remained negative throughout. The patient was discharged in stable condition and is currently awaiting bone marrow transplantation.
Methods: Case report.
Results: This case highlights the diagnostic complexity of necrotic skin lesions in immunocompromised patients and underscores the critical importance of early biopsy and communication of preliminary findings. Differentiating leukemic infiltration from fungal infection is essential to avoid misdiagnosis and therapeutic delay. Histopathologic confirmation enabled timely management despite negative blood cultures. Multidisciplinary collaboration and early antifungal therapy contributed to a favourable outcome.
Conclusion: Cutaneous fusariosis should be considered in neutropenic patients with necrotic skin lesions. Early biopsy and histologic evaluation are essential for diagnosis. Successful management depends on prompt antifungal treatment and immune recovery, with dermatopathology playing a key role.

E-PS-05-058

Non-dermatophytic mold onychomycosis mimicking subungual malignant tumour

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Background & Objectives: Onychomycosis, a fungal infection of nails, is primarily caused by dermatophytes and yeasts. Recently, non-dermatophyte molds (NDM), such as Acremonium spp., have also been implicated. These molds are more common in elderly and immunocompromised patients, with prevalence rates ranging from 1.45% to 17.6%. In immunocompetent patients, infections are rare.
Methods: A 34-year-old HIV-negative male presented with a painful subungual mass on his left great toe for three months, following minor trauma. Examination revealed an ulcerated, oozing nodule deforming the nail plate, with surrounding erythema and oedema extending to the second digit. The differential diagnosis included onychomycosis, verruca vulgaris, mycobacterial infection, benign tumours (e.g., pyogenic granuloma, keratoacanthoma), and malignant tumours (e.g., squamous cell carcinoma, melanoma).
Results: Routine haematological, biochemical and immunological investigations were either negative or within normal range. Mantoux test was negative. No significant pathologic findings were detected on X-ray examination and Magnetic Resonance Imaging of the affected limb. Biopsy and tissue cultures obtained from the nail bed revealed infection by Acremonium spp. The patient responded satisfactorily to treatment with i.v. liposomal amphotericin B (4 mg/kg/d) for ten days followed by surgical debulking of the subungual mass and a three-month course of p.o. voriconazole (200 mg b.i.d.). There was no evidence of relapse at his follow-up visit, six months later.
Conclusion: Non-dermatophyte molds may be involved in onychomycosis as primary pathogens in up to 2.3% of all onychomycoses, or as contaminant agents. Acremonium spp. in particular, is an uncommon cause of onychomycosis, especially in immunocompetent individuals. Optimal treatment of Acremonium infections is not well defined due to the rarity of this infection. Based on anecdotal reports, treatment of most invasive infections requires a combination of surgical intervention, when possible, and a regimen of amphotericin B and azoles.

E-PS-05-059

Darier's disease: case series of a rare entity

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Background & Objectives: Darier's disease (DD) is a rare autosomal dominant genodermatosis characterized by a keratinization disorder involving the skin, mucous membranes, and nails. It is characterized by oily, keratotic, yellow-red/brown, crusted papules or plaques. The lesions most commonly affect seborrheic areas. Here we present a case series of 6 patients with DD.
Methods: Six patients (3 females, 3 males; age range 17–67 years) presented with similar clinical manifestations to the dermatology outpatient clinic, including persistent skin eruptions and papules. The localization of the lesions varied, including head and neck/eyelid, trunk, upper extremities, and vulvar regions. Incisional skin biopsies performed on each patient revealed overlapping histomorphological features.
Results: Biopsy findings included focal parakeratosis in the epidermis, marked suprabasal acantholysis, and cleft formation. The retained single layer of basal keratinocytes overlying the dermal papillae protruding into the cavity irregularly formed a villous appearance. Acantholytic "corps ronds" and "grains" cells were observed within the clefts. DIF microscopic examination revealed no IgG, IgA, IgM, C3, or fibrinogen accumulation. Mild perivascular inflammatory cell infiltration was also observed.
Conclusion: DD's estimated prevalence is 1 in 30,000-100,000. Mutations in the ATP2A2 gene on chromosome 12q24.1 are identified in DD cases. Although DD is known to be a hereditary disease, cases can present with no family history of illness or with atypical clinical findings. The disease usually starts around puberty and runs a chronic course. The severity of the manifestations varies with exacerbations induced by sun exposure, heat, friction, infections, and pregnancy. The hallmark histologic feature is focal acantholytic dyskeratosis involving the suprabasal epidermis. DIF examination is essential in the differentiation from other acantholytic dermatitis, as a Darier-like pattern is observed within several acantholytic diseases, such as Hailey-Hailey disease, Grover's disease, warty dyskeratoma, seborrheic dermatitis, pemphigus vegetans, and pityriasis amiantacea. Clinicopathologic correlation is the last word used to arrive at a diagnosis.

E-PS-05-060

Basal acantholytic dyskeratosis as Wolf's isotopic response after herpes zoster infection

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Background & Objectives: Wolf's isotopic response occurs when a new skin disorder develops at the site of a healed, unrelated skin disease. Herpes zoster (HZ) is the most common preceding condition. Reported disorders are primarily granulomatous and lichenoid reactions.
Methods: Diagnosis was made using a routine staining. We reviewed the medical record to obtain data such as age, site and clinical suspicion. Additionally, we performed a review of the literature in the last ten years.
Results: A 69-year-old female consulted for a linear eruption of asymptomatic hyperpigmented and crusted plaques on her right thoracic region. The lesions were located on the same site where, eighteen months before, she had suffered a HZ, that had completely disappeared after treatment. With the clinical diagnosis of lichen planus, a biopsy was made. This revealed basal acantholytic dyskeratosis along the whole epidermis, with no herpetic changes. These findings were interpreted as a Wolf's isotopic response.
Conclusion: Many disorders have been described as Wolf's isotopic response in healing or healed herpes zoster scars. To our knowledge, this is the first reported case of basal acantholytic dyskeratosis occurring as this reaction after a HZ infection. This finding expands the spectrum of conditions included in this phenomenon.

E-PS-05-061

Mogamulizumab-associated rash and the overlap histopathological features with Cutaneous T cell lymphoma: a case report

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Background & Objectives: Mogamulizumab is a monoclonal antibody targeting CCR4 used as a therapeutic option for mycosis fungoides (MF) and Sézary syndrome (SS).
Nevertheless, Mogamulizumab-associated rash (MAR) can be defiant to distinguish from MF or SS, clinically and histopathologically, which may result in treatment withdrawal due to severe drug response or incorrect diagnosis of recurrence or disease progression.

Methods: A 60 year-old woman previously diagnosed with Sézary Syndrome has been treated with methotrexate for two months. However due to lack of response, mogamulizumab was initiated.
After three months of treatment, the patient presented a disseminated, monomorphous, and grossly symmetrical dermatosis characterized by lichenoid papules surrounding hair follicles with occasional scale. Erythrodermic lesions were also accentuated in the face.
A recent biopsy was performed.
Results: Histopathological study revealed an epidermis with mild acanthosis, parakeratosis, scattered apoptotic keratinocytes and exocytosis of lymphocytes. In the papillary and superficial dermis, there is a mild to moderate lichenoid inflammatory infiltrate, composed predominantly of lymphocytes and histiocytes, with a focal granulomatous pattern.
Immunohistochemistry showed positivity of the abundant T cell population for CD3, CD2, CD5, CD7, CD8 in the dermal infiltrate but also highlighted alignment of lymphocytes among the basal keratinocytes.
CD4 was negative and CD30 was positive in scattered cells.
Conclusion: The histopathological findings were in favour of MAR, still the alignment of lymphocytes in the basal layer raised concern of disease persistence.
Therefore, the rearrangements study of T cell receptor genes was performed in this biopsy and in the previous where the diagnosis of SS was made.
A polyclonal population of T cells were detected in the current biopsy in contrast to the first one.
Then, the patient was submitted to corticoid therapy but also maintained treatment with mogamulizumab leading to complete response, reinforcing the fact that mogamulizumab therapy continuation or retreatment should be considered for a favourable outcome.

E-PS-05-062
Cutaneous chromomycosis in an elderly agricultural worker. A case report
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Background & Objectives: Cutaneous chromomycosis is a chronic fungal infection of the skin caused by various species of dematiaceous fungi found in nature and common in the tropical zone. This report presents a disease that is rare in Europe, which poses difficulty in its diagnosis.
Methods: An 81-year-old woman, residing in the rural area of Silvianópolis, Minas Gerais, Brazil, reports a history of a cutting trauma on her right and left forearms caused by a bird during her work. Following the incident, a vegetating lesion with a central crust appeared.
Results: The patient had a previous history of two skin biopsies with a diagnosis of skin carcinoma and sought treatment after noticing the growth of the lesion. Microscopic analysis, with H.E. staining, revealed skin with pseudoepitheliomatous hyperplasia and granulomatous inflammation with Langhans giant cells, intraepidermal abscesses, and brownish, birefringent membrane structures, consistent with Chromomycosis sp. Grocott's staining was positive for fungi. Treatment with Itraconazole 100mg daily for two months resulted in the complete resolution of symptoms.
Conclusion: Cutaneous inflammatory processes show an important differential diagnosis with skin cancer. It is important to emphasize that fungal lesions, of occupational origin, can also lead to severe infections, and that timely diagnosis and appropriate treatment can lead to successful outcomes.

E-PS-05-063
Molecular profiling of advanced melanoma
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Background & Objectives: Melanoma is the fifth most common cancer worldwide, characterized by a high mutation rate driven by environmental and genetic factors. Next-Generation Sequencing (NGS) has revolutionized cutaneous melanoma (CM) management, particularly in identifying mutations for targeted therapies. This study assesses the frequency of driver mutations in advanced melanoma cases in Nova Scotia and compares these findings with broader literature.
Methods: We analysed data from 799 melanoma patients who underwent NGS and/or BRAF immunohistochemistry (IHC) testing between 2017 and 2023. Associations between mutation types, age, tumour stage, and anatomical location were evaluated.
Results: The mean patient age was 71, with a male-to-female ratio of 1.6. BRAF mutations were found in 297 (37%) cases, NRAS in 211 (26%), KIT in 34 (4%), and GNAQ/GNA11 in 15 (2%). A mutation of clinical significance was not detected in 243 (30%) cases. Among BRAF-positive cases, 201 (68%) had V600E mutations, 69 (23%) had V600K/R/D, and 27 (9%) had non-V600 mutations. BRAF mutations were significantly associated with younger age ($p < 0.00001$), lower T-category ($p = 0.0002$), and were most frequently observed in CM of the torso (54%). NRAS mutations correlated with older age (≥60 years, $p = 0.009$), but not with T-category. NRAS mutations were most frequent in CM of the extremity (38%). KIT mutations were relatively rare in our cohort, but were most frequent in CM of mucosal (25%) and acral (17%) sites.
Conclusion: BRAF mutations, particularly V600E, were the most common but occurred at a lower frequency than often reported in literature. NRAS mutations were relatively frequent in Nova Scotia. Appropriate molecular testing is essential for optimizing management of advanced CM, and knowledge of expected local trends influences resource planning and quality assurance practices.

E-PS-05-064
Calcinocis cutis appearing as a vascular lesion on MRI
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Background & Objectives: Calcinosis cutis is a rare disease characterised by calcium salts deposition in the skin and subcutaneous tissue. It is classified as dystrophic (the most common, associated with connective tissue disease), metastatic (associated with abnormal serum levels of calcium and phosphorus), idiopathic, iatrogenic, and calciphylaxis (calcification of blood vessels).
Methods: An 18-year-old female presented with painful swelling in the posterior compartment of the forearm. Clinical examination identified a subcutaneous mass, and MRI suggested the presence of a vascular lesion, possibly a haemangioma. Fine needle aspiration (FNA) was performed in another centre and was compatible with a vascular neoplasm. A wedge-shaped excision of the lesion was performed, and we received a skin specimen measuring 54x47x36mm.
Results: Microscopically, we recognised a lobular and relatively well-demarcated lesion that occupied the reticular dermis and the subcutaneous adipose tissue. Its main characteristic was the extensive presence of basophilic, amorphous, irregular aggregates indicating calcium deposits and establishing the diagnosis of calcinosis cutis. The calcium deposits were separated by fibrotic bundles containing thin-walled blood vessels without calcifications; therefore, we excluded

calciphylaxis. A moderate inflammatory infiltrate was present with occasional lymphoid nodules and focal foreign body reaction with multinucleated giant cells. Despite the classic morphology of the lesion, we performed immunohistochemistry with classic vascular markers to exclude the presence of a vascular neoplasm that was suggested by imaging and FNA.
Conclusion: This is a typical case of calcinosis cutis that was evaluated by imaging and cytopathology as a vascular neoplasm. The typical differential diagnosis of calcinosis cutis includes mycetoma, xanthoma, and gout/pseudogout but not vascular lesions. Clinicopathological correlation is required for determining the aetiology of calcinosis cutis. We suggested that vitamin D, calcium and phosphate levels should be measured and a follow-up investigation was required to rule out autoimmune systemic diseases that cause connective tissue damage.

E-PS-05-065
MYO5A::NTRK3 fusion in Spitz tumours: comparison between a Spitz melanocytoma and a Spitz melanoma
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Background & Objectives: Melanocytic lesions with MYO5A::NTRK3 fusion are a subset of Spitz tumours, associated with a spindle cell morphology and a neuroid appearance.
This presentation highlights the morphological, immunohistochemical and molecular features of a Spitz melanocytoma and a Spitz melanoma, in which a MYO5A::NTRK3 fusion was detected.
Methods: Case 1: A 45-year-old female presented on the left arm an atypical pigmented lesion of 7x8 mm.
Case 2: A 47-year-old male presented a tumour on the ear, measuring 32x12 mm, initially suspected as squamous cell carcinoma.
The two lesions were excised and underwent pathological examination.
Results: Both cases showed a compound melanocytic proliferation with fusiform morphology, focal neuroid pattern and immunohistochemical expression of pan-TRK.
Case 1: Microscopic examination revealed a biphasic melanocytic population: a central fusiform component with desmoplastic stroma, surrounded by a peripheral nevoid component. Focally, the cellularity was increased and some nuclei were hyperchromatic. No dermal mitoses were found.
The expression of p16 and MelanA was diminished in the fusiform component. The diagnosis of Spitz melanocytoma was established.
Case 2: The histological examination showed a densely cellular, ulcerated melanocytic lesion with focal necrosis. The architecture was fascicular, with neuroid appearance. Pseudo-Verrocay bodies were focally noted. In some areas, the spindle cells were monomorphic, while other areas showed significant pleomorphism. Deep dermal mitoses were present (4 mitoses / mm^2).
P16 expression was partially absent. The proliferation index was high.
DNA sequencing revealed a TERT gene mutation. The TMB was 19.8 mutations/Mb.
RNA sequencing was performed in an external reference laboratory and a MYO5A::NTRK3 fusion was detected. A diagnosis of Spitz melanoma was rendered.
Conclusion: The fusiform morphology and the neuroid pattern strongly correlate with the presence of MYO5A::NTRK3 fusion and are consistent with the data described in the literature.
The identification of an NTRK3 fusion could represent a potential therapeutic target for melanoma cases.

E-PS-05-066
Merkel cell carcinoma in a young immunocompetent patient with MCPyV positivity
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Background & Objectives: Merkel cell carcinoma (MCC) is an aggressive neuroendocrine carcinoma of the skin, typically seen in elderly patients. Although extremely rare, MCC can occur in younger individuals. Immunosuppression, especially related to solid organ transplantation, hematologic malignancies, and HIV, is a significant risk factor for younger patients. However, the occurrence of MCC in immunocompetent younger patients remain exceptional. Herein, we present a case of MCC in an immunocompetent young patient diagnosed through Merkel cell polyomavirus (MCPyV) antibody positivity, despite initially negative CK20 staining.
Methods: A 45-year-old male patient presented with a palpable, firm mass in the left gluteal region. Patient had no prior medical history. Diagnostic biopsy revealed a tumour composed of nests and trabecular arrangements of round-shaped, blue cells with narrow cytoplasm, occasionally exhibiting plasmacytoid appearance. Differential diagnoses included small round cell tumours, metastatic carcinoma, and lymphoma.
Results: Immunohistochemically, tumour cells were negative for CK20, positive for pan-cytokeratin, NSE, chromogranin, synaptophysin, INSM1, and MCPyV clone Ab3, with a high Ki-67 proliferation index. Local wide excision revealed a 2.2 cm nodular lesion in deep dermis. Repeat CK20 staining demonstrated focal and weak perinuclear dot-like positivity. Crucially, MCPyV antibody clone Ab3 was positive and MCC was diagnosed.
Conclusion: MCC predominantly affects patients over the seventh decade of life, with only 4% diagnosed below the fifth decade. Our patient's young age, immunocompetent status, and initially negative CK20 biopsy made diagnosis challenging. The identification of MCPyV positivity was crucial for diagnostic confirmation.
Although rare, MCC should be considered in younger immunocompetent patients presenting with atypical skin lesions. In such challenging scenarios, utilizing MCPyV testing can significantly aid in accurate diagnosis. Small number of MCC cases in young, immunocompetent patients have been reported, but MCPyV status is documented in only two cases. To our knowledge, this is the second MCC report with MCPyV positivity in a young, immunocompetent patient.

E-PS-05-067
Cutaneous involvement of extranodal NK/T cell lymphoma, nasal type, a clinical and histopathological presentation of two cases
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Background & Objectives: Extranodal natural killer/T-cell (ENK/T) lymphoma is a rare Epstein-Barr virus (EBV)-associated neoplasm. The skin is the second most common site of involvment after the upper aerodigestive tract. It has various histopathological findings and numerous differential diagnoses.
Methods: We present two cases of cutaneous involvement of Extranodal NK/T Cell Lymphoma, nasal type, emphasizing its clinical presentation and histopathological findings.
Results: The first case is a 34-year-old man presented with multiple plaques infiltrating the trunk and limbs for 3 months, in the context of weakness and fever. Physical examination revealed the presence of an inguinal lymph node. Microscopic examination showed cutaneous tissue with extensive ulceration and necrosis in the epidermis. The dermis and subcutaneous tissue contained a diffuse lymphoid infiltrate composed of small to medium-sized cells. Angiotropism with angiodestruction and thrombosis was observed. Immunohistochemical study demonstrated intense and diffuse positivity of the tumour cells for CD56 and CD3, with rare lymphocytes expressing CD20.
The second case is a 52-year-old woman presented with a 5 cm erythematous to violaceous nodule on her back, which had been evolving for 6 months, and a similar 1.5 cm nodule on her right leg. Microscopic examination revealed cutaneous tissue with focal epidermal ulceration.

The dermis and subcutaneous tissue showed a dense malignant lymphoid proliferation organized in diffuse sheets. The cells were medium to large. There were areas of tumour necrosis and angiotropism. Immunohistochemical analysis showed positivity of the tumour cells for CD3 and CD56, while they were negative for CD20, ALK, CD4, and CD8. CD30 marked some active lymphocytes. The search for EBV by in situ hybridization showed nuclear positivity.
Conclusion: ENK/T cell lymphoma is characterized by the coexistence of tumour necrosis and angioinvasion. The differential diagnosis includes primary cutaneous Gamma Delta T-cell lymphoma, and peripheral T-cell lymphoma.

E-PS-05-068
Differential diagnosis challenges. Overlapping histological features between IgG4 related desease and EPGA
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Background & Objectives: IgG4-related disease (IgG4-RD) is an inflammatory disorder responsible for fibrosing, tumefactive lesions that can involve the lacrimal gland as well as the extraocular muscles, orbital soft tissues, sclera, and local nerves. Eosinophilic granulomatosis with polyangiitis (EGPA) constitutes an unusual disorder which is characterized histopathologically by necrotizing vasculitis, extravascular granulomas and tissue infiltration by eosinophils. The differential diagnosis between these conditions can be complex.
Methods: A 12-year-old patient underwent biopsy sampling for a right orbital neoformation. The main specimen measured 23x8x7 mm and contained two whitish lesions measuring 10x5 mm and 7x4 mm, while a second conjunctival sampling measured 4x3x3 mm. Immunohistochemical analysis showed positivity for CD68++, CD163++, CD38++, CD138+ and IgG4+ (>10/HPF), with mixed infiltration of B (CD20+) and T (CD2+) lymphocytes. The absence of immunoreactivity for BRAF V600E, S100 and CD56 excluded some differential diagnoses of neoplastic nature.
Results: Histological analysis revealed a mixed cellular infiltrate characterized by numerous IgG4+ polytypic plasma cells and a storiform arrangement of fibrous tissue, elements suggestive of IgG4-RD. However, the presence of foci of necrosis and neutrophilic granulocytes made it necessary to consider a differential diagnosis with EGPA. Negativity for BRAF V600E and S100 ruled out a neoplastic process. These histologic findings, although indicative, require clinical and laboratory framing to define with certainty the nature of the lesion, thus guiding therapeutic management.
Conclusion: The case highlights the difficulty in the differential diagnosis between IgG4-RD and EGPA, given the overlapping histological features. The presence of IgG4+ plasma cells points toward IgG4-RD, but the necrosis and mixed infiltrate dictate careful evaluation. A multidisciplinary approach, with clinicopathologic correlation, is essential to establish the definitive diagnosis and set the correct treatment.

E-PS-05-069
Folliculotropic mycosis fungoides: a clinicopathological study of a case series of 12 patients
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Background & Objectives: Folliculotropic mycosis fungoides (FMF) is a rare variant of cutaneous T-cell lymphoma (CTCL), comprising only 10% of all mycosis fungoides cases. Distinct clinical and histological features have been identified in patients with FMF. In this study, our aim was to provide through a case-series additional information regarding its clinicopathological features.
Methods: Twelve patients diagnosed in the department of pathology of Habib Thameur Hospital between 2008 and 2024 were identified. The clinical data and microscopic features of these cases were reviewed and analysed.
Results: Patients mean age was 46.1 years [15–73] with a male-to-female ratio of 1.4:1. The median diagnostic delay was 130 days [65-303]. Clinically, all patients presented with erythematous plaques, 58% of which were infiltrated. One case also exhibited a tumour on the right cheek. Lesions were localized to the trunk and extremities in seven cases, to the face and neck in 4 cases and were generalized in 3 cases. Three cases showed alopecic plaques, with one case associated with eyebrow depilation. A total of 22 biopsies were performed. Histopathological analysis revealed epidermotropism in 20 cases and pilotropism in all cases. Immunohistochemical analysis demonstrated a CD3 positive staining and a high CD4/CD8 ratio in all cases. A CD7 loss was found in 71% of biopsies.
Conclusion: FMF occurs more frequently in male patients and in those in the fifth decade of life. Skin lesions often persist for months before diagnosis, with a diagnostic delay varying between 18. Clinically, FMF presents with plaques, acneiform lesions, follicular keratosis, and alopecia. Lesions primarily affect the head, neck, upper extremities, and torso, distinguishing FMF from classical MF. Histopathologically, FMF is characterized by dense lymphocytic infiltrates around hair follicles, often accompanied by follicular mucinosis. Loss of T-cell antigens like CD7 is common. Multiple biopsies may be necessary before a definitive diagnosis could be rendered.

E-PS-05-070
Melan-A-positive cells in re-excision samples for skin cancer and melanoma: a possible diagnostic trap
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Background & Objectives: Rutinary diagnostics of malignant melanoma involves the evaluation of skin re-excision specimens.
It is also possible to observe the presence of factors that may complicate the diagnosis such as a dense inflammatory infiltrate and/or the presence of melanophages and/or melanin in the dermis of the observed specimen.
Methods: We retrospectively re-evaluated the malignant melanoma re-excision samples in our database, in which case Melan-A immunohistochemical staining was used to exclude the presence of malignant melanoma.
Results: Of the retrospectively identified cases in which excisional enlargement was performed following the diagnosis of malignant melanoma, immunohistochemical staining with Melan-A was performed in eight cases, Melan-A-positive cells were observed in the dermis without an additional associated melanocytic lesion. These were always single cells in the dermis without cytological atypia or mitotic activity. In those cases where it was performed, immunohistochemical staining for HMB45 did not show aberrant expression.
In two cases subsequent histological processing with serial sections of the specimen showed the presence of an associated melanocytic nevus; in one case, (associated with the presence of inflammatory infiltrate) melanocytes were present in the border zone between dermis or subcutaneous tissue ; the subsequent processing of the sample showed the presence of atypical melanocytes, present in aggregates and not individually, suggestive for malignant melanoma.
Conclusion: The data in our observation suggest that the rare, Melan-A positive dermal cells melanoma could be found in re-excisions specimens due to malignant melanoma diagnosis made earlier.

The absence of cytologic atypia and HMB45 abnormal recation support the diagnosis of benign, melanocytes.
An accurate and careful evaluation of other morphological parameters (such as inflammatory infiltrate or the localization of melanocytes in the vicinity of subcutaneous tissue) requires a thorough examination of the histological sample with serial sections to exclude the presence of melanocytic nevi or malignant melanoma residues.

E-PS-06 E-Posters Digestive Diseases Pathology (GI)

E-PS-06-001

Bichromatic squamous epithelium: an artifact associated with the use of Lugol's iodine solution in oesophageal endoscopic submucosal dissection specimens

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Background & Objectives: Endoscopic Submucosal Dissection (ESD) is a minimally invasive endoscopic technique used for the en bloc resection of precancerous lesions and early-stage cancers in the oesophagus. For squamous neoplasia, Lugol's iodine is used during ESD procedures to better delineate the lesion, enhancing visualization during resection. This study highlights a notable histopathological artifact observed in the squamous epithelium of oesophageal ESD specimens treated with Lugol's iodine.
Methods: This is a retrospective review of nine oesophageal ESD cases performed at our institute between 2018 and 2024. Prior oesophageal biopsies were available in five of these patients. The cohort included individuals diagnosed with squamous dysplasia and/or invasive squamous cell carcinoma. Clinical procedure notes, endoscopic images, histopathology slides, and pathology reports from both biopsy and ESD specimens were reviewed to assess findings related to Lugol's iodine.
Results: Lugol's iodine was applied in all biopsy and ESD procedures. In ESD cases with squamous dysplasia (low and high grade) and/or squamous cell carcinoma, the dysplastic squamous epithelium exhibited a distinctive layered bichromatic (two-toned) appearance with a superficial band-like zone where the cells displayed cytoplasmic eosinophilia and nuclear pyknosis. This distorted histology presented a diagnostic challenge, as the artifact was confined to the superficial layer of the dysplastic epithelium, mimicking a less severe degree of dysplasia. No biopsy specimen exhibited this artifact, likely due to shorter iodine exposure time pre-formalin fixation compared to ESD specimens. This artifact was absent in normal squamous epithelium. The concentration of Lugol's iodine (variable; 1.25-2.5 %) did not affect this artifact development.
Conclusion: As ESD is increasingly used to treat oesophageal squamous neoplasia, recognizing this epithelial artifact associated with Lugol's iodine application is important for the surgical pathologist. The nuclear changes and altered nuclear-cytoplasmic ratio in the superficial squamous epithelium may interfere with accurate histological diagnosis of dysplasia severity.

E-PS-06-002

E-Cadherin and P53 expression in colorectal adenocarcinoma: impact on prognosis and survival

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Background & Objectives: Colorectal cancer (CRC) is a major public health concern worldwide, including in Tunisia. Despite therapeutic advances, recurrence and metastasis remain the leading causes of mortality after surgery. We investigated the expression of P53 and E-cadherin and their association with histo-prognostic factors, prognosis, and overall survival.
Methods: We included 100 patients diagnosed with colorectal adenocarcinoma over 88 months. Histopathological data were collected from the University Hospital of Medenine and the private laboratory of Dr. Nejib Ben Yahia in Djerba. Immunohistochemical (IHC) analysis was performed on paraffin-embedded tissues for E-cadherin and P53 antibodies. Immunostaining was semi-quantified based on the percentage of stained cells and staining intensity. A final score was calculated for each case and dichotomized into positive and negative categories based on a predefined threshold. Statistical analyses were performed using SPSS version 22.
Results: IHC analysis was conclusive for both antibodies in 75 patients. Loss of E-cadherin expression was significantly associated with advanced tumour stages (III and IV; $p = 0.047$), lymph node involvement ($p = 0.002$) and lymphatic invasion ($p = 0.035$). P53 expression was significantly linked to the presence of an additional tumour component (e.g., mucinous) ($p = 0.022$) and venous invasion ($p = 0.046$). A positive correlation was found between high E-cadherin and P53 expression ($p = 0.009$). Patients with low E-cadherin expression had better 3-year overall survival ($p = 0.008$). No significant association was found between P53 expression and survival.
Conclusion: Loss of E-cadherin expression is associated with a poorer prognosis. In contrast, the prognostic value of P53 in colorectal adenocarcinoma remains controversial, with our study showing no significant impact of its expression on overall survival. These findings highlight the need for further exploration of biomarkers to refine prognosis and optimize CRC management.

E-PS-06-003

A challenging case of three concomitant tumours in a young woman

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Background & Objectives: Primary small bowel adenocarcinoma (SBA) is a rare gastrointestinal cancer with a low incidence among young people. The atypical clinical presentations, the potential to metastasize to the ovary and the association with a primary ovarian cancer constitute a diagnostic and therapeutic challenge.
Methods: We present the case of a 39-year-old female patient which was admitted to the surgical clinic for upper abdominal pain accompanied by vomiting. Imagistic investigations detected the presence of a right ovarian tumour mass and a jejunal stenosing lesion, for which segmental enterectomy and right adnexectomy was performed through laparoscopy. The specimens were processed by classic histopathological methods with additional immunohistochemical tests.
Results: Gross examination of intestinal specimen revealed the presence of an exophytic polypoid and stenosing lesion, the microscopic examination establishing the diagnosis of low-grade adenocarcinoma of the jejunum, invasive to the subserosal layer. Histopathological examination of ovarian specimen revealed the presence of two distinct entities: an ovarian metastasis of intestinal adenocarcinoma and a cystic teratoma with mature tissues with an ovarian strumal carcinoid component. Additional immunohistochemical tests, positive for Villin, CDX2 and CK20 markers in the tumour area, confirmed the diagnosis of ovarian metastasis of intestinal adenocarcinoma. Synaptophysin, chromogranin A and CD56 positivity markers but calcitonin negativity established the diagnosis of ovarian strumal carcinoid. Postoperative

evolution of the patient was favourable, but given the association of these tumours, genetic testing for Lynch syndrome was recommended.
Conclusion: This case highlights an unusual diagnostic association, jejunal adenocarcinoma with ovarian metastasis, being entities rarely reported in the literature to date. The incidental discovery of ovarian strumal carcinoid adds an increased level of complexity to this case, thus emphasizing the importance of histopathological diagnosis with additional immunohistochemical tests for establishing the suitable therapy.

E-PS-06-004
Early gastric cancer specimens resected by endoscopic submucosal dissection – is tumour microenvironment CD10 expression significant?
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Background & Objectives: Cancer-associated fibroblasts are a dominant stromal component assisting in tumour development by influencing tumour growth, invasion and metastasis. CD10 is a cell surface type II zinc-dependent metalloprotease structurally similar to MMPs that inactivates various signalling peptides. The role of CD10 positive stromal cells is known in breast and colo-rectal carcinoma, but understudied in gastric carcinoma. This study aims to investigate whether CD10 expression is correlated with other pathological parameters in early gastric carcinoma.
Methods: Twelve patients diagnosed with early gastric carcinoma completely resected by endoscopic submucosal dissection represented the cohort. Most representative paraffin-embedded blocks were selected for analysis. CD 10 and p53 expression were evaluated using immunohistochemistry and correlated with lympho-vascular invasion and degree of local extension.
Results: The study analysed 12 patients, 8 men and 4 women with ages between 62 and 87 (median age 69 years). All cases were intestinal type early gastric carcinoma (pT1a 58.3% and pT1b 41.7%), 5 of which were located in the body (41.7%), 5 in the antrum (41.7%) and 2 in the gastroesophageal junction (16.7%). Stromal CD10 expression was detected in 5 cases (41.7%), while the remaining 7 (58.3%) were negative. CD10-positive cases associated mutant p53 pattern of expression, with complete loss of expression or overexpression. CD10 positivity also had significant correlation with tumour grade and lympho-vascular invasion.
Conclusion: Stromal CD10 expression seems to correlate with other histologic markers of aggressive behaviour. The study has limitations due to cohort size, but it emphasizes the effect tumour microenvironment has on tumour behaviour and potential to invade.

E-PS-06-005
Colorectal adenocarcinoma with regional lymph node metastases from other primary foci of cancer
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Background & Objectives: Colorectal cancer is one of the commonest malignancies that the pathologist encounters in his daily work. Examination of the lymph nodes in the submitted resected specimen is a basic task, essential for correct staging and subsequent appropriate therapy for the patient. However, lymph node metastases in the colon are not always from a primary focus of colorectal adenocarcinoma.
Methods: A case study is made in which 4 cases of resected specimens of colorectal cancer with regional lymph node metastases with proven origin from other primary foci are examined using histochemical and immunohistochemical methods for period of 2 years.
Results: The results of the immunohistochemistry are the following: in the patient with colorectal and prostatic cancer all metastatic lymph nodes, which are fifteen, show origin from prostatic acinar cancer; in the patient with colorectal and serous cystadenocarcinoma of the ovaries all metastases in the lymph nodes are from the ovarian tumour; in the patient with colorectal and endometrial adenocarcinoma all the metastatic lymph nodes are from the endometrial tumour and in the patient with colorectal and invasive ductal carcinoma of the breast from 15 isolated lymph nodes, 2 of them are metastatic, 1 of which is from the invasive ductal carcinoma of the breast.
Conclusion: This case-report series aims to show that not always metastases in regional lymph nodes originate from the primary foci and to emphasize how important is the connection between the pathologist and the clinician, as well as the immunohistochemistry, so that the patient can receive the most appropriate treatment.

E-PS-06-006
A rare case of tactile corpuscle-like bodies in the rectum mimicking amyloidosis
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Background & Objectives: Tactile Corpuscle-Like Bodies (TCLB) are benign, neural structures incidentally found in gastrointestinal biopsies. Fewer than 30 cases have been documented, from which only 2 located in the rectal mucosa. Due to their rarity, TCLBs may pose significant diagnostic challenges.
Methods: We present the only case of TCLB in the rectum found in the archive of The Emergency University Hospital, Bucharest. The specimen was obtained by colonoscopy and evaluated histologically with haematoxylin and eosin (H&E) and Congo red stains. Immunohistochemical analysis was performed as part of the diagnostic workup.
Results: A 45-year-old male with a history of bladder cancer underwent routine surveillance colonoscopy, during which a $3 \times 3 \times 2$ mm sessile rectal polyp was identified and resected. Histological examination revealed mucosa with relatively normal epithelium and multiple well-circumscribed, non-encapsulated, eosinophilic nodules in the lamina propria. The nodules were negative on Congo red and presented rare concentrically-arranged spindle cells with eosinophilic cytoplasm and elongated nuclei. Based on these features, a diagnosis of rectal TCLBs was established. At one-year follow-up, the patient remained asymptomatic, with no recurrence or complications.
Conclusion: TCLBs are rare, under-recognized lesions that are increasingly identified with the growing use of endoscopy. Several ethiopathogenical hypothesis have been proposed regarding TCLBs, including reactive, hamartomatous, or early neoplasic process. Few reports of peripheral nerve sheath tumours containing TCLB-like areas raised the possibility of a precursor relationship. Although they have a benign prognosis, their resemblance to other conditions such as amyloidosis or granulomatous lesions may raise diagnostic challenges. Recognizing this entity is essential to prevent misdiagnosis and avoid unnecessary interventions.

E-PS-06-007
Small bowel ganglioneuromatosis in a NF1 patient: a case report
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Background & Objectives: Ganglioneuromatosis is a rare benign proliferation of ganglion cells, Schwann cells, and nerve fibres, associated with neurofibromatosis type 1 (NF1), multiple endocrine neoplasia type 2b (MEN2b) and Cowden syndrome. Intestinal involvement can lead to bowel obstruction. We report a case of diffuse small bowel ganglioneuromatosis in a patient with NF1, presenting with intestinal occlusion.
Methods: A 53-year-old man with NF1 presented with acute abdominal pain, distension, and absence of bowel movements. Imaging revealed small bowel obstruction. Exploratory laparotomy with segmental resection was performed. Histopathological analysis and immunohistochemistry (S100, SOX10, Synaptophysin, CD34, CD117, SMA, AE1/AE3, Ki67) were conducted for diagnosis.
Results: The resected bowel segment showed diffuse mural thickening and luminal dilatation. Histologically, there was a dense mesenchymal proliferation predominantly located in the submucosa, with extension into the lamina propria (including ulcerated mucosal areas), the muscularis propria, and the subserosa. The lesion was composed primarily of spindle-shaped Schwannian cells (S100+) and scattered ganglion cell aggregates (SOX10+, Synaptophysin+). It extended to the proximal resection margin and was associated with fibrotic and degenerative nerve changes in the subserosal space. An abundant eosinophilic infiltrate was also noted. Ki67 proliferation index was <1%. Concurrent skin biopsies revealed multiple neurofibromas. The findings established a diagnosis of diffuse intestinal ganglioneuromatosis, associated with NF1.
Conclusion: Ganglioneuromatosis is a rare complication of NF1, with limited reported cases. Diffuse intestinal ganglioneuromatosis in NF1 is unusual, with most cases affecting the large intestine. Reported small bowel cases primarily involve young adults, making our case an uncommon presentation. Beyond its potential to mimic malignancy, it may also point toward an underlying genetic syndrome. Its identification in such scenarios underscores the importance of linking histological findings to potential systemic or genetic implications.

E-PS-06-008
Comparison of CMV density with serological findings and Nancy Scores in active Ulcerative Colitis
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Background & Objectives: Ulcerative colitis (UC) is a chronic inflammatory disease characterized by alternating periods of remission and exacerbation. Cytomegalovirus (CMV) infection is known to influence disease severity, contribute to immunosuppressive therapy resistance, and trigger exacerbations. This study aimed to investigate the correlation between CMV density, serological markers, and histological findings in patients with active UC.
Methods: We retrospectively analysed biopsies from hospitalized UC patients with CMV infection at Ege University's Gastroenterology Department between 2018 and 2023. CMV immunohistochemistry was performed in all cases. Histological activity was assessed using the Nancy histological scoring system. CMV density was quantified by counting positively stained nuclei per high-power field (HPF) (Olympus BX50 microscope, 40× objective, r = 0.54 mm). Data were analysed using nonparametric tests.
Results: A total of 47 patients (18 females, 29 males) were included, with a median age of 50 ± 18 years (range: 20–86). CMV infection was detected via serology in 21 cases, tissue PCR in 31, and immunohistochemistry in 24. Among immunohistochemically positive cases, serology was positive in 13, while tissue PCR was positive in 12 ($p = 0.047$, Chi-square test). The mean CMV density was 2.61 ± 2.29 per HPF (range: 1–9). Most patients (78.7%, n = 37) had a Nancy score of 4, indicating severe histological activity. Steroid resistance was observed in 32 cases (70.2%), 27 of whom had a Nancy score of 4. No correlation was found between CMV density, age, gender, and histological scores, serological markers, or PCR results.
Conclusion: CMV infection was more frequent in patients with a Nancy score of 4. Immunohistochemistry correlated better with tissue PCR than with serology. Whether CMV is a bystander or a pathogenic factor in UC remains unclear and requires further investigation

E-PS-06-009
Two rare cases of radiation-induced sarcoma: pleomorphic sarcoma and angiosarcoma
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Background & Objectives: Radiation-induced sarcoma (RIS) is a rare, aggressive cancer that typically develops 10-15 years after radiation therapy. It occurs in irradiated tissues and is associated with high recurrence rates and poor prognosis due to late diagnosis and chemotherapy resistance. This report presents two cases of radiation-induced sarcoma in patients with a history of radiotherapy.
Methods: First case: A 53-year-old female, diagnosed with oesophageal squamous cell carcinoma in 2016, underwent chemotherapy and radiotherapy but declined surgery. 9 years post-radiotherapy, she presented with dysphagia, and an endoscopic examination revealed a mass. The esophagectomy specimen showed a polypoid tumour (4.5 x 2.3 x 1.3 cm) in the same area as the prior tumour. Histologically, the tumour was composed of pleomorphic spindle cells in fascicles. Immunohistochemistry showed focal smooth muscle actin (SMA) positivity. The diagnosis was radiation-induced pleomorphic sarcoma. Next-generation sequencing (NGS) was performed for further analysis.
Second case: A 61-year-old female, diagnosed with moderately differentiated gastric adenocarcinoma in 2014, underwent total gastrectomy followed by chemotherapy and radiotherapy. 11 years post-radiotherapy, she presented with nausea and vomiting, and ileus was diagnosed. Small bowel resection revealed a haemorrhagic, poorly circumscribed tumour of atypical spindle cells. Immunohistochemical staining was positive for ERG and CD34, confirming the diagnosis of radiation-induced angiosarcoma.
Results: The first case involved radiation-induced pleomorphic sarcoma, diagnosed 9 years after radiotherapy for oesophageal squamous cell carcinoma. The second case involved radiation-induced angiosarcoma, diagnosed 11 years after radiotherapy for gastric adenocarcinoma.
Conclusion: Radiation-induced sarcomas are rare but serious complications of radiation therapy, characterized by aggressive behaviour and poor prognosis. Their development poses a significant challenge in managing patients with a history of radiation exposure.

E-PS-06-010
A 14-year experience with appendiceal mucinous neoplasms: insights from a single-centre case series
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Background & Objectives: Appendiceal mucinous neoplasms (AMNs) are rare epithelial tumours with varying risks of peritoneal dissemination. This study aimed to retrospectively evaluate the clinicopathological features of AMN cases diagnosed at a single centre over 14 years.
Methods: Sixty AMN cases diagnosed between 2010 and 2024 were retrospectively analysed. Patient demographics, histopathological features, pT stage, presence of appendiceal diverticulum, and accompanying neoplastic lesions were evaluated. Haematoxylin-eosin (H&E) stained slides were reviewed for grade of nuclear dysplasia, mucin extrusion, invasion depth, and related pathological findings. All cases were staged according to the 9th edition of the AJCC system.
Results: Among the 60 cases, 18 were male (30%) and 42 female (70%), with a mean age of 58 (35–89) years. Histopathological examination revealed that 56 cases (93.3%) exhibited low-grade appendiceal mucinous neoplasm (LAMN) morphology throughout, while 4 cases (6.7%) displayed high-grade features. pT staging was as follows: pTis in 29 cases (48.3%), pT3 in 4 (6.7%), pT4a in 18 (30%), and pT4b in 9 (15%). High-grade appendiceal mucinous neoplasm (HAMN) cases were all pT4. Appendiceal diverticula were found in 17 cases (28.3%). Accompanying neoplastic lesions were identified in 10 cases (16.7%), including 7 colonic adenocarcinomas (11.7%), 1 malignant mesenchymal tumour (1.7%), and 2 appendiceal neuroendocrine tumours (3.3%).
Conclusion: The analysed cases showed a broad age range, with a mean age in the late 50s, consistent with the literature. Although AMNs are reported to be slightly more frequent in females, the marked female predominance in our series is notable. The distribution of pT stages was generally in line with prior studies; notably, the low number of pT3 cases may reflect a brief or less detectable transitional phase. The relatively high frequency of diverticula and coexisting neoplasms suggests possible associations with AMN development. Further studies and large series are needed to clarify prognostic factors.

E-PS-06-011
Loss of PTEN expression as a poor prognostic marker in colorectal cancer: a Tunisian case series' study
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Background & Objectives: Colorectal cancer (CRC) is one of the most common cancers and the third cause of death by cancer worldwide. Discovering new prognostic markers such as PTEN and developing new targeted therapies could improve patients' care. Loss of PTEN expression in CRC could indicate an aggressive clinical course, impacting patients' prognoses and outcomes.
Methods: This is a retrospective monocentric study at the Pathology department of Salah Azaiez Institute using Tissue micro-array samples and immunohistochemical techniques for studying PTEN expression in CRC in a Tunisian case series.
Results: Our case series included 21 patients (12 males and 9 females). The mean age was 52 years. PTEN expression was retained in 71.43% of cases and lost in 9.52% of cases. Loss of PTEN expression was observed in tumours which size exceeded 10cm in largest diameter. Loss of PTEN expression was also observed in tumours with advanced pT stage (pT3 or pT4) and those with lymph node metastases.
Conclusion: In our series, PTEN expression was lost in 9.52% of cases. These results are consistent with those reported in literature, where loss of PTEN expression in CRCs accounted for nearly 8% of cases in most studies. Loss of PTEN expression was observed in tumours with large size and advanced pT and pN stages. According to literature, loss of PTEN expression in CRC is associated with more advanced stages of the disease, local recurrence and distant metastases, notably liver metastases. Our results are consistent with those reported in the literature.

E-PS-06-012
Expecting the unexpected: a case report of a MiNEN in the ampullary region with a NET G3 component in a patient with BRCA2 mutation
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Background & Objectives: This study describes a rare case of Mixed Neuroendocrine / non-neuroendocrine Neoplasm (MiNEN) of the ampullary region composed of adenocarcinoma and NET G3, along with a systematic review of the few similar cases in literature.
Methods: A 47yo female patient with BRCA2 germinal mutation and breast cancer presented with US-diagnosed bile ducts dilation. Endoscopically, the duodenal papilla was bulging and eroded and a biopsy was diagnosed as "carcinoma, NOS". She underwent duodenocefalopancreatectomy.
Results: Microscopically, an ampullary neoplasms composed of two different cell population was found: one showed glandular adenocarcinoma morphology and the other showed a solid-trabecular growth of polygonal cells with round nuclei and granular cytoplasm. Negative immunostains for GATA3 and Mammaglobin ruled out a metastatic breast carcinoma. CK7 was diffusely positive in the glandular part and negative in the solid-trabecular one. Chromogranin A and Synaptophysin were positive in the solid-trabecular component and negative in the glandular one. Ki67 PI was 25% in the solid-trabecular component and mitotic index was 17 mitoses x2mm^2. p53 and Rb1 showed a wild type pattern at immunohistochemistry. A MiNEN composed of adenocarcinoma (40%) and NET G3 (60%) was diagnosed. A systematic review of the literature retrived only 12 known cases of MiNEN: 11 mixed adenocarcinoma-NEC and only 1 adenocarcinoma-NET.
Conclusion: MiNENs of the ampullary region are exceedingly rare, with only 13 known cases (including ours). Here, we report the second case of mixed adenocarcinoma-NET of this site. Since the symptoms are similar to other types of neoplasia of the same region, and since the gold standard for an optimal diagnosis is an extensive sampling, the final diagnosis could be delayed.

E-PS-06-013
Neoadjuvant chemotherapy combined with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with peritoneal colorectal carcinomatosis: an observational study of 178 patients
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Background & Objectives: Colorectal cancer (CRC) is the second leading cause of cancer-related death worldwide, primarily attributed to metastatic disease. Selected patients with peritoneal colorectal carcinomatosis could be offered a curative-intent strategy based on CRS combined with HIPEC, following neoadjuvant systemic chemotherapy.
Methods: We searched the pathology archives of our department between 2003 and 2019 and retrospectively analysed sociodemographic (age and sex), clinical and surgical (timing of peritoneal carcinomatosis (synchronous vs metachronous), chemotherapy regimens, CRS and HIPEC intervention date, Peritoneal Cancer Index (PCI), Completeness of Cytoreduction (CC) score, relapse date, severe complications, mortality) and histological data (tumour histological subtype, TNM status, immunohistochemical and molecular status and histological response evaluated using Peritoneal Regression Grading Score (PRGS)).
Results: 178 patients were retrospectively studied, 50% males and 50% females, with median age of 60 years. All patients received CRS combined with HIPEC, after neoadjuvant systemic chemotherapy and were divided into two groups based on histological response [complete (18) and incomplete (160)], with 10,1% of complete response, consistent with the literature. The statistical analysis showed that tumour histological subtype, lymph node involvement, KRAS status and PCI are significantly associated with the histological response (p=0.007, 0.006, 0.036 and 0.000, respectively) and consequently with progression-free survival (PFS).
Conclusion: Selected patients with peritoneal colorectal carcinomatosis could be offered a curative-intent strategy based on CRS combined with HIPEC, following a neoadjuvant systemic chemotherapy and some of them can achieve pathological complete response, offering prognostic information. Significant predictor factors of pathological response could be helpful to enable a better selection of patients who are candidates for this treatment, with the aim of optimizing benefits and minimizing risks within the context of personalized medicine.

E-PS-06-014
Mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs): first case-series in an Oncology Hospital in Portugal
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Background & Objectives: Mixed neuroendocrine-non-neuroendocrine neoplasms (MiNEN) are a rare occurrence in the gastrointestinal tract (GI). These tumours have both neuroendocrine and non-neuroendocrine differentiation, each component representing at least 30%. We report the first case-series of MiNEN in an Oncology Hospital in Portugal.
Methods: We performed a retrospective analysis of patients with MiNEN diagnosis from January 2010 to February 2025 at IPO Porto, Portugal. Information regarding clinical data, tumour details, immunohistochemical markers, pathological stage, treatment modalities, clinical and oncological outcomes were collected.
Results: Twelve patients with diagnosis of MiNEN in the GI tract were found in our centre. Four patients were females and the average age at diagnosis was 67,9 (26 - 83) years. The most common tumour location was the stomach in eight patients, two in right colon and two in the oesophagus/gastroesophageal junction. All patients underwent surgery. In the entire patient group, the neuroendocrine component was a poorly differentiated neuroendocrine tumour, small or large cell carcinoma (NEC), and the non-neuroendocrine component was adenocarcinoma. One tumour had amphicrine features. All patients had lymph nodes metastases.
Conclusion: To our knowledge this report details the first case-series of MiNEN of the GI tract diagnosed in a Portuguese Oncology Hospital. The results obtained, which show a NEC component in association with an adenocarcinoma, are consistent with the findings presented in previous studies. This association is linked to poor prognosis, predominantly due to the high grade neuroendocrine tumour. Furthermore, we report an amphicrine tumour diagnosed in the right colon. Overall, this report gathers further insights into knowledge of MiNEN.

E-PS-06-015
BRAF and PD-L1 protein signatures in early colon cancer – correlations with intratumor lymphocytes
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Background & Objectives: Endoscopic submucosal dissection (ESD) for early colonic cancer (ECC) is an emerging therapeutical option, that allows a curative minimal invasive approach, offering for microscopical assessment full-thickness mucosa malignant lesions. This study evaluates, on a small prospective cohort, the expression of various histopathological and immunohistochemical parameters, correlated with tumour progression: differentiation, desmoplasia, intratumor lymph cells (TILs), BRAF and PD-L1 expression.
Methods: Twenty consecutive patients with ESD fully resected ECC were included in this study. The whole tumour was assessed on multiple sections according to European guidelines. TILs and desmoplasia were evaluated using a four-steps qualitative scale. Immunohistochemical assays were performed on the most representative paraffin blocks. BRAF expression was assessed in tumour cells from the invasive component, while PD-L1 in stromal and inflammatory cells within the invasive tumour.
Results: Ten tumours exhibited submucosal invasion (pT1), while the other 10 invaded only the lamina propria (pTis). Histologic grade was usually high (15 lesions), without any correlation with invasion stage. BRAF was negative in all lesions. PD-L1 was positive in 10 cases, usually in small proportion of cells (median value 10 percent, ranging from 1 to 30 percent). There was a significant positive correlation between PD-L1 expression and number of TILs (two-tailed P value 0.0091), cases with more TILs having a constantly higher expression of PD-L1. Also, PD-L1 expression was higher (without statistical significance) in stromal component of pT1 tumours, than in pTis ones. Tumours with high levels of desmoplasia had, also, higher expression of PD-L1 (but not of TILs).
Conclusion: PDL-1 overexpression, known to correlate with short overall survival in colonic cancer, is also correlated, in ECC, with the presence of TILs, feature that has a positive prognosis value. These interesting data from a small study, are tackling the insides of immune response and effects of immunotherapy in colorectal cancer.

E-PS-06-016
Chondroid metaplasia of peritoneum incidentally detected after total gastrectomy: a case report
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Background & Objectives: Chondroid metaplasia of the peritoneum is a rare condition in which mesothelial or fibroblastic cells transform into chondrocytes, forming cartilage-like tissue without atypia and independent of malignant mesothelial neoplasms, metastatic carcinoma, or foetal implantation. The primary causes are previous abdominal surgeries and trauma. Here, we present a case of chondroid metaplasia of peritoneum in a patient with both trauma and malignancy, suggesting alternative pathogenic mechanisms.
Methods: A 64-year-old woman with a history of rib fractures due to a car accident and Herpes Zoster infection 1.5 years ago presented with stomach pain. Abdominal CT revealed a 27x21 mm irregularly

bordered, heterogeneous contrast-enhancing mass attached to the gastric wall at the hepatogastric ligament. Endoscopy identified an infiltrative tumour mass in the antrum and angulus, and biopsy confirmed gastric adenocarcinoma. The patient received four cycles of neoadjuvant FLOT treatment and showed a nearly complete response according to the PET findings. Total gastrectomy with D2 dissection was performed.
Results: Histopathological examination of the total gastrectomy specimen confirmed the diagnosis of poorly differentiated gastric adenocarcinoma in microscopic foci. Immunohistochemical analysis showed that HER-2 was negative. According to the TNM classification, the case was reported as ypT2 ypN1. Additionally, a firm, single, flesh-coloured nodule, measuring 3 cm, was incidentally found on the peritoneal surface of the perigastric fat tissue. Histopathological evaluation confirmed the presence of mature hyaline cartilage without cytological atypia, leading to the diagnosis of chondroid metaplasia.
Conclusion: Chondroid metaplasia of the peritoneum is rarely reported and is usually found incidentally. Our case is the first in the literature to involve both a history of trauma and a malignant tumour diagnosis. Further research is needed to better understand the various aetiologies of chondroid metaplasia.

E-PS-06-017
A rare tumour of the gallbladder: mixed lymphoepithelioma-like carcinoma and adenocarcinoma
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Background & Objectives: Lymphoepithelioma-like carcinoma (LELC) is a rare malignancy characterized by poorly differentiated epithelial cells with dense lymphoplasmacytic infiltration. Although it is most commonly found in the nasopharynx, lung, and thymus, gallbladder involvement is extremely rare. Due to the limited number of reported cases, its prognosis and optimal treatment approach remain uncertain. We present a rare case of gallbladder carcinoma with mixed histology of LELC and adenocarcinoma, contributing to the scarce literature on this entity.
Methods: An 86-year-old woman presented with abdominal pain and distension in February 2025. Imaging revealed a polypoid lesion with exophytic growth in the gallbladder wall, leading to a cholecystectomy.
Results: Macroscopic examination revealed a 2 cm polypoid tumoral lesion located 1 mm from the surgical margin. Histologic evaluation showed poorly differentiated tumour cells with dense lymphoid infiltration in some areas and glandular structures in others. Immunohistochemistry demonstrated cytokeratin 7 and cytokeratin 19 positivity in both the undifferentiated tumour cells and glandular areas. Vimentin positivity was observed only in the solid areas with undifferentiated tumour cells. Based on these findings, a diagnosis of mixed LELC and adenocarcinoma was made. Epstein-Barr virus (EBV) was negative in immunohistochemical staining. Microsatellite instability (MSI) testing revealed preserved mismatch repair (MMR) proteins.
Conclusion: Gallbladder LELC is an exceptionally rare tumour and should be considered in the differential diagnosis of gallbladder neoplasms. LELC is generally associated with a more favourable prognosis compared to conventional gallbladder carcinoma. Further studies are needed to clarify its biological behaviour and guide treatment strategies.

E-PS-06-018
Imatinib and immunosuppression: an overlooked side effect?
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Background & Objectives: Gastrointestinal stromal tumours (GIST) are rare malignancies mainly found in the stomach and small intestine, known for their variable malignancy. Here, we present a case involving Tuberculosis (TB) in conjunction with GIST.
Methods: A unique case was retrieved from the hospital record
Results: A 37-year-old male with a history of Gastrointestinal Stromal Tumour (GIST) and prior surgical resection presented with recurrent abdominal pain. Ultrasound revealed a mesenteric mass indicating GIST recurrence, confirmed by biopsy. During exploratory laparotomy, dense adhesions and extensive mesenteric involvement halted the procedure. Six months of Imatinib therapy followed, with partial response seen on CT scans. Treatment continued for two years, but a subsequent scan showed a 28% mass increase with fibrosis and calcified granulomas. An enterocutaneous fistula appeared, leading to a three-month Sunitinib course, but no improvement was observed on follow-up scans. Regorafenib was initiated, but cavitary lung lesions, fibrotic changes, and lymphadenopathy raised suspicion of tuberculosis. Regorafenib was stopped, and Anti-tuberculosis therapy (ATT) was administered. After nine months, continued chest symptoms required a six-month ATT extension. The patient's condition stabilized, but an abdominal mass remained, suggesting old tuberculosis. Follow-up is ongoing.
Conclusion: This case report highlights the challenges posed by the coexistence of recurrent GIST and TB infection in a patient. Imatinib, a cornerstone of GIST therapy, not only targets cancer-specific receptors but also modulates T cell function. While not typically considered a predisposing factor for TB, previous reports have suggested potential associations between Imatinib therapies leading to immune-suppression followed by flaring up of tuberculosis. This raises questions about its impact on immune susceptibility.

E-PS-06-019
Submucosal lipomatosis of the appendix: a rare clinical entity
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Background & Objectives: Submucosal lipomatosis of the appendix was first described histopathologically by Antonci in 1956. It is a rare clinical entity that can sometimes be mistaken for a tumour on clinical and radiological evaluation. This condition is often associated with localized symptoms or acute appendicitis, for which it is frequently the underlying cause. Unlike a true lipoma, submucosal lipomatosis lacks a well-defined capsule.
Methods: We present the case of a 48-year-old patient who arrived at the Emergency Department with severe abdominal pain that initially began in the epigastrium before migrating to the lower right quadrant. Abdominal ultrasound revealed a tubular, aperistaltic structure measuring 1.1 cm in diameter with a "targetoid" appearance in the ileocecal region. Blood tests showed elevated leukocyte and C-reactive protein levels, prompting the surgical team to proceed with an appendectomy.
Results: Macroscopic examination of the resected appendix, which measured 8 cm in length and up to 2 cm in diameter, revealed a markedly thickened, whitish wall forming a tumour-like mass of 1.5 cm in length. The serosa appeared gray, inflamed, and exhibited increased vascularity. Histological analysis demonstrated pronounced lobules and sheets of mature adipocytes within the appendiceal wall. The appendix also showed partial necrosis and dense granulocytic inflammatory infiltrate, which extended into the tumour-like mass, contributing to its characteristic macroscopic appearance.
Conclusion: While some authors argue that small amounts of submucosal fat within the appendiceal wall are common, submucosal lipomatosis is distinguished by its size and mass-like appearance. Recognizing this condition through both radiological and histopathological examinations is crucial, as it can lead to complications such as intussusception, torsion, and inflammation. The main radiological differential diagnoses include isolated acute appendicitis, small and large bowel obstruction, and carcinoma. Furthermore, due to the presence of necrosis and

degenerative changes in the adipocytes at the histopathological level, careful evaluation is necessary to rule out malignancy.

E-PS-06-020

Grossing the Whipple: a tertiary cancer centre's experience with ampullary lesions and a review of major macroscopic features

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Background & Objectives: Ampullary adenocarcinomas constitute 6-9% of all periampullary malignancies. These lesions can cause exuberant clinical manifestations, such as obstructive jaundice and weight loss, and thus motivate surgical intervention, representing approximately 15% of pancreaticoduodenectomies. The Whipple procedure remains a cornerstone of treatment for such lesions, although less invasive interventions are preferable when possible. Establishing an intra-or peri-ampullary origin for tumours poses a diagnostic challenge, and proper grossing is crucial in demonstrating the specific localization of these neoplasms. Likewise, adenomyomatous hyperplasia is a rare cause of biliary obstruction and common bile duct dilation, mimicking malignancy and posing a diagnostic challenge prior to surgical intervention, possibly leading to overtreatment. We propose to review ampullary lesions in our institute that motivated surgical intervention, including adenomyomatous hyperplasia centred in the ampulla.
Methods: We performed a review of cases with ampullary lesions treated primarily with cephalic duodenopancreatectomy in our institution over a 15-year period, through a query of internal records. Relevant clinical and pathological information was retrieved and analysed. Histological slide analysis is ongoing.
Results: Preliminary results of our review show that, between January 2010 and December 2024, 47 cases of ampullary lesions were treated with cephalic duodenopancreatectomy, with a slight predominance of intra-ampullary lesions. Notably, 25.3% (12/47) of these cases presented with concurrent or isolated adenomyomatous hyperplasia. Further analysis and review of the histological slides are required to confirm these initial observations.
Conclusion: Our preliminary review underscores the diagnostic difficulties in distinguishing between various types of ampullary lesions, highlighting the need for thorough gross examination, detailed histological assessment, and consideration of clinical presentation. In particular, the presence of adenomyomatous hyperplasia in a subset of cases may have implications for both diagnosis and management. Ultimately, our findings may contribute to refining diagnostic protocols and improving patient outcomes.

E-PS-06-021

Evaluation of non-conventional dysplasias associated with inflammatory bowel disease – a single centre experience

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Background & Objectives: Patients with inflammatory bowel disease (IBD) have a higher risk of developing neoplasms, due to chronic inflammatory milieu. In the last couple of years, new, non-conventional entities have been identified, reflecting generally poorer prognosis. Our study aimed to examine and compare all IBD-associated dysplasias, to identify their frequency in a Southern Hungarian population, and to further characterize their clinicopathologic features, as well.
Methods: A consecutive database was built from all IBD patients, who were diagnosed and/or treated in the Albert Szent-Györgyi Clinical Centre of the University of Szeged between 2011 and 2023. Basic clinicopathological data were collected from medical charts, and all neoplastic samples have been reevaluated. Statistical analysis was carried out by using khi-square, Mann-Whitney, and Kruskal-Wallis tests, with SPSS Statistics V 23.0 software (Armonk, USA).
Results: In the examined 13 years, 2397 patients were either diagnosed or treated with IBD, and 176 of them had a neoplastic sample. Non-conventional dysplasia was diagnosed in 50 patients. The most frequent subtype proved to be serrated lesion NOS (n=20; 40%), followed by hypermucinous (n=14; 28%), goblet cell deficient (n=9; 18%), sessile serrated lesion-like (n=6; 12%) and traditional serrated adenoma-like dysplasia (n=1; 2%). Significant association was found between the presence of non-conventional dysplasia and patient's age (p=0.003), IBD subtype (p=0.037), endoscopic appearance (p=0.01), the development (p<0.001), localisation (p<0.001), size (p<0.001), macroscopic appearance (p<0.001), grade (p<0.001), histological subtype (p<0.001), T (p=0.003) and M stage (p=0.012), mismatch repair protein status (p=0.007) of carcinoma, and the presence of lymphovascular invasion (p=0.024).

Conclusion: Based on our results, it can be stated that non-conventional dysplasias are fairly common in IBD-associated neoplastic samples (50/176; 28%). Due to their uncertain behaviour, complete resection needs to be proven, and patients may benefit from a closer follow-up.

Funding: This work was supported by the University of Szeged, Faculty of Medicine Research Fund-Heténi Géza Grant (IV-134-62-1/2024. SZAOK)

E-PS-06-022

Reproducibility examination of histopathological growth patterns of liver metastases in a retrospective, consecutive, single-centre, cohort study

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Background & Objectives: Histopathological growth patterns (HGPs) of liver metastases have been determined to have prognostic value. So far, only 2 studies have analysed the reproducibility of HGPs. Our study aimed to examine the reproducibility of the assessment of HGPs.
Methods: In our retrospective, consecutive, single-centre, cohort study, a database was built from patients who were operated on due to liver metastases at the University of Szeged, between 2011 and 2023. In each case, basic histopathological data were registered. Histological slides were collected and individually evaluated by 5 doctors and 2 medical students, with different years of experience in gastrointestinal pathology. Statistical analysis was carried out, and our methods were intraclass correlation and Fleiss' kappa.
Results: Our study comprised the resection specimens of 205 patients, with altogether 336 metastatic foci, of mostly gastrointestinal origin (n=188). Excellent agreement was reached between both the pathology specialist trainees (ICC score: 0.903) and the board-certified pathologists (ICC score: 0.983). The general agreement between all 7 evaluators proved to be moderate, with an ICC score of 0.738.
Conclusion: Our study proves that HGPs could be reliably determined for those who have at least 2 years of work experience in general pathology. This is the first study that includes the most board-trained pathologists included in the reproducibility examination of HGPs.

Funding: This work was supported by the University of Szeged, Faculty of Medicine Research Fund-Heténi Géza Grant (IV-134-62-1/2024. SZAOK)

E-PS-06-023

Down-regulation of long intergenic non-protein coding RNA 261 confers favourable prognosis and improved response to neoadjuvant CCRT in patient with rectal cancers

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Background & Objectives: The introduction of neoadjuvant concurrent chemoradiotherapy (CCRT) for patients with resectable rectal cancer not only improves survival rates but also increases the likelihood of curative surgeries. long intergenic non-protein coding RNA 261 (LINC00261), a long non-coding RNA (lncRNA), has been extensively documented as playing diverse roles across various cancer types and participating in numerous cellular processes. However, no comprehensive evaluation has been conducted on the relationship between LINC00261 expression, response to neoadjuvant CCRT, and survival rates in patients with rectal cancer.
Methods: A comparative analysis of gene expression profiles from the transcriptomic dataset (GSE35452) identified LINC00261as the most significantly up-regulated lncRNA. Tumour samples were collected from 343 primary rectal cancer patients who underwent neoadjuvant CCRT followed by surgical resection. The expression level of LINC00261 was semi-quantitatively assessed using in situ hybridization. Subsequently, statistical analyses were conducted to examine the relationship between LINC00261 expression, various clinicopathological features, and survival outcomes. Real-time RT-PCR was used to validate the transcription level between responders and non-responders in an independent cohort ($n = 8$ in each group).
Results: Decreased expression of LINC00261 showed significant correlations with less advanced post-treatment tumour invasiveness, negative post-treatment nodal metastasis, absence of vascular invasion and perineural invasion, and improved response to neoadjuvant CCRT (all $p \leq 0.024$). Diminished expression of LINC00261 was associated not only with favourable disease-specific survival (DSS), local recurrence-free survival (LRFS) and metastasis-free survival (MeFS) (all $p < 0.0001$) in univariate analysis but also functioned as an independent predictor signifying enhanced clinical outcomes, including DSS, LRFS, and MeFS (all $p < 0.001$). In the real-time RT-PCR analysis, the transcriptomic levels were significantly lower in the responder group compared to the non-responder group ($p = 0.007$).
Conclusion: LINC00261 may play a significant role in rectal cancer progression and response to neoadjuvant CCRT, serving as a novel prognostic factor.

E-PS-06-024

Unveiling medullary rectosigmoid carcinoma: a rare clinical presentation and comprehensive review of literature

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Background & Objectives: Medullary carcinoma (MC) of the rectosigmoid is an extremely rare and poorly understood subtype of colorectal cancer, constituting a small percentage of cases. It is characterized by its unique histological features, including solid, syncytial sheets of large eosinophilic cells with abundant lymphocytic infiltration and the absence of glandular differentiation. MC is frequently associated with microsatellite instability (MSI) and mismatch repair (MMR) protein deficiencies, particularly MLH1 and PMS2, and it often demonstrates a favourable prognosis, particularly in the absence of distant metastases. The diagnosis of MC is challenging due to its overlap with other poorly differentiated carcinomas.
Methods: A 50-year-old male with a history of sarcoidosis and chronic steroid use presented with left lower quadrant abdominal pain and altered bowel habits. Imaging studies revealed a rectosigmoid mass with regional lymphadenopathy. A left-sided colectomy, revealed features consistent with MC. IHC demonstrated positivity for calretinin and loss of MLH1 and PMS2, confirming the diagnosis of MC with microsatellite instability. The tumour was staged as pT3N0Mx, with no evidence of lymphovascular space invasion or perineural invasion.
Results: The histological and immunohistochemical findings, combined with the patient's favourable prognosis, underscore the importance of accurate diagnosis. MC, with its unique immune microenvironment and association with MSI, may exhibit a more favourable clinical course compared to other poorly differentiated colorectal carcinomas, making early recognition and surgical resection pivotal for optimal outcomes. This case contributes to the growing body of literature on the diverse clinical presentations of MC and reinforces the need for a comprehensive diagnostic approach to guide management.
Conclusion: Based on a literature review conducted from 2012 to 2023, our case is the first reported instance of a male patient with rectosigmoid medullary carcinoma. This case highlights the clinical and molecular variability of MC, which contrasts with the typical presentation in older females and the proximal colon.

E-PS-06-025

Complete response rate analysis in neoadjuvant therapy with FLOT (Fluorouracil, Leucovorin, Oxaliplatin and Taxol) in adenocarcinoma of oesophagogastric junction

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Background & Objectives: The incidence of adenocarcinoma of oesophagogastric junction (AOJ) has increased in recent years due to obesity and gastroesophageal reflux disease. It is the tumour with the highest mortality among gastrointestinal tumours. The rate of increase in incidence over the past four decades is the highest of any cancer, especially in high-income countries.
The aim of this study was to analyse the response of AOJ to the neoadjuvant perioperative chemotherapy regimen FLOT (Fluorouracil, Leucovorin, Oxaliplatin and Taxol) through histopathological analysis of the surgical specimen after esophagectomy.
Methods: Twenty patients who underwent video-assisted thoracoscopic esophagectomy with oesophagogastroplasty after a FLOT neoadjuvant regimen (average of 4 sessions) were analysed and divided into 2 subgroups: complete and incomplete responses.
Results: Surgical specimen analysis showed a complete response to FLOT in 4 patients (20%) (pT0N0M0 – 3 cases and pT0N1M0 – 1 case), including one poorly differentiated tumour with signet ring cells in the preoperative biopsy. The four received four cycles of neoadjuvant FLOT regimen with 100% of the dose calculated by weight. Approximately 40 days after esophagectomy, all 20 patients received other four sessions of FLOT. However, 10 (50%) required reduced doses or postponement of the adjuvant therapy intervals due to toxicity/weakness. The median survival was 19 months, with a maximum of 60 months. Patient pT0N1M0 developed lung metastasis and survived for 13 months. Among the 13 patients who are still alive, 8 are disease-free.

Conclusion: When other modalities of neoadjuvant therapy are considered and similar case series in current literature are analysed, the perioperative FLOT chemotherapy regimen in AOJ is proving to be an effective option. Indeed, it was associated with a disease free status in

almost half of the patients in the present study. Larger case series could be performed in order to place the FLOT regimen among the treatment options with better response in AOJ.

Funding: Educorp - State University of Campinas (UNICAMP)

E-PS-06-026

Systemic sclerosis of colon with severe constipation and colonic pseudo-obstruction

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Background & Objectives: Systemic sclerosis of the digestive tract is very rare and commonly occurs in the oesophagus, large intestine, small intestine and stomach in that order.
Methods: A 72-year-old woman presented with severe constipation and abdominal pain. Right hemicolectomy was performed because the patient did not respond to medical treatment.
Results: Grossly, the specimen showed a dilatation of the lumen of the ascending colon (megacolon) measuring approximately 20cm in length. Histologically, Muscularis propria showed multifocal atrophy with replacement by fibrosis. There was extensive collagenization in the submucosa and fibrosis in small vessels. Immunohistochemically, infiltrating lymphocytes were predominantly CD4 rather than CD8. Congo red staining was negative.
Conclusion: We report a rare case of systemic sclerosis of colon that is histologically difficult to experience.

E-PS-06-027

Human epidermal growth factor receptor 2 (HER2) expression prevalence in gastroesophageal adenocarcinomas in Malaysia

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Background & Objectives: The 5-year prevalence of gastric and oesophageal adenocarcinomas in Malaysia, are 6.8 and 1.7 per 100 000 population and is a major cause of mortality and morbidity. Gene amplification and overexpression of *HER2* in gastroesophageal adenocarcinomas (GEA) are associated with aggressive disease and the introduction of targeted therapy has demonstrated significant benefit. *HER2* testing in GEA is sporadically performed in Malaysia with limited local data.
Methods: HER2 immunoexpression in 41 biopsies and 13 resection specimens from 54 patients (39 males, 15 females) aged between 23-77 years with advanced GEA from two government hospitals between 2022 to 2025 were studied. Two sample groups were tested with HER2 immunohistochemistry (IHC); patients for an industry driven research (IDR) preliminary screening (28) with confirmatory testing [IHC and Dual-colour dual-hapten in situ hybridization (DDISH)] and the other upon clinical request (26). IHC was interpreted as 0 /1+(negative); 2+(equivocal) and 3+(positive) by two pathologists following 2016 CAP-ASCP-ASCO HER2 testing in gastroesophageal adenocarcinoma guideline and compared with DDISH results when available.
Results: From the 54 samples, 49 were from primary site (Oesophagus, cardio-oesophageal junction[COJ], stomach) and 5 from metastatic sites. 39 (72%) of IHC were interpreted as negative, 10 (19%) as equivocal and 5(9%) as positive. Overall, 10 cases (19%) showed HER-2 DDISH amplification (6) and 3+ IHC (4). Tumour with intestinal differentiation were HER2 amplified/ overexpressed in 7/30 cases (23%) compared to diffuse type 2/21(10%). HER2 positivity was higher in COJ/oesophagus specimens (9/10) and in biopsies (10/10).
Conclusion: 28% of the cases were either equivocal or positive for HER2 IHC with 19% displaying *HER2* amplification or 3+ IHC, in keeping with range of 6.8% to 26.8% described in literature. Most positive samples were COJ/oesophagus biopsies with propensity to GEA with intestinal differentiation. Despite the limited cases, GEA HER2 immunoexpression in Malaysia appears consistent with other countries.

E-PS-06-028

Perianal ectopic breast fibroadenoma: a rare case report

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Background & Objectives: Ectopic breast tissue is an uncommon phenomenon and is situated along the so-called Milk Line that extends from the axilla to the vulva [1]. Various histopathological appearances have been described ranging from normal breast tissue to cancer [2]. We report an unusual case of fibroadenomatous type changes in perineum in a woman who presented with an anal lesion/mass clinically.
Methods: A 43 years old woman complained of persistent perianal lesion causing discomfort. Clinically it appeared a soft cystic mass and an excision biopsy was then undertaken.
Results: Grossly, the specimen was a well-defined firm white nodule measuring 21x15mm. Microscopically, the mass was composed of proliferating ductal tissue showing minimal epithelial hyperplasia embedded in spindle cell breast type stroma resembling fibroadenomatoid hyperplasia (figure 1a). Immunohistochemical stains for CK7 (figure 1b), ER (figure 1c), and GATA3 (figure 1d) were strongly positive confirming breast tissue phenotype.
Conclusion: Ectopic female breast tissue is often seen in the axilla but can be anywhere along the milk line/mammary ridge which extends from the breast to the groin including the vulva and perineum and less commonly reported in the buttock, neck, face, flank, arms, hips, shoulders and back [3, 4, 5]. Ectopic breast tissue may become more pronounced owing to hormonal changes during puberty and pregnancy. In our case, there were focal changes suggestive of fibroadenomatoid hyperplasia but there was no evidence of atypia or malignancy in the tissue examined. This is a rare phenomenon in which the pathologist should be aware of and be included in the differential diagnosis of any perianal mass.

E-PS-06-029

Intracholecystic papillary neoplasm, an incidental finding: report of two cases

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Background & Objectives: Intracholecystic papillary neoplasm of the gallbladder (ICPN) is a rare, premalignant lesion of the gallbladder, with the potential for progression to invasive gallbladder carcinoma. It was first recognized by the World Health Organization (WHO) in 2010 and proposed in the 2019 WHO classification, as a unique preinvasive neoplasm of gallbladder. Despite its malignant potential, ICPN generally has a better prognosis than invasive carcinoma. This report highlights two cases which were diagnosed after routine cholecystectomy and underlines the importance of early detection and histopathological diagnosis.

Methods: The first case we present is a 57-year-old female, with a history of recurrent right upper quadrant pain and gallstones, who underwent abdominal ultrasound that revealed two non-mobile, echogenic lesions in the gallbladder. Post-cholecystectomy histology confirmed ICPN, with a mixture of gastric pyloric-type epithelium, foveolar, and oncocytic epithelium. The second case is a 62-year-old male, who was referred to general surgery due to a suspicious polypoid mass in the gallbladder fundus on CT imaging. Laparoscopic cholecystectomy revealed a mass measuring 1.6 cm and confirmed on histology as ICPN. None of those lesion showed high-grade dysplasia or invasive carcinoma.
Results: ICPN is often found incidentally during imaging or post-cholecystectomy histological evaluation and it may present with symptoms similar to cholelithiasis. Most cases are non-invasive, however there is potential for malignancy, especially in the presence of high grade dysplasia or papillary growth pattern. This underscores the importance of histopathological examination in confirming the diagnosis and determining the risk of malignancy.
Conclusion: ICPN is a rare gallbladder lesion, but a small fraction can progress into invasive carcinoma. The need for screening guidelines is essential for early detection of the disease to prevent malignant transformation into invasive carcinoma. Pathological study of this type of lesion is important to identify the main characteristics that influence patient prognosis and survival.

E-PS-06-030
A rare case of primary pancreatic ductal adenocarcinoma and synchronous serous carcinoma of the ovary
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Background & Objectives: An 82-year-old female patient is diagnosed, via Endoscopic ultrasound-guided fine needle biopsy, with pancreatic ductal adenocarcinoma and subsequently undergoes distal pancreatosplenectomy. During the procedure two additional masses are found in the woman's abdominal and pelvic cavity and are therefore sent in the Pathology Department for evaluation.
Methods: An Intraoperative Frozen Section Consultation of the abdominal mass revealed a tumour with papillary growth and fluid-filled cysts, microscopically suggestive of malignancy with papillary architecture. Following surgery, the rest of the resected specimens, consisting of the pancreas, spleen and pelvic mass, were sent for further studying.
Results: Morphological and immunohistochemical analysis confirmed the two macroscopically similar masses as extraovarian presentations of serous carcinoma of the ovary [WT1(+), ER (+), PR (+), p16 (+), p53(+)]. Specifically, the abdominal mass consisted mostly of a borderline serous component with low-grade and high-grade areas, whereas the pelvic mass consisted solely of a high-grade serous component. Histopathological examination of the pancreas confirmed the diagnosis of pancreatic ductal adenocarcinoma [CK7(+), CK17(+), CK20(+), WT1(-), ER (-), PR (-), p16 (-), p53(-)].
Conclusion: The identification of synchronous ovarian and pancreatic malignancies raises the possibility of an inherited genetic predisposition, including Hereditary Non-Polyposis Colorectal Cancer/Lynch Syndrome, Familial Adenomatous Polyposis (FAP), Hereditary Breast and Ovarian Cancer (BRCA 1 or 2 mutation), Peutz-Jeghers Syndrome and Li-Fraumeni syndromes. Genetic counselling for the patient's immediate family should be considered.

E-PS-06-031
Squamous cell carcinoma following treated oesophageal intramucosal adenocarcinoma: an unusual scenario
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Background & Objectives: Radiofrequency ablation (RFA) is an established treatment for high grade dysplasia and intramucosal adenocarcinoma, where it may be used in combination with endoscopic mucosal resection (EMR). Squamous cell carcinoma (SCC) is a very rare complication of these interventions. To our knowledge, this is the first case of SCC arising following combined EMR and RFA for intramucosal adenocarcinoma.
Methods: A 75-year-old male with a history of Barrett's oesophagus (BO) diagnosed in 2002 was lost to follow-up. Upon re-referral in 2017, endoscopy revealed a suspicious lesion at 39cm from the incisors. Biopsy confirmed intramucosal adenocarcinoma on a background of BO with high-grade dysplasia (HGD).
Results: The patient was treated with two rounds of neoadjuvant chemotherapy (carboplatin/capecitabine), followed by EMR. Microscopy confirmed ypT1a (m3) intramucosal adenocarcinoma close to deep margin in the EMR specimen. Follow-up biopsies at 2 and 6 months showed chronic inflammation and intestinal metaplasia without dysplasia or malignancy. He subsequently received RFA. At 12 months follow-up, endoscopy revealed a stricture suspicious for malignancy and repeat biopsies confirmed a poorly differentiated SCC. This was confirmed by immunohistochemistry. Imaging (CT and CT-PET) staged the SCC as T2/T3, with no nodal or distant metastases. The radical curative surgical approach was declined by the patient. Given the recent interventions (EMR & RFA) and risk of worsening dysphagia with radiotherapy, the multidisciplinary team opted for palliative stenting.
Conclusion: This case illustrates a rare but serious complication of combined EMR and RFA for treatment of early adenocarcinoma arising in BO and highlights the necessity of long-term surveillance and repeat biopsies.

E-PS-06-033
Gastroesophageal adenocarcinoma and Human epidermal growth factor receptor 2 (HER2) testing validation in Malaysia
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Background & Objectives: HER2 immunohistochemistry (IHC) with confirmatory in-situ hybridisation is routinely performed on breast cancers in hospitals in Malaysia but sparsely performed in Gastroesophageal Adenocarcinomas (GEA) despite evidence of targeted therapy benefit in patients with HER2 overexpression and gene amplification. The challenges of staining variability and heterogeneity of HER2 IHC interpretation is recognised worldwide. This study investigates the interobserver variability between two pathologists while validating HER2 immunohistochemistry at respective laboratories.
Methods: HER2 immunoexpression for 54 patients with advanced GEA from two government hospitals between 2022 to 2025 were studied. Two sample groups were tested with HER2 immunohistochemistry (IHC); patients for an industry driven research (IDR) preliminary screening (28) with confirmatory testing [IHC and Dual-colour dual-hapten in situ hybridization (DDISH)]and upon clinical request (26). IHC was interpreted as 0 /1+(negative); 2+(equivocal)

and 3+(positive) by two pathologists, independently following 2016 CAP-ASCP-ASCO HER2 testing in gastroesophageal adenocarcinoma guideline and compared with confirmatory IHC/DDISH. Both pathologists are trained and certified for IHC interpretation. Weighted Kappa was performed for assessment of agreement.
Results: Out of the 54 cases, the pathologists achieved agreement in 52 cases with a weighted Kappa = 0.932 (95% CI). Two discrepant cases were reported as 1+ vs 2+ and 2+ vs 3+. Concordance between the pathologist and IDR confirmatory tests (either IHC or IHC & DDISH, n=28) was substantial with weighted Kappa =0.729 (95%CI). Discrepancies were present in 5 cases.
Conclusion: The interpretation of GEA HER2 IHC requires practise as it is different from breast cancer and the heterogenous nature complicates interpretation. The excellent agreement of HER2 IHC interpretation between both pathologists and good concordance between pathologist and confirmatory tests in an established laboratory is an encouragement for pathologist to perform HER2 IHC testing for GEA confidently in all laboratories within Malaysia.

E-PS-06-034
Value of flow cytometry in the diagnosis of complex celiac disease
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Background & Objectives: The analysis of intraepithelial lymphocytes (IELs) in the duodenal mucosa by flow cytometry (lymphogram) identifies a specific lymphocyte profile in celiac disease (CD), serving as a complementary diagnostic tool in borderline or discordant cases and even in the follow-up of suspected refractory CD. It is also useful in patients who have initiated a gluten-free diet (GFD) without prior diagnosis, since certain IELs subpopulations remain elevated. This study describes cytometric and histological findings in various clinical scenarios of suspected CD.
Methods: Thirty-five patients with suspected CD were retrospectively reviewed between August 2023 and February 2025, and classified into five groups: (1) inconclusive serology and intraepithelial lymphocytosis (n=8), (2) villous atrophy with negative serology (n=5), (3) GFD without prior diagnosis (n=16), (4) paediatric patients with borderline serology (anti-TG2: 7–16 AU/mL) (n=4), and (5) suspected refractory CD type II (n=2), defined by >15–20% aberrant T cells ($sCD3^-$, $icCD3^+$). The lymphogram in our series included the evaluation of $TCR\gamma\delta^+$, $CD45^+$, and $CD3^-$ NK-like IELs. A CD-compatible lymphogram was defined by $TCR\gamma\delta^+$ IELs >15%.
Results: The lymphogram was compatible with CD in 14 of 35 patients, distributed among groups 1 (n=2), 2 (n=3), 3 (n=8), and 4 (n=1). Aberrant T cells (<10%) were identified in 1 patient from group 5 and 2 additional patients from group 2.
Conclusion: IELs profiling contributed to the diagnosis of CD in 40% of the patients evaluated, demonstrating its complementary value in complex clinical settings, particularly in patients on a GFD without a confirmed diagnosis. Additionally, it may also help in seronegative cases (regardless of the degree of atrophy), in borderline histology or non-celiac lymphocytosis, and in the early detection and monitoring of refractory CD type II. Nonetheless, this case series is limited, and larger studies are needed to confirm these findings.

E-PS-06-035
Spatial mapping reveals heterogeneous immune microenvironments in the evolution of colitis-associated colorectal cancer
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Background & Objectives: Patients with inflammatory bowel disease have a higher risk of colitis-associated colorectal cancer (CA-CRC), but microenvironmental factors driving progression remain unclear. This study explores evolution of the immune microenvironment in two human ulcerative colitis (UC) whole colons through space and time.
Methods: Cellular microenvironments of two total panproctocolectomy specimens (UC1 and UC2), including preoperative biopsies, were digitally analysed using 166 H&E-stained whole slide images (WSI) from tissue sections sampled every 2 cm around the entire bowel. A state-of-the-art convolutional neural network-based cell classifier examined 592 pathologist-annotated regions of interest (ROIs) across non-dysplastic mucosa, dysplasia, and carcinoma to quantify densities of four immune cell types (lymphocyte, neutrophil, eosinophil, and plasma cell), along with epithelium and fibroblasts. T-cell receptor (TCR) sequencing (n=35 UC1; n=76 UC2) profiled T-cell clonal composition and dynamics across colons and through time.
Results: UC1 comprised 124 WSI with 23 dysplasia samples and four cecal adenocarcinomas, while UC2 contained 42 WSI with three foci of "indefinite for dysplasia". The rectosigmoid showed the highest mean lymphocyte density and unique TCR clonotype count in both colons. TCR sequencing revealed diverse clonotype distribution patterns in the UC bowels, ranging from ubiquitous presence throughout to localized patches, with some clonotypes persisting for up to 2 years. Significantly higher neutrophil densities (p=0.04) were observed cancer-near (mean 119.0/mm^2; cecum and ascending) versus -far (71.2/mm^2; transverse and below), but significantly less in dysplasia (53.6/mm^2) compared to non-dysplastic mucosa (76.2/mm^2; p=0.03). In UC1, signet-ring cell type CA-CRC exhibited much lower lymphocyte density (278.75/mm^2) compared to two conventional adenocarcinomas (1095.12/mm^2 and 1276.83/mm^2).
Conclusion: In UC, the immune microenvironment varies regionally, with the distal colon having the highest lymphocyte density and TCR diversity, whereas in CA-CRC it is subtype-dependent, but overall suggestive of an immune-privileged environment during carcinogenesis.

Funding: KB was funded by the Swiss National Science Foundation (P500PM_217647 / 1)

E-PS-06-036
Russell Body Esophagitis in Barrett's oesophagus
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Background & Objectives: Russell Body Barrett's Esophagitis (RBBE)is a rare and chronic inflammatory condition that has been associated with Barrett's oesophagus and, in some cases, an increased risk of malignancy. It can be linked to various factors HIV, gastric carcinoma, monoclonal gammopathy, and hepatitis C. It is characterized by accumulation of immunoglobulin-filled plasma cells, known as Russell bodies,which can sometimes be mistaken for neoplastic cells.

It has been linked to various conditions, including H. pylori infection, gastric carcinoma, and immunological disorders.
Methods: We report a case of Russell body Barett's Esophagitis in a 82 year-old female who is on Omeprazole 20 mg and endoscopic surveillance for low-grade dysplasia and 12 cm Barrett's oesophagus diagnoses since 2015. The patient has no gastrointestinal or oesophageal symptoms. Endoscopic findings are 12 cm Barrett's mucosa and 4 cm hiatus hernia.
Results: The biopsy from oesophagus showed numerous Russell bodies with excessive plasma cells in lamina propria which are showing positive staining for CD138, kappa and lambda light chains (polyclonal) and negative for pancytokeratin AE1/AE3. Congo red stain for amiloid and Modified Giemsa for H pylori is negative. The mucosa is negative for dysplasia.
Conclusion: The inflammation in RBBE is caused by overstimulation of plasma cells, leading to the accumulation of nondegradable immunoglobulin in the endoplasmic reticulum, forming Russell bodies. Recognizing this pattern is crucial for conducting a thorough workup to exclude associated conditions. Additionally, it can sometimes be mistaken for extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue, plasmacytoma, or signet ring cell carcinoma. Given the risk of chronic inflammation potentially leading to metaplastic or neoplastic changes, patients diagnosed with Russell body gastroenteritis, especially with additional risk factors such as smoking, may require close surveillance. Further research is needed to fully understand the clinical significance of this condition and its possible long-term implications.

E-PS-06-037
Monophasic gastric tumour with MALAT1-GLI1 fusion: another variant of gastroblastoma
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Background & Objectives: Gastroblastoma is an exceptionally rare gastric neoplasm, traditionally characterized as a biphasic lesion composed of epithelial and spindle cell components, originating in the muscularis propria. Most cases exhibit GLI1 gene fusions, with the MALAT1-GLI1 fusion being the most prevalent and serving as a diagnostic biomarker. Here, we present a case of an aggressive, metastasizing gastroblastoma, confirmed to harbour the MALAT1-GLI1 fusion, which exclusively displayed an epithelial pattern, thus demonstrating an atypical monophasic morphology.
Methods: See below
Results: A 50-year-old female patient was diagnosed with a 5 cm submucosal tumour in the pylorus, concomitant with two hepatic metastases. Two months following gastrectomy and liver resection, the patient required a second surgical intervention due to the development of new hepatic lesions. Nine months later, the patient underwent surgery again after multiple distant metastases were identified in the liver and peritoneum.
Histological evaluation of the aforementioned surgical samples revealed relatively uniform epithelioid cells arranged in nests and cords, with occasional microcystic changes and vague glandular formations containing eosinophilic material. The tumour cells exhibited scant to moderate eosinophilic cytoplasm and round, monotonous nuclei with fine, infrequent nucleoli, rare mitotic figures (1/5 mm²), and occasional apoptotic bodies. Tumour cells were strongly positive for keratin cocktail (CK AE1/3), CD56, and CD10. No expression of c-KIT, DOG1, CD34, SMA, desmin, synaptophysin, chromogranin or S100 was detected. Despite extensive examination, the lesions did not show a spindle cell component. The MALAT1-GLI1 gene fusion was identified in the tumour tissue.
Conclusion: Due to their extremely low incidence and the lack of distinct characteristics, gastroblastomas pose a diagnostic challenge. Their biphasic nature, characterized by the presence of both epithelial and spindle cell components, normally serves as a key diagnostic criterion. However, in our case, as well as in two recently published clinical cases, a new variant of GLI1-rearranged gastrointestinal monophasic tumours is described.

E-PS-06-038
Chondrolipoma of the oesophagus-a case report
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Background & Objectives: Chondrolipoma is a rare, benign mesenchymal tumour composed of both mature adipose and cartilaginous tissue. It is a subtype of lipoma, a common mesenchymal tumour, distinguished by areas of cartilaginous differentiation. Chondrolipomas can develop in various anatomical sites, including soft tissues, the head and neck region, and, rarely, internal organs such as the intestines and stomach. Here, we present a case of chondrolipoma arising from the oesophagus which appears to be the first reported case in English literature.
Methods: A tumour was incidentally detected in the cervical oesophagus of a 15-year-old male three years ago. Fine needle aspiration via endoscopic ultrasound revealed mature squamous epithelial cells and subepithelial connective tissue fragments. Due to the development of dysphagia, radiologic evaluations were repeated, and magnetic resonance imaging showed a thick-walled tumour, measuring 6x4x3cm, located in the cervical oesophagus, extending into and obliterating the oesophageal lumen. Most of the mass exhibited fat signal intensity, with non-lipomatous soft tissue components. The tumour was in the submucosal layer and displaced the trachea to the right. Submucosal mass excision was performed, and haematoxylin&eosin-stained slides were evaluated.
Results: Macroscopically, a well-circumscribed, yellow-coloured lesion containing patchy white solid areas was observed. Microscopic examination revealed a lesion with mature cartilaginous and adipose tissue. No lipoblasts were identified, and no atypia, mitosis, or necrosis was observed. Focal osseous metaplasia was noted. Chondroid lipoma, hamartoma, and chondrolipoma were included in the differential diagnosis. Histomorphologic findings were consistent with lipoma with chondroid metaplasia, also known as chondrolipoma.
Conclusion: Oesophageal chondrolipoma is a rare tumour. Even though without suspicious radiologic findings for malignancy, causing symptoms may lead surgical intervention. To the best of our knowledge, this is the first reported case of oesophageal chondrolipoma. Awareness of this unusual location is important for accurate diagnosis and management.

E-PS-06-039
Combination of Hirschsprung's disease and Epstein-Barr virus infection in children
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Background & Objectives: The combination of two conditions - Hirschprung's disease (HD) and Epstein-Barr infection (EBV) create

difficulties in diagnosis and treatment. A novel perspective is the investigation of the role of microcirculatory vessels and glial cells in the pathogenesis of intestinal disorders, as well as the interplay between these components and viral agents. The objective of the study is to conduct a morphological analysis of rectal biopsy samples from children presenting with a combination of Hirschprung's disease and EBV-infection.
Methods: Rectal biopsy specimens of 15 children diagnosed with Hirschprung's disease were used in the study. Histological analysis using haematoxylin and eosin and Van Gieson staining, and immunohistochemical staining with antibodies to calretinin and viral antigens (EBV, HSV, CMV) were performed.
Results: All cases were divided into three groups according to the duration of the disease: less than 2 years, 2 to 3 years, and more than 3 years. In each case, only one ganglion was found in the field of vision. Foci of sclerosis in the intestinal mucosa and muscular layers were detected. HSV and CMV antigens were not detected. In 10 cases EBV antigen was detected in vascular endothelium and ganglion neurons, and in 2 cases - in glial cells. In one case EBV antigen was found in individual nerve trunks. Lymphocytic infiltration and large lymphoid follicles were also observed.
Conclusion: The evidence suggests that EBV affects the endothelial, neuronal, and glial cells, which may influence the morphology of Hirschsprung's disease. This highlights the need to investigate the mechanisms of this pathology. The findings open new perspectives for understanding the role of viral infection in the pathogenesis of Hirschsprung's disease and developing effective treatment strategies.

E-PS-06-040
Diagnostic significance of determining herpes viruses in epithelial tumours of colorectal localization
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Background & Objectives: Determination of the role of herpes viruses in colorectal carcinogenesis remains controversial and poorly understood, and the study of this issue is an extremely important and urgent problem within the framework of the theory of viral carcinogenesis.
Objective: Comparative assessment of clinical, morphological and molecular genetic features of benign and malignant tumours with and without herpes viruses.
Methods: We studied 134 observations with benign and malignant neoplasms of colorectal localization. The comprehensive analysis included: clinical, morphological, immunohistochemical, molecular genetic methods, as well as the method of transmission electron microscopy. Herpes viruses were determined by real-time PCR.
Results: Among all observations, Epstein-Barr virus (EBV) was detected in 22% of cases, herpes virus type 6 (HHV6) in 19%, and cytomegalovirus (CMV) in 5.2%. Herpes viruses were more often detected in malignant than in benign neoplasms (88% and 12%, respectively; $p=0.004$). In patients with benign neoplasms, infection with one of the analysed viruses was determined in almost all observations, while malignant neoplasms were characterized by a combination of several viruses, and the most common was a combination of EBV and HHV6. We obtained statistically significant data indicating a more frequent lymphovascular ($p=0.002$) and perineural ($p<0.001$) invasion in observations where herpes viruses were detected. We did not find statistically significant differences when comparing the frequency of detection of somatic mutations of *KRAS*, *BRAF* and *NRAS* and the presence of herpes viruses. The study by electron microscopy methods allowed us to identify the presence of viral agents in most samples of malignant epithelial tumours of the colon.
Conclusion: Our study demonstrates the contribution of herpes viruses to the progression of malignant tumours of colorectal localization. Statistically significant results were obtained in relation to lymphovascular and perineural invasion, undoubtedly indicating a more aggressive biological behaviour of the tumour in the presence of herpes viruses.

Funding: The study was carried out within the framework of state budget funding (No 124021600057-0)

E-PS-06-041
Pathomorphological features of eosinophilic esophagitis at presentation and after treatment
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Background & Objectives: Eosinophilic esophagitis (EoE) is a chronic immune-mediated oesophageal disease, that shows predominantly eosinophilic infiltration of oesophageal mucosa ($\geq$ 15 eos/hpf) and various degree of subepithelial fibrosis. The aim of our study was to analyse histological features of EoE in patient at first biopsy and after treatment with proton pomp inhibitors (PPI).
Methods: Biopsy was performed in 70 patients with endoscopic features of EoE (EREFS $\geq$ 2) and in 25 patients with history of EoE after treatment with PPI. Biopsy specimens were fixed in 10%-neutral buffered formalin and stained with haematoxylin and eosin. Additional Mallory staining was performed for assessment of fibrosis. EoE histology scoring system (EoEHSS) and EoE Histology Remission Score (EoEHRS) were applied for histological evaluation of specimens.
Results: EoE was confirmed in all 70 patients, among them 51 were men (72,86%), median age was 29.5 (21; 42.25). Peak eosinophil count (PEC) ranged from 17 to 222 (Me 52 eos/hpf). Basal zone hyperplasia presented in 100% of cases and varied from 20 to 80%. Dilated intercellular spaces were noticed in 97,14%, surface epithelial alteration – in 60%, eosinophilic abscesses – in 48,57%, surface layering – in 17,14% and dyskeratotic epithelial cells – in 11,42% of patients. Lamina propria of mucosa could be assessed in 71,43% of biopsy specimens, among them various degree of fibrosis was observed. EoEHSS median grade score comprised 12 (8; 14.5), median stage score was 10 (8; 12). After treatment 92% of patients (23 from 25 patients) fulfilled EoEHRS criteria of histological remission.
Conclusion: EoEHSS is a powerful tools to evaluate pathomorphological features of EoE. Assessment of biopsy specimens obtained after treatment with EoEHRS helps to establish histological remission. Treatment with PPI was effective in 92% of patients.

Funding: The study was carried out within the framework of state budget funding (No 123030700111-1)

E-PS-06-042
Histological features and immunohistochemical markers of oesophageal cancer
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Background & Objectives: Worldwide oesophageal cancer is the eighth most commonly diagnosed cancer and is the sixth leading cause of cancer death. Incidence of adenocarcinoma (EAC) rises more rapidly than squamous cell cancer (ESCC). The aim of our morphological study was to assess histological type, grade and immunohistochemical profile of oesophageal cancer.
Methods: Biopsy was performed in 71 patients with oesophageal cancer. Biopsy specimens were stained with haematoxylin and eosin and combined PAS/Alcian blue. Immunohistochemical evaluation was performed using p53 (D0-7), p16 (SP49), Ki67 (MIB-1). All cases of ESCC expressed CK5/6 and p63. 77% of EAC expressed Muc5AC, 53,84% of EAC expressed Muc6 and 38,46% of EAC expressed Muc2.
Results: Median age of patients comprised 70,5 years (63-78), male-to-female ratio was 2,2:1. 46 patients were diagnosed wih EAC (G1 – 9 patients, G2 – 20 patients, G3 – 17 patients), 18 patients had SSCC (G1 – 5 patients, G2 – 8 patients, G3 – 5 patients) and 7 patients had undifferentiated cancer . Immunohistochemical evaluation was performed in 39 cases (26 patients with EAC and 13 patients with ESCC). Positive p53 expression (mutant-type) presented in 6 patients with ESCC (50%) and in 7 patients with EAC (46,15%). Expression of p16 was negative in all but 1 ESCC case (7,69%) and positive in 14 patients with EAC (53.84%). Positive expression of 16 was associated with positive p53 expression in EAC. Higher Ki67 level was associated with positive p53 expression in both cancer types ($p<0.01$).
Conclusion: Mutant-type expression of p53 was noticed in almost half of patients with ESCC and EAC that highlights the key role of *TP53* in oesophageal carcinogenesis. Moreover, mutant expression of p53 was associated with positive expression of p16 in EAC and with higher level of Ki67 in both cancer types. Further studies are needed to establish the role of immunohistochemical markers expression in prognosis of oesophageal cancer.

Funding: The study was carried out within the framework of state budget funding (No 122032100086-3)

E-PS-06-043
Jejunal perforation by histoplasmosis: case report
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Background & Objectives: Histoplasmosis is an opportunistic fungal infection caused by Histoplasma species. Disseminated forms, although rare, often involve the gastrointestinal tract and primarily affect immunocompromised patients. This paper presents an unusual case of gastrointestinal histoplasmosis with jejunal perforation.
Methods: A 57-year-old man presented with chronic abdominal pain, intermittent fever, cough, diaphoresis, nausea, and rapid weight loss.
Results: Findings on CT scans showed thickening and malignant lesions in the intestine, further evaluated through laparotomy, in addition to pulmonary involvement. Jejunal perforation and septic shock were identified and
treated with antibiotics. The clinical course was unfavourable, resulting in death. Peritoneal liquid cultures and haemocultures were negative, but the biopsy histological analysis revealed the presence of Histoplasma yeast.
Conclusion: This case underscores the importance of considering invasive fungal infections in apparently immunocompetent critically ill patients and reassessing the diagnostic methods for timely and effective treatment.

E-PS-06-044
Radiation-induced angiosarcoma of the breast metastatic to the upper gastrointestinal tract
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Background & Objectives: Radiation-induced angiosarcoma of the breast is a rare and aggressive tumour with poor prognosis and increasing prevalence. Widespread metastasis is common, however secondary involvement of the gastrointestinal tract is exceptionally rare.
Methods: We present the case of a 56-year-old woman who was diagnosed with angiosarcoma of the breast seven years after resection of breast cancer, followed by adjuvant external radiotherapy. Within one year, widespread bone metastasis occurred. The patient was referred to the hospital with severe abdominal pain and iron deficiency anaemia.
Results: Upper endoscopy was performed and showed multiple polypous and ulcerated lesions in stomach and duodenum; corresponding to diffuse thickening of the stomach wall on CT scan. Biopsies were taken and demonstrated highly vascularized nodular infiltrates of atypical spindle cells with marked nuclear pleomorphism and increased mitosis. Upon immunohistochemistry, the atypical spindle cells were negative for pan-keratin and SOX10, yet positive for CD31, ERG and MYC, prompting final diagnosis of radiation-induced angiosarcoma metastatic to stomach and duodenum.
Conclusion: Secondary tumours of the gastrointestinal tract are infrequent and mainly attributable to malignant melanoma, breast and lung cancer, while metastasis of sarcoma is even rarer. Reports of gastrointestinal metastasis due to radiation-induced angiosarcoma are currently lacking in the English literature. Our case highlights the differential diagnosis in separating the lesion from spindle cell carcinoma and other spindle cell malignancies.

E-PS-06-045
Gastric manifestation of cystinosis
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Background & Objectives: A 21-year-old female patient is known to have cystinosis (infantile nephropathic form). As a result, renal insufficiency requiring dialysis, growth retardation and arterial hypertension developed.
Methods: A gastroscopy, which was performed due to recurrent haemoptysis, revealed a leathery gastric mucosa.
Histologically, chronic and highly active HP gastritis can be diagnosed. In addition, rectangular to polygonal birefringent crystals are found intracapillary, which appear light yellow in H&E stain.
Results: These correspond to cystine crystals.
We therefore diagnose a gastrointestinal manifestation of cystinosis.
Conclusion: Cystinosis is a very rare autosomal recessive storage disease that primarily damages the kidneys. As the disease progresses, the eyes, musculoskeletal system, endocrine organs and CNS are particularly affected.

E-PS-06-046

Prognostic value of Epstein–Barr virus and stromal tumour-infiltrating lymphocytes in gastric cancer: a single-institution Polish study

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Background & Objectives: There is still a quest for identifying prognostic factors in gastric cancer (GC). This retrospective single-institution study aimed to analyse overall survival (OS), evaluating the prognostic value of Epstein–Barr virus (EBV) and stromal tumour-infiltrating lymphocytes (sTILs) adjusted for other variables such as neoadjuvant chemotherapy, sex, age, and the parameters (y)pT, (y)pN, (y)pM.
Methods: A total of 262 patients with primary GC, who underwent gastrectomy between 2008 and 2018 at the National Research Institute of Oncology, Warsaw, Poland, were included. The tumour staging was assessed according to the 8th edition of the TNM classification. EBV was detected by chromogenic in situ hybridization with the INFORM EBER Probe. TILs were examined by a semi-quantitative method described by International Immuno-Oncology Biomarker Working Group. All statistical analyses were conducted using R4.1.1 (R Core Team, 2021) package. The Akaike Information Criterion (AIC) model comparison procedure was performed. ΔAIC values <-2 were considered indicative of a significant predictor effect.
Results: Univariate and multivariate Cox regression analyses revealed no significant differences in OS between EBV positive and negative GC. Upon univariate analysis, higher percentage values of sTILs within the invasive margin (p=0.025, ΔAIC=-3.61), and combined central area and invasive margin of tumour (p=0.031, ΔAIC=-3.23), were identified as favourable prognostic factors, though these findings were not statistically significant in multivariate analysis. In multivariate analysis, the most significant independent prognostic predictors were (y)pT (p=0.004, ΔAIC=-6.41), (y)pN (p<0.001, ΔAIC =-33.42), (y)pM (p<0.001, ΔAIC=-8.96) and age (p<0.001, ΔAIC=-17.05).
Conclusion: Multivariate Cox regression analysis has identified (y)pTNM, particularly the (y)pN parameter, and patient age as the independent prognostic factors in GC. Incorporating other covariables into the AIC-based prognostic model did not improve prognostic accuracy. However, univariate analysis revealed statistical significance for sTILs within primary tumour, but not for EBV, indicating sTILs hold a higher prognostic value than EBV for GC.

Funding: The work was co-financed by a donation from Roche company for the purchase of the INFORM EBER probe – donation number 54/D/7/8/2016

E-PS-06-048

SWI/SNF-deficient malignant tumours of the gastrointestinal tract: a case-series of a rare and highly aggressive malignancy

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Background & Objectives: Switch/sucrose nonfermentable (SWI/SNF) complex-deficient carcinomas are rare, aggressive malignancies recently recognized in the gastrointestinal tract (GIT). They result from *SMARCB1* or *SMARCA4* inactivation, key components of the chromatin-remodelling SWI/SNF complex. Given emerging therapeutic implications (EZH2-inhibitors, immunotherapy), accurate diagnosis is crucial.
Methods: We retrospectively reviewed all SWI/SNF-deficient GIT carcinomas diagnosed at our institution from 2015 to 2025. Tumours were identified by complete loss of SMARCB1 or SMARCA4 protein expression in tumour cells, with intact internal controls.
Results: Six cases were identified: three SMARCB1-deficient and three SMARCA4-deficient carcinomas. Median age was 33.7 years (range: 16–61), with a male-to-female ratio of 1:2. Tumour sites included the stomach (n=3), gallbladder (n=2), and pancreas (n=1). One patient had an unresectable tumour, and three had distant metastases. Three underwent surgery. The median tumour size was 9 cm. Histology revealed high-grade undifferentiated carcinoma, with rhabdoid (n=3), yolk sac-like (n=1), and glandular (n=1) features. One case had multiseptate, empty vacuoles. All tumours expressed keratins, and three each showed complete loss of *SMARCB1* or *SMARCA4*. Mismatch repair proteins were retained; PD-L1 CPS scores were <3. One patient was lost to follow-up. With a median follow-up of 8 months, four progressed on palliative chemotherapy, and one died of disease.
Conclusion: SWI/SNF-deficient GIT carcinomas are rare, aggressive, and have poor outcomes. Key histologic clues include undifferentiated, rhabdoid, and yolk sac-like morphology. Immunohistochemistry is essential for diagnosis and guiding trial enrolment.

E-PS-06-049

Histopathological spectrum and αE-catenin expression of gastric cancers from carriers of germline *CTNNA1* truncating variants: insights from the largest reported cohort

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Background & Objectives: Germline truncating variants in *CTNNA1* gene, encoding αE-catenin, account for approximately 2% of hereditary diffuse gastric cancer (HDGC) cases. Loss of αE-catenin expression has been reported on a case-by-case basis in carriers of germline *CTNNA1*-variants. However, the detailed histological/immunohistochemical features of *CTNNA1*-associated gastric cancer (GC) are not well characterized.
Methods: Eleven tumour samples, including six primary GCs and five (peritoneal and nodal) metastases, from nine *CTNNA1* truncating carriers fulfilling the 2020 HDGC genetic testing criteria [doi:10.1016/S1470-2045(20)30219-9] were studied. According to WHO classification, GC was classified as signet-ring-cell-carcinoma (SRCC) /

poorly-cohesive-carcinoma (PCC) (diffuse-subtype by Laurén). Immunohistochemistry for αE-catenin (clone EP1793Y) was performed on eight samples from seven patients.
Results: Median age at GC diagnosis was 48 years (range:37–75). One case was detected at early stage (pT1a) in a prophylactic-total-gastrectomy, while the remaining eight were diagnosed at advanced stage (≥pT2), five with metastases.
The pT1a carcinoma, adjacent to pagetoid spread of SRCs (pTis), showed classic SRCs. Advanced-stage GCs showed predominantly PCC morphology with variable SRC component: <5% in five cases, 5–10% in two, and 10–50% in three. In two patients, the SRC proportion increased from 10% in primary tumours to 50% in corresponding metastases. All metastatic sites showed pure diffuse morphology with prominent desmoplastic stroma. In contrast, primary tumours displayed additional patterns, including nested, trabecular, rosetoid and true microglandular structures.
In all advanced-stage GCs, aberrant αE-catenin immunoexpression was demonstrated: complete loss in 62.5% (5/8) of samples analysed, and faint/incomplete membranous, paranuclear dotted, and/or cytoplasmic staining in the remaining 37.5% (3/8).
Conclusion: This is the largest cohort to date characterizing histopathological features and αE-catenin expression in *CTNNA1*-associated GCs. The morphological diversity observed in primary tumours may represent a diagnostic pitfall in the recognition of HDGC cases. The utility of αE-catenin expression as a marker for genetic triage in these cases warrants further investigation.

E-PS-06-050
Collagenous gastritis: from microscope to clinic, a diagnostic challenge in children and adults
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Background & Objectives: Collagenous gastritis (CG) is a rare condition defined by subepithelial collagen band deposition in the gastric mucosa. It has two clinical phenotypes: a paediatric form characterized by abdominal pain and microcytic anaemia, and an adult form associated with malabsorption and autoimmune diseases. Histologically, CG shows three main patterns: lymphocytic gastritis-like, eosinophil-rich, and atrophic. Endoscopic findings are non-specific. Differential diagnoses include amyloidosis, autoimmune gastritis, radiation injury, and scleroderma. Treatment includes dietary modifications, proton pump inhibitors (PPIs), sucralfate, corticosteroids, and oral budesonide.
Methods: We describe a case series of two patients one paediatric and one adult highlighting the phenotypic and histopathologic spectrum of CG.
Results: **Case 1:** An 8-year-old girl with atopy and a family history of autoimmunity presented with abdominal pain, anorexia, pallor, abdominal distension, and constipation. Labs revealed severe iron-deficiency anaemia and hepatosplenomegaly. Initial biopsy showed chronic gastritis and duodenitis. Persistent symptoms led to repeat endoscopy showing pangastritis and follicular duodenitis. Histology confirmed CG with >10 μm subepithelial collagen, marked lymphoplasmacytic and eosinophilic infiltrate (>40 eos/hpf), and oxyntic atrophy. Treatment included elemental formula, corticosteroids, PPIs, and dietary restrictions, resulting in clinical improvement.
Case 2: A 65-year-old woman with hypertension and dyslipidemia presented with chronic abdominal pain. Endoscopy revealed fundocorporal nodularity and erythema. Biopsy showed chronic erosive gastritis, severe oxyntic gland atrophy, pseudopyloric metaplasia (gastrin-negative), smooth muscle hyperplasia, and a thickened subepithelial collagen band (10–15 μm, Masson trichrome). Neuroendocrine cell hyperplasia was confirmed by chromogranin stain and reactive antral gastropathy. Findings were consistent with the atrophic pattern of CG. PPI therapy was initiated.
Conclusion: CG demonstrates age-dependent clinical and histologic variability. These cases emphasize its diagnostic complexity and the critical role of histopathology. Early recognition enables targeted treatment and may significantly improve outcomes, especially in paediatric patients with allergic or autoimmune tendencies.

E-PS-06-052
ChatGPT-4o as a pathologist's assistant: a new era in colon polyp classification
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Background & Objectives: Colon polyps represent an enormous number of diagnoses in the daily work of pathologists specialized in Gastrointestinal Pathology. Also, differentiate tubular adenomas (TA) from sessile serrated lesion with low-grade dysplasia (SSL-LGD) in not always easy. Waiting for the advent of AI algorithms that will help us decrease the burden of care, we have explored how adept the tools we now have available are.
Methods: We selected from our files a series of 158 colon polyps including 61 TA, one of them with high-grade dysplasia (TA-HGD), 33 SSL without dysplasia (SSL-ND), 62 SSL-LGD and 1 SSL-HGD. We use ChapGPT-4o of OpenIA as an AI tool. We trained it with the definitions of each type of polyp given in the WHO Classification of Tumours, Tumours of the Digestive Tract, 5th edition, and defined the differences between LGD and HGD. Once this was done, we showed it the images of the polyps so that it could make the diagnosis.
Results: ChatGPT-4o correctly diagnosed all 33 (100%) SSL-ND and the 2 (100%) HGD polyps, one TA and one SSL. It also correctly classified 56 (92%) TA-LGD and 44 (71%) SSL-LGD.
Conclusion: Given the good results obtained with the available AI in classifying colon polyps, we should not have to wait too long for the arrival of better tools to help the pathologist in the daily work of classifying this type of lesions to free him/her from this repetitive and low complexity task.

E-PS-06-054
The "2" faces of gastric carcinoma: a comparative study of early-onset (EOGC) and late-onset gastric carcinoma (LOGC) using MUC2, CDX2, HER2, and MMP2
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Background & Objectives: Gastric carcinoma is a heterogeneous disease with distinct clinical, pathological, and molecular characteristics influenced by the age of onset. This study seeks to elucidate mechanisms behind the increased aggressiveness of EOGC and explore potential implications for targeted therapeutic strategies by analysing the expression of key immunomarkers of **tumour differentiation, invasiveness, and therapeutic potential**.
Methods: The most representative paraffin blocks from the gastric resection specimens of 10 EOGC (onset <45 years of age) and 10 LOGC (onset >45 years of age) patients were selected. Immunohistochemical expression of MUC2, CDX2, HER2 and MMP2 was evaluated.

Results: EOGC is known to be more aggressive than LOGC. We found significantly lower MUC2 positivity in EOGC (12.5%) compared to LOGC (37.5%), while CDX2 positivity was similar in both groups (62.5%). This suggests that while both subtypes share a similar rate of intestinal differentiation (CDX2+), EOGC exhibits a more primitive, poorly organized intestinal phenotype, whereas LOGC may represent a more mature, mucin-producing tumour, potentially correlating with a less aggressive course.
HER2 was positive in 25% of LOGC cases but absent in EOGC, indicating that HER2 overexpression may contribute to the aggressiveness of LOGC. This finding shows a decreased opportunity for HER2-targeted therapies in EOGC.
MMP2 was positive in 80% of both subtypes, highlighting its role in tumour invasiveness and metastasis. This suggests that MMP2-targeted therapies could be beneficial for both EOGC and LOGC.
Conclusion: These findings highlight distinct molecular differences between EOGC and LOGC that may inform future treatment strategies. While both subtypes share common features such as CDX2 positivity and MMP2 involvement, HER2 overexpression and mucinous differentiation may be more relevant in LOGC. Further studies are needed to explore the prognostic implications of these markers and their potential in guiding personalized therapeutic approaches in clinical practice.

E-PS-06-055
Molecular testing in colorectal cancer: a single-centre experience
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Background & Objectives: Colorectal cancer (CRC) is a heterogeneous disease with distinct molecular subtypes that influence prognosis and treatment response.
Methods: The archival material from the Institute of Pathology, Belgrade, was analysed, encompassing all cases of CRC submitted for consultative review, in which predictive immunohistochemical and molecular biomarkers were assessed. Over five years, these analyses were conducted on 89 patients. Exactly half were male and half female. The average age was 60.8 ± 12.77 years, with the youngest 23 and the oldest 84. The majority (40.4%) were in clinical stage 2; one-third in stage 4, and nearly a quarter in stage 3. Only two female patients were in stage 1, both under 40.
Results: Microsatellite instability was evaluated by determining MMR status in 58 cases, using the RT-PCR method in 11 patients, and both methods in 5 patients (with consistent conclusions). A total of 15.9% of the examined tumours were classified as dMMR/MSI-H. The RAS/BRAF status was assessed in 21 cases; 7 patients had no mutations in either of these genes. In one young patient with MLH1 loss, BRAF-wildtype was identified, strongly suggesting Lynch syndrome.
PD-L1 testing is rarely performed in our institution (tested in 13.5% of tumours), with only three tumours exhibiting expression. HER2 testing in CRC was also infrequent (18%), and no cases showed expression of this marker.
Conclusion: These findings highlight the molecular diversity of CRC and reinforce the importance of biomarker testing for personalized treatment strategies. The relatively high proportion of MSI-H tumours underscores the need for routine screening for Lynch syndrome in younger patients. Limited PD-L1 and HER2 expression suggests a low likelihood of response to targeted therapies against these markers in our cohort. Expanding molecular profiling in CRC patients could improve patient stratification and therapeutic decision-making.

Funding: This research was funded by the Ministry of Science, Technological Development and Innovation, Republic of Serbia: 451-03-137/2025-03/ 200110

E-PS-06-056
Sarcomas involving the digestive system: a single-centre, 10-year experience
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Background & Objectives: Sarcomas involving the digestive system are rare and can be challenging to classify, with the major differential diagnoses including sarcomatoid carcinoma and gastrointestinal stromal tumours (GIST). To facilitate diagnosis and management, we present our single-centre experience on the clinicopathologic characteristics of these sarcomas.
Methods: A retrospective review of non-GIST digestive system sarcomas in adults was conducted using an institutional pathology database query of cases received from January 2015 to March 2025 (IRB protocol 812420). The analysed parameters included demographics, clinical presentation, tumour site, histologic type, stage, and outcome.
Results: A total of 72 cases were identified, accounting for approximately 1% of all malignancies involving the digestive system over the 10-year period. There was a male predilection (63.9%) and a wide age range (23–92 years; mean 56.7 ± 17.2 years). The most common tumour type was well-differentiated/dedifferentiated liposarcoma (30.6%), which primarily involved the digestive system through direct extension. This was followed by metastatic sarcoma (19.4%), Kaposi sarcoma (18.0%), leiomyosarcoma (11.1%), desmoplastic small round cell tumour (5.6%), angiosarcoma (4.2%), epithelioid haemangioendothelioma (2.8%), malignant peripheral nerve sheath tumour (2.8%), myeloid sarcoma (2.8%), pleomorphic rhabdomyosarcoma (1.4%), malignant glomus tumour (1.4%), and gastrointestinal neuroendocrine tumour (1.4%). Three primary tumours (4.2%) remained unclassifiable despite extensive workup. Notably, metastatic sarcomas may present following a remote history of sarcoma or as intussusception due to polypoid mucosal involvement, posing a diagnostic challenge and potential delay. Most cases were high stage (pT4 20.8% vs. pT1 8.3%). Two cases exhibited nodal metastasis (3%). Among 40 patients with complete follow-up data, 25 succumbed 1–56 months (mean 14.3 ± 16.2 months) after diagnosis, resulting in a mortality rate of 62.5%.
Conclusion: Non-GIST digestive system sarcomas are associated with high mortality, particularly in cases of high-stage or high-grade disease. Large intra-abdominal or retroperitoneal sarcomas involving the digestive system represent the most common scenario, followed by metastatic sarcomas.

E-PS-06-057
Claudin 18.2: emergin therapeutic target in HER2-negative gastroesophageal adenocarcinoma
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Background & Objectives: Claudin-18.2 is an intercellular binding molecule that is naturally expressed in non-malignant gastric epithelium. With tumour transformation and loss of cell polarity claudin is exposed allowing it to work as a therapeutic target with encouraging preliminary results in clinical trials. We have evaluated the expression pattern of this marker in a cohort of gastric tumours and its correlation with histological type, epidemiological determinants and the expression of other markers.
Methods: Forty-eight cases of gastroesophageal adenocarcinomas were recorded over a one-year period, 29 of them were HER2 negative. 51% were women and 49% were men. Their ages ranged from 47 to 96 years

with a median of 70 years. 16 were intestinal, 9 were diffuse, 3 were mixed and 1 was poorly differentiated. Those sections with adequate tumour representation were selected and immunohistochemical staining was performed. Subsequently, claudin staining was evaluated in each of them, recording the intensity and distribution of staining.
Results: Claudin 18.2 expression was studied in 27 of these cases. Two, were excluded due to lack of material at the time of the study. 13 cases were positive (48%) and 14 negative (52%). Regarding staining intensity, 77% of positive cases (10) showed 3+ intensity and 23% (3) were 2+. One case showed heterogeneous staining with 3+ at the superficial level of the tumour and 2+ at the deep level. It is important to highlight the need to have an adequate representation to carry out the study.
Conclusion: Given the heterogeneity of the marker expression and the still scarce literature supporting it in this field, further studies are needed to evaluate the need to reduce the positivity cutoff and optimize its usefulness as a biomarker in the diagnosis and treatment of advanced gastroesophageal cancer, allowing for better identification of patients candidates for targeted therapies and increasing clinical efficacy of these interventions.

E-PS-06-058

IL-17-positive immune cells in right-sided, left-sided colon cancer and in rectal cancer.IL-17A-197 A/G single nucleotide polymorphisms in colorectal cancer and their connection with IL-17 cell density in the tumour

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Background & Objectives: IL-17 supports tumour growth by facilitating angiogenesis and by promoting T cell-mediated tumour rejection. Expression of IL-17 cytokines in colorectal cancer is associated with genetic polymorphisms in the IL17A gene. The rs227S913 SNP has been shown to affect the IL17A gene expression and A allele has been associated with worse prognosis and higher susceptibility for colorectal cancer.
The aim of our study is to reveal IL-17 cell density in RCC, LCC and rectal cancer and to correlate these results with MMR status, survival and genetic polymorphisms of rs227S913 SNP.
Methods: Tissue samples resected from 92 patients with RCC (n=21), LCC (n=32) and rectal cancer (n=39) are investigated by immunohistochemistry for IL-17 in the tumour stroma (TS) and in the invasive front (IF) and for MMR proteins and for the (IL-17A-197 A/G SNP conducting the PCR-RELP method.
Results: IL-17$^+$ immune cells are less in number in RCC (11%) compared to those in LCC (36%) (χ2=2.512; p=0.113). Higher numbers of IL-17$^+$ cells in IF are mostly dMMR in RCC patients (χ2=5.661;p=0.59). On the opposite, higher IL-17 cell density in the IF is associated with pMMR status in LCC patients (χ2=6.967; p=0.008). Patients, who have more IL-17$^+$ cells in TS have pMMR status (χ2=5.333; p=0.25). Respectively, IL-17$^+$ cells are higher in the IF of pMMR status (χ2=7.149; p=0.009). In rectal cancer IL-17$^+$ cells are less in number compared to RCC and LCC. When IL-17$^+$ cells are $\geq$ 12.24 cells/mm2 in the IF, patients have pMMR status. In rectal cancer patients with IL-17$^+$ cells $\geq$ 5.44 cells/mm2 we find tertiary lymphoid structures (TLS). We observed higher density of IL-17$^+$ cells in the carriers of the G-allele genotypes (AG +GG).
Conclusion: In conclusion we confirm the negative effect of the A-allele for the IL-17A-197 A/G SNP for the immune response in the tumour microenvironment.

E-PS-06-059

Differences in mismatch repair protein expression between primary gastric tumours and lymph node metastases: clinicopathological insights

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Background & Objectives: Heterogeneity in mismatch repair (MMR) protein expression between primary tumours and metastases remains understudied in gastric cancer (GC). We aimed to assess the prevalence of heterogeneous MMR status (hMMR) in lymph node metastases of GC and explore its associations with clinicopathological features to inform prognosis and therapy.
Methods: We analysed 33 GC patients with confirmed lymph node metastases and no prior neoadjuvant therapy. Full-sized surgical specimens were evaluated immunohistochemically using antibodies against MSH2 (79H11), MSH6 (EP49), MLH1 (ES05), and PMS2 (EP51). hMMR was defined as uneven staining ($\geq$20% variability) of any marker in primary tumours or metastases. We correlated hMMR in metastases with sex, age, tumour site, macroscopic type, size, histologic subtype, differentiation, vascular emboli, TNM stage, and clinical stage. Statistical significance was assessed using χ^2 or Fisher's exact tests in Statistica 12.5.192.7, with $p<0.05$ considered significant.
Results: hMMR in lymph node metastases occurred in 5/33 cases (15.2%): three showed hMMR in both primary tumour and metastases, while two had stable primary tumour staining but hMMR in metastases. One additional case revealed microsatellite instability (MSI) exclusively in metastases, not the primary tumour. The mucinous subtype was significantly enriched in the hMMR-metastases group (p=0.024), contrasting with the intestinal subtype dominating the stable-MMR group. hMMR in metastases strongly correlated with advanced N stages (N3, $p<0.001$) compared to stable MMR (N1-2). No associations with sex, age, or tumour size were observed.
Conclusion: Heterogeneous MMR status in GC lymph node metastases, though uncommon (15.2%), is linked to mucinous histology and advanced nodal spread. This suggests clonal evolution with potential implications for prognosis and immunotherapy responsiveness.

E-PS-06-060

Spatial molecular heterogeneity of small bowel adenocarcinoma: when the metastasis tells a different story

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Background & Objectives: Metastatic small bowel adenocarcinoma (SBA) is a rare and aggressive malignancy with limited therapeutic options. Molecular discrepancies between primary tumours and their distant metastases may impact treatment decisions. This study aims to

evaluate the molecular profile concordance between primary tumour and paired distant metastasis in patients with metastatic SBA.
Methods: Next-generation sequencing (NGS) was performed using the Illumina MiSeq platform. Library preparation was conducted with the AmoyDx HANDLE Classic NGS Panel. Bioinformatic analysis was carried out using the AmoyDx NGS Data System (ANDAS). Immunohistochemistry (IHC) for mismatch repair proteins (BenchMark Ultra system) was performed.
Results: Five patients (all females; median age: 70 years) were included; the primary tumour was duodenal in three cases and jejunoileal in two cases. The distant metastases (four synchronous and one metachronous) were peritoneal in all cases. Molecular differences between the primary tumour and the corresponding metastasis was observed in one patient (20%). This patient, who had a history of Crohn's disease and received adjuvant chemotherapy after surgical resection of a stage II SBA (pT4N0) at the age of 61 years, developed a peritoneal metastasis 5 years later. Both primary tumour and metastasis harboured a TP53 and an IDH2 mutation, whereas an additional KRAS mutation (G12V) was identified in the metastatic tissue. The primary tumour of this patient was MMR-proficient by IHC and microsatellite stable (MSS) by NGS, while the metastasis exhibited MMR-deficiency by IHC (loss of MLH1 and PMS2 expression) and it was MSS by NGS.
Conclusion: Spatial molecular heterogeneity may occur in metastatic SBA, suggesting that adding molecular profiling of metastatic tissue, especially in case of metachronous metastases, may improve selection of patients with advanced SBA for targeted therapies and/or immunotherapy.

E-PS-06-061
Colonical estenosis. a case report
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Background & Objectives: Amoebic colitis is an infection of the large intestine caused by the protozoan parasite Entamoeba histolytica which can spread to the liver and other organs such as the brain or lungs.
This infection is most common in tropical and subtropical regions and rare in developed countries. It is transmitted by ingestion of Entamoeba histolytica cysts via the faecal-oral or oral-anal route.
Methods: A 48-year-old woman with no past history of interest consulted for fever >39-40º for 8 days and non-specific digestive symptoms. Laboratory tests showed leukocytosis of 22,750, increased CRP (352.4) and procalcitonin (3.08), alterations in liver function (ALT=68, ALP=422 and Bilirubin=1.6). Micro-organism studies were negative. CT findings suggested a possible neoplasm in the ascending colon, with inflammatory changes in the abscess phase and large hepatic LOES that could be hepatic abscesses. Right hemicolectomy and drainage of liver abscesses were performed.
Results: We received a 29 cm segment of large bowel with a 10X6 cm ulcerated lesion and nearby millimetric cottony exudates. Samples were not sent to microbiology due to the initial suspicion of neoplasia and not of an infectious process. Microscopic examination showed large flask-shaped ulcerations and transmural abscesses that sometimes reached the serosa without perforating it. Numerous trophozoites (suggestive of Entamoeba) were identified in the mucosa and submucosa, showing intense magenta PAS positivity and CD68 negative (being positive in macrophages). No areas of dysplasia or tumour infiltrates were identified and the final diagnosis was Entamoeba histolytica amoebic colitis.
Conclusion: Amoeboma (amoebic pseudotumour) presents as a firm, well-defined, annular inflammatory thickening of the colon wall, usually in the cecum or ascending colon, which can be confused with a neoplasm, the definitive diagnosis being anatomopathological, with visualisation of trophozoites invading the intestinal mucosa.

E-PS-06-062
A 16-year-old girl with inflammatory bowel disease-associated colorectal cancer
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Background & Objectives: Inflammatory bowel disease (IBD) increases the risk of colorectal cancer (CRC). Patients with IBD-associated CRC (IBD-CRC) are younger (typically 40s to 60s), more likely to develop right-sided colonic tumours, and have a poorer prognosis. IBD-CRC arises in a background of chronic mucosal inflammation and exhibits an aggressive growth pattern. *TP53* mutations are frequently observed in IBD-CRC.
Methods: We present a 16-year-old girl with a decade-long history of ulcerative colitis and newly diagnosed IBD-CRC. Clinical history, histopathological features, and immunohistochemical findings are described.
Results: Diagnosed with ulcerative colitis at age 5, the patient recently experienced intermittent vomiting, raising suspicion of severe ileus. Contrast-enhanced computed tomography revealed mucosal thickening in the ascending colon. She underwent extended right hemicolectomy, which revealed a 4.5 × 3.5 cm polypoid tumour with adjacent inflammatory ulcerations. Histopathology showed a well-differentiated adenocarcinoma invading the visceral peritoneum, with lymphovascular and perineural invasion. Dense peritumoral lymphocytic infiltration was also noted. The background displayed chronic mucosal inflammation, ulceration, crypt architectural distortion, and focal dysplasia. Immunohistochemistry demonstrated diffuse, strong nuclear p53 staining in the carcinoma, SATB2 loss in the dysplastic foci, and retained mismatch repair protein (PMS2, MSH6) expression.
Conclusion: We report a rare case of IBD-CRC in a very young patient. Despite her age, she had fluctuating ulcerative colitis activity for a decade. IBD-CRC demonstrates distinct histological features, with adenocarcinoma arising from chronic active colitis, crypt architectural distortion, and focal dysplasia. p53 overexpression and MMR proficiency align with previously reported findings. This case highlights the aggressive nature of IBD-CRC, even in young patients, emphasizing the need for vigilant surveillance and timely surgical intervention to improve outcomes.

E-PS-06-063
Morphological heterogeneity in gastric poorly-cohesive carcinoma. Impact on prognosis and on the expression of predictive markers
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Background & Objectives: The WHO Classification drew attention to the distinction between signet-ring cell and poorly cohesive NOS gastric cancer, as a possible indication of different prognosis in these subsets of patients. The high morphological heterogeneity within individual lesions could impact on patients survival, but also on the mutational profile and the expression of markers predictive of response to therapy. The aim of the present study is to analyse the survival and response to therapy on a group of poorly-cohesive gastric carcinomas (PCGC) on biopsy.

Methods: All consecutive patients with a diagnosis of PCGC on biopsy in the last year were enrolled. All clinical and histopathological features were collected, including the percentage of signet-ring and non-signet poorly-cohesive component in each case. After histological revision, immunohistochemistry for MLH1 (clone MI), PMS2 (A16-4), MSH2 (G219-1129), MSH6 (SP93), Claudin-18.2 (43-14A), Her-2 (4B5), and PD-L1 (22C3) was performed.
Results: Sixteen patients (12 males, 4 females; mean age 69,43 years) were enrolled, among which 5 (31.2%) died of disease after a mean follow-up of 229 days.
The presence of a signet-ring component in a heterogeneous PCGC (i.e. signet-ring and non-signet component) was significantly correlated with a better survival, while 3 out of the 5 deceased patients had PCGC with a pure non-signet component (p=0.012, cox regression analysis). No significant differences in the expression of the predictive markers were observed among groups.
Conclusion: We studied a group of patients with poorly cohesive gastric carcinomas, focusing on the different cell subpopulations. The most important finding is that we can confirm that the presence of a not signet-ring cell component is an independent predictor of worse outcome. The case enrolment is ongoing, to confirm this finding, as well as to analyse the role of PCGC heterogeneity in the response to systemic therapy.

E-PS-06-064
Molecular and histopathological features of metastatic gastrointestinal stromal tumours (GISTs)
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Background & Objectives: Gastrointestinal stromal tumours (GISTs) are rare mesenchymal neoplasms that can metastasize, typically to the liver, peritoneum, and lungs. Metastatic GISTs present significant diagnostic challenges due to their morphological diversity. This study aims to evaluate the clinical and histopathological characteristics of metastatic GISTs.
Methods: We report five cases of metastatic GISTs diagnosed between 2023 and 2025 at our laboratory. Histopathological diagnosis was based on the examination of biopsy and surgical resection specimens. Immunohistochemistry was performed to detect CD117 (c-kit) and DOG-1 expression. The mitotic index was assessed by counting mitoses in 10 high-power fields (400×). Clinical data were collected from patients' medical records.
Results: All five patients were male, with a mean age of 59.4 years (range: 49–75). Clinical symptoms varied: two presented with abdominal pain and epigastric discomfort, one with a palpable abdominal mass, and two with general health deterioration. Primary tumour sites included the stomach (2 cases), small intestine (2 cases), and colon (1 case). The average tumour size was 12.1 cm (range: 10.5–18 cm). Metastases occurred in the peritoneum (3 cases), liver (1 case), and scapula (1 case). Histologically, all tumours showed fascicular or myxoid architecture with spindle cells. Necrosis was observed in 3 cases, and vascular emboli in 1 case. According tothe Miettinen and Lasota classification, 3 cases were classified as high-risk, while 2 were classified as moderate-risk. All tumours were positive for CD117 and DOG-1.
Conclusion: Metastatic GISTs are rare but significant, with primary sites commonly in the stomach and small intestine. Tumour size and mitotic index are key prognostic factors. This study highlights the importance of these factors for predicting disease progression, emphasizing the need for long-term follow-up due to the high recurrence rate, especially in high-risk cases.

E-PS-06-065
Metastasis sequence of gastric carcinomas – involvement of Claudin-7
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Background & Objectives: Abnormal Claudin-7 expression has been related to carcinogenesis, progression, and metastasis in different cancers, but only few studies have targeted Claudin-7 in gastric cancer (GC). Our work aims to analyse the pattern of Claudin-7 expression in primary GC, tumour emboli and lymph node metastases, and its relationship with clinicopathological features and survival.
Methods: The study group consists of 33 cases of GC with lymph node metastases. Claudin-7 immunoexpression was evaluated in tumour core, invasive front, tumour emboli and lymph node metastases, and statistically correlated with clinicopathological characteristics (age, gender, tumour grading and TNM pathological staging) and survival extracted from medical records.
Results: The univariate analysis showed a statistically significant correlation between Claudin-7 expression in tumour core and gender, as well between Claudin-7 expression in lymph node metastasis and extramural vascular invasion. Kaplan-Meyer curves showed a statistically significant association between Claudin-7 expression in tumour core and overall survival, a lower expression indicating a poor prognosis. Moreover, multivariable Cox proportional hazard model highlighted that Claudin-7 expression in tumour core, along with prognostic stage group and lymphovascular invasion could serve as an independent prognostic factor, signifying that the hazard rate for death is grater in patients with Claudin-7 low expression as opposed to patients with high Claudin-7 expression.
Conclusion: To our knowledge, a complete assessment of Claudin-7 expression in primary GC, tumour emboli and lymph node metastases, correlated with clinicopathological parameters and survival, has not yet been reported. Our study confirmed the correlation between Claudin-7 expression in lymph node metastasis and extramural vascular invasion in primary GC. Moreover, Claudin-7 low expression in tumour core, along with prognostic stage group and lymphovascular invasion, are independent prognostic factors, being correlated with a poor prognosis. Thus, our data contribute to further the knowledge of the involvement of this molecule in metastasis sequence of GC.

E-PS-06-066
Histopathological and molecular correlation of heterogeneous MMR expression in colorectal cancer
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Background & Objectives: Immunohistochemical (IHC) staining for mismatch repair (MMR) proteins is essential for detecting deficient MMR (dMMR), which occurs in approximately 15-20% of colorectal carcinomas (CRC) and is often associated with microsatellite instability (MSI). Although dMMR tumours show a uniform loss of nuclear staining, up to 2.2% of CRCs exhibit heterogeneous expression patterns possibly associated with MSI and/or BRAF mutations. The frequency and clinical significance of these patterns are poorly documented due to limited studies.

Methods: We retrospectively analysed all cases of colorectal adenocarcinoma diagnosed in 2024 at the University Hospital of Navarra. Cases with heterogeneous MMR protein staining (MLH1, PMS2, MSH2, and MSH6) were selected and classified according to their heterogeneity patterns (intraglandular, subclonal, or regional). Correlations were made between MMR status determined by PCR (MSS, MSI-low, or MSI-high) and BRAF V600E mutation status assessed by IHC in cases with heterogeneous staining of MLH1 and/or PMS2.
Results: Among the 398 patients with CRC, 10 (2.5%) showed heterogeneous MMR protein expression. MLH1 and PMS2 were altered in four cases; three had intraglandular MLH1 loss and subclonal PMS2 loss, and one had intraglandular loss of both proteins. Isolated PMS2 and MSH6 heterogeneity was observed in two cases each (intraglandular and subclonal patterns). Two cases showed MSH2, MSH6, and PMS2 abnormalities with an intraglandular pattern, one also with a subclonal PMS2 loss. Four cases analysed by PCR revealed MSI-high status in two cases. BRAF V600E IHC was performed in four of the eight cases with MLH1 and/or PMS2 alteration, detecting the mutation in one case. Analysis of the remaining cases is pending.
Conclusion: The heterogeneous expression of MMR proteins in CRC is recognized in daily practice and may be associated with MSI and BRAF mutations. Its identification and reporting are important and recommended, as they may have diagnostic and therapeutic implications.

E-PS-06-067
PD-L1 and PD-1 expression in Right-Sided versus Left-Sided Colon Cancer
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Background & Objectives: Programmed cell death protein-1 (PD-1) and its ligand (PD-L1) pathway has emerged as a key predictor of prognosis and immunotherapy response in various solid tumours. Right-sided colon cancers (RSCC) and left-sided colon cancers (LSCC) exhibit distinct clinicopathological and molecular profiles, which may influence the expression of these markers and, consequently, immunotherapy implications. This study evaluates PD-L1 and PD-1 expression patterns based on tumour laterality in colon cancer.
Methods: A retrospective study was carried out involving cases of colorectal carcinoma diagnosed between 2014 and 2016. Tumour laterality was defined as right (cecum to proximal transverse) or left (distal transverse to descending colon). Tissue microarrays were used for immunohistochemical study. PD-L1 expression was assessed using combined positive score (CPS) with a cutoff of 1%.PD-1 expression was considered high if stained cells represented 10% or more of the stromal surface. Patients with bifocal tumours including both RSCC and LSCC were excluded. Statistical analysis was performed using SPSS.
Results: The study included 91 cases with a mean age of 61.7 years (range 19-89), and 55 (60.4%) were male. There were 35 RSCC (38.5%) and 56 LSCC (61.5%). PD-L1 positivity was observed in 10 cases (5 RSCC, 5 LSCC), corresponding to 14.3% of RSCC vs. 8.9% of LSCC (p=0.499). High PD-1 expression was detected in 25 cases, representing 20% of RSCC vs. 32.1% of LSCC (p=0.207). No significant association was found between tumour laterality and PD-L1/PD-1 expression.
Conclusion: Although RSCC and LSCC are prognostically and molecularly distinct (e.g., higher BRAF/KRAS mutations in RSCC), ourstudyrevealed no significantdifference in PD-L1/PD-1 expression by laterality. The trend toward higher PD-1 in LSCC mayreflectdifferential immune microenvironments.
While our results do not support laterality as a sole predictor of PD-L1/PD-1 expression, they highlight the need for larger studies itegrating molecular and immune profiling.

E-PS-06-068
Cyclin D1 expression in colorectal cancer and its association with clinicopathological features
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Background & Objectives: Colorectal cancer (CRC) is a major public health problem due to its high morbidity and mortality worldwide. Understanding the mechanisms of CRCs' carcinogenesis and the signalling pathways, including Cyclin D1, is important for the development of new effective therapies the aim of this study was to evaluate Cyclin D1 expression in CRC in a Tunisian case series and identify its association with clinicopathological features.
Methods: A retrospective study including cases of CRC at Salah Azaiez Institute. An immunohistochemical study with anti-Cyclin D1 antibody using the "Tissue Microarray" technique was carried out.
Results: Our case-series included 33 cases. The mean age was 58 years (38-77). CRCs were mainly located in the left colon and rectum. Tumour size was greater than 50mm in nearly 58% of cases. Cyclin D1 expression was retained in 64% of cases. We found a statistically significant association between Cyclin D1 expression and large tumour size ($p = 0.003$), presence of metastases at diagnosis ($p = 0.022$), and the time to onset of metastases of 1 year ($p = 0.03$). No statistically significant association was found between CyclinD1 expression and other clinicopathological features.
Conclusion: Studies on the expression of Cyclin D1 in CRC and its associations with anatomo-clinical aspects are rare. Understanding the carcinogenesis pathways involving Cyclin D1 in CRC could help develop a prognostic, and/or predictive biomarker of response to certain therapies.

E-PS-06-069
Deciphering the tumour-immune landscape in GISTs: immunotherapy-relevant insights from multiplex immunohistochemistry
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Background & Objectives: Gastrointestinal stromal tumours (GISTs) are driven by KIT or PDGFRA mutations and treated with tyrosine kinase inhibitors (TKIs), but responses in the metastatic setting remain suboptimal. Immunotherapy may offer a new frontier, yet its integration requires a precise molecular understanding of the tumour immune microenvironment (TME), still largely unexplored in GISTs. This study

aims to generate immune profiling data to support rational design of future targeted therapy.
Methods: Twenty-eight FFPE GIST surgical samples were selected. Multiplex immunohistochemistry for CD3/CD20/CD163, and PD-L1/CD68 was performed with Ventana Discovery Ultra platform, and digitally quantified using QuPath v0.5.0. Additional markers (Arginase-1, HLA class I) were assessed by manual scoring.
Results: Immune infiltration was detected in all samples, with a dominant presence of CD163+ M2 macrophages (mean 15.5%), and a consistent, albeit lower, CD3+ T cell infiltration (mean 3.6%). Notably, primary tumours harboured a significantly richer immune microenvironment than metastatic lesions, particularly in macrophages ($p<0.05$), but also in T and B cells, suggesting a progressive immune escape during metastasis.
PDGFRA-mutant GISTs showed a trend toward higher CD20+ B cell density and PD-L1 expression compared to KIT-mutant tumours, suggesting potential subtype-specific immunogenicity.
PD-L1 expression was higher in primary tumours than in metastases, reinforcing the idea of dynamic immune modulation during progression.
HLA-I expression was retained in most samples, while Arginase-1 staining was consistently negative, excluding a major role for myeloid-derived suppressor cells and suggesting that immune evasion in GISTs does not rely on classical MHC downregulation or myeloid suppression.
Conclusion: This study unveils a nuanced immune landscape in GISTs, with implications for immunotherapeutic strategies. The presence of immune targets—especially in primary tumours—lays the groundwork for rational combinations of TKIs and immunotherapy in selected patient subsets.

Funding: The research leading to these results has received funding from AIRC under IG 2021 - ID. 26010 project – P.I. Maria Abbondanza Pantaleo

E-PS-06-070
Peritoneal mesothelioma: a report of two cases
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Background & Objectives: Peritoneal mesothelioma (PeM) is a rare malignant neoplasm with poor survival that accounts for approximately 10% of all mesotheliomas. It is generally diffuse and, compared with pleural mesothelioma; it shows weaker association with asbestos exposure, and involves more frequently women and young patients.
Methods: We studied the histopathological findings of two patients diagnosed with PeM. For clinical data, we reviewed the patients' electronic medical records.
Results: We report two cases of PeM, both belonging to males without asbestos exposure, who presented with multiple nodules involving the serosal lining in the peritoneal cavity. The first patient was a 53-year-old diagnosed in 2022 and treated with chemotherapy that recurred in December 2024. In January 2025, he underwent a procedure combining cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. The second patient was a 72-year-old with nodules affecting the peritoneum and multiple abdominal organs that died without a diagnosis and underwent an autopsy. Histologically, the tumours consisted of a predominant solid proliferation of monotonous, round cells; with eosinophilic cytoplasm; and atypical nuclei with mitosis and necrosis. In the first case, there were focal areas of the tumour with atypical cells lying in a myxoid stroma that showed positivity with Alcian Blue-PAS stain. In both cases, the microscopic examination confirmed the mesothelial nature of the tumour (positivity for WT1, calretinin, and podoplanin) and its invasive nature. The first case showed loss of BAP1. The final diagnosis in both cases was high-grade diffuse epithelioid mesothelioma.
Conclusion: PeM is a rare neoplasm that can represent a diagnostic challenge. Ancillary testing, including immunohistochemical stains, in situ hybridization for CDKN2A or NF2, and molecular studies, in selected cases, allows its correct diagnosis. While the standard TNM staging system is used for pleural mesothelioma, there is not a universally accepted TNM staging system for peritoneal mesothelioma due to its rarity and unique characteristics.

E-PS-06-071
A rare case of an amphicrine tumour in the right colon: case report and literature review
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Background & Objectives: Amphicrine tumour exhibits both neuroendocrine and non-neuroendocrine morphological and immunohistochemical (IHC) features in the same neoplastic cells. This rare tumour is by many included in a spectrum of mixed adenoneuroendocrine tumours (MiNEN), a group of neoplasms occurring in the digestive tract.
Methods: We herein report a case of a right colon MiNEN with amphicrine characteristics in a 80-year-old female who presented with diarrhoea and weight loss. She underwent a colonoscopy that revealed an ulcerated lesion in the right colon that was biopsied. The biopsy showed a malignant epithelial neoplasm with high proliferative index and neuroendocrine differentiation.
Results: After appropriate staging with MRI showing multiple images suggestive of hepatic metastasis, she underwent a right colectomy. A gross examination of the surgical specimen showed an ulcerated tumour at the right colon with 3.8cm. The final histopathological examination confirmed a MiNEN diagnosis with a single neoplastic cell population presenting dual differentiation: secretory granules (neuroendocrine) and intra-cellular mucin (adenocarcinoma). On IHC, neoplastic cells showed positivity for CAM5.2, CK7, CDX2, sinaptophysin, chromogranin and INSM1. In addition, PAS-D stain showed intracellular mucin in the same cells. We counted 72 mitotic figures in 2mm2 and the proliferative index (Ki67) was >90%. The final pathological stage was pT4aN1bM1.
Conclusion: This report details a rare subtype of MiNEN originating in the right colon with neoplastic cells presenting simultaneously neuroendocrine and glandular differentiation.
Although, amphicrine tumour is still not acknowledge in the most recent WHO Classification of Endocrine and Neuroendocrine Tumours, it poses a challenge for pathologists and for clinical management of patients. This very rare tumour adds to the scant documented cases and complements the knowledge regarding the clinical presentation, pathology, management and prognosis of MiNEN.

E-PS-06-072
eCura score in early gastric cancer patients – a solid tool for assessing endoscopical curability
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Background & Objectives: Endoscopic submucosal dissection has been widely accepted as a minimally invasive, effective method to

achieve curative treatment for early gastric cancer. The eCura score helps in stratifying patients based on the risk of lymph node metastasis. It represents a good histological tool to quantify endoscopic curability supporting optimal decision regarding further treatment. This study aims to evaluate the reproducibility of the eCura score and system.
Methods: Eleven patients who underwent endoscopic submucosal dissection for early gastric carcinoma were included in the study. Two pathologists with different experience (3, respectively 20 years) used the most representative tumour slides for calculating the eCura score and assessing endoscopic curability.
Results: 11 patients, 7 men and 4 women with ages between 62 and 87 (median age 69 years) represented the analysed cohort. The eCura score varied between 0 and 4, with the majority (63.6%) being 0. The eCura system showed 8 cases classified as eCura A (72.7%), 2 cases as eCura B (18.2%) and 1 as eCura C-2 (9.1%). The majority of the patients showed a low risk of lymph node metastasis risk, while the rest showed an intermediate risk. Comparing between the two pathologists' quantifications showed similar results in cases without lympho-vascular invasion, venous invasion and submucosal invasion depth above 500 microns, while in more advanced cases the results were slightly different. Adding immunohistochemical stains for smooth muscle and lymphatics to better visualize them corrected the score differences, making the scoring system less dependent on the pathologist's experience.
Conclusion: The eCura score and system are reproducible in curative cases, while adding immunohistochemical stains to better assess lympho-vascular invasion and submucosal invasion depth could eliminate interobserver variability.

E-PS-06-073
Histological patterns of anti-PD-1 induced colitis
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Background & Objectives: Programmed cell death protein 1 (PD-1) blocking agents are novel immunotherapeutics used for treatment of advanced-stage malignancies however toxicity is common and may occur many months after the therapy stopped. Immune related adverse events may affect multiple organs including gastrointestinal system and the most widely reported is colitis as an important complication. There is little information on the pathologic features of anti-PD-1 colitis.
Methods: We describe six patients with a history of lung cancer who developed colitis while on anti-PD-1 monotherapy. The patients presented with acute onset of diarrhoea (+/- blood) 3 to 6 months after the anti–PD-1/PD-L1 therapy. Endoscopy showed oedema, erythema, loss of vascular pattern, granularity, ulcerations and even normal mucosa. The patients did not have a previous history of idiopathic inflammatory bowel disease (IBD) or microscopic colitis.
Results: The colon biopsies showed active colitis with neutrophilic infiltration in the lamina propria, cryptitis, crypt microabscesses, basal plasmacytosis and prominent crypt epithelial cell apoptosis reminiscent of graft-versus-host disease and focal crypt atrophy/dropout as in ischemic colitis. Increased intraepithelial lymphocytes (CD3+),a lymphocytic colitis-like pattern was observed in two cases. A mixed colitis pattern combining features of active colitis and ischemic colitis were found in two cases. Two of the patients showed active colitis IBD-like, especially ulcerative colitis but due to CMV positivity were excluded from our study.
The differential diagnosis includes infectionsinjury by other drugs, graft-versus-host disease, and IBD.
Conclusion: As anti-PD-1 agents are increasingly used in oncology, we present these cases to increase awareness of anti-PD-1 colitis among pathologists, to facilitate its timely diagnosis and treatment. The anti-PDL-1 therapy–induced colonic injury can present in a number of histopathologic patterns that can be an overlap. The loss of epithelial barrier integrity may be implicated in the initiation of the pathogenetic process.

E-PS-06-074
Hematoidin crystals in a vessel wall: a rare peculiar histological finding
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Background & Objectives: Hematoidin is a product of heme metabolism that is deposited in tissues under low oxygen tension conditions in association with blood extravasation and appears 10 - 12 days postinjury. In contrast to hemosiderin, hematoidin is lacking iron and therefore is not highlighted with histochemical staining for iron. Following erythrocyte degeneration, porphyrin is released from haemoglobin and is converted to biliverdin, which is reduced to crystalline hematoidin. Because hematoidin can be converted back to biliverdin, it is not always seen. This may explain its rarity.
Methods: A 59-year-old man which admitted to surgical department with abdominal pain of three days duration. The CT showed signs of ischemic colitis and the patient underwent partial colectomy of small intestine.
Results: The pathological examination revealed findings of ischemic type colitis with necrosis of the mucosal and vessel dilation with haemorrhage of submucosal and mesenteric fat. In a vessel wall especially in the inner layer of the mesenteric fat observed a golden-brown/yellow-orange crystalline pigment and that is composed of thread-like filaments arranged in star-shaped clusters. The Perl's staining for hemosiderin was negative.
Conclusion: May persist for years within haemorrhagic lesions and organizing hematomas. Hematoidin has been documented in a variety of conditions typically associated with chronic haemorrhage. Hematoidin crystals is non-specific phenomenon that can be seen in variety of conditions, it is a combination of acute lung injury and thrombotic microangiopathy in Covid-19 pneumonia, pulmonary infarcts and necrotizing lung lesions. Hematoidin was also reported in patients with traumatic and spontaneous cerebral haemorrhages, acute gastrointestinal bleeding and in the skin.

E-PS-06-075
Kaposi sarcoma in perinodal adipose tissue without lymph node parenchymal involvement: an unusual presentation. A case report
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Background & Objectives: Kaposi sarcoma (KS) is an angioproliferative disorder associated with human herpesvirus 8 (HHV-8) infection, primarily affecting immunocompromised patients. The skin is the most affected site, followed by mucosal surfaces, lymph nodes, and visceral organs. Primary lymph node involvement is relatively rare. Here, we present a case of KS involving perinodal adipose tissue without intranodal involvement, which appears to be the first reported case.
Methods: A 70-year-old female with a 12-year history of ulcerative colitis (UC) underwent distal subtotal gastrectomy and D2 lymphadenectomy for gastric adenocarcinoma. Haematoxylin and eosin-stained slides of the tumour, normal gastric mucosa, and regional lymph nodes were evaluated.

Results: The patient was diagnosed with pT1bN2M0 gastric adenocarcinoma. Among the regional lymph nodes, nine exhibited abnormal vascular proliferation in the perinodal adipose tissue. Higher magnification revealed slit-like vascular proliferations, some of which were associated with afferent and efferent vessels of the lymph nodes, with no involvement of the lymph node parenchyma. Immunohistochemical analysis showed positive immunoreactivity for CD34 and HHV-8, confirming the diagnosis of KS. No evidence of KS was detected in the tumour or non-tumour sections of the gastrectomy specimen.
A comprehensive evaluation was conducted to assess potential KS involvement at other sites, revealing no mucocutaneous lesions or colonoscopic abnormalities. The patient had not received any immunosuppressive treatment for UC, and HIV testing was negative. No evidence of immunosuppression was found.
Conclusion: KS can occur in unusual anatomical sites, complicating its recognition and potentially leading to underdiagnosis. To the best of our knowledge this may be the first reported case of KS involving perinodal adipose tissue, associated with lymph node vessels, without affecting the lymph node parenchyma. Pathologists should be aware of this presentation and consider further evaluation for involvement at other sites, as well as an assessment of the patient's immunosuppressive status.

E-PS-06-076
Histopathological characteristics of different types of amyloidosis with gastroduodenal involvement
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Background & Objectives: Diagnosing gastrointestinal amyloidosis can be challenging, as the symptoms are non-specific. The aim of this study is to describe histoanatomical and immunohistochemical features of the most common types of amyloidosis with gastroduodenal involvement in biopsy and autopsy specimens.
Methods: Histological sections were stained with haematoxylin and eosin and Congo red. Immunohistochemistry with a broad panel of antibodies against various amyloid types was used.
Results: The study included 39 cases of duodenal amyloidosis (24 biopsies and 15 autopsies) and 32 cases of amyloid deposits in the stomach (21 biopsies and 11 autopsies). Patient ages ranged from 32 to 91 years.
Immunophenotyping of amyloid in the duodenum revealed AL lambda type in 17 (44%) cases, AL kappa – in 6 (15%), AA – in 11 (28%), and ATTR – in 5 (13%) of cases.
In the gastric specimens, AL lambda amyloidosis was found in 10 (31%) cases, AL kappa – in 11 (34%), AA – in 7 (22%), ATTR – in 4 (13%) cases.
The analysis of histoanatomical distribution of amyloid deposits in the stomach and duodenum demonstrated that AL kappa amyloidosis often affected the duodenal (83%) and gastric (90%) mucosa. However, in patients with ATTR amyloidosis the submucosal layer was involved in 100% of cases and the lamina propria – only in 11%.
Conclusion: As shown in the study, AL lambda was the most common amyloid type detected in the duodenum, while in the stomach lambda and kappa varieties of AL were found in a similar number of cases.
The most extensive amyloid deposits were determined in cases of AL amyloidosis of kappa type suggesting that such patients may have a more rapid progression of the disease.
As ATTR amyloid is deposited mostly within the submucosal and muscular layers, it is recommended to enclose submucosal tissues in the biopsy specimens in order to avoid false negative histological results.

Funding: This work was supported by the Ministry of Education and Science of the Russian Federation within the framework of the state order No 123030700032-9

E-PS-06-077
Relevance of OLGA/OLGIM staging systems revisited: background mucosal changes in a large series of gastric adenomas
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Background & Objectives: Gastric adenomas (GAs) are premalignant lesions with a potential to progress to gastric carcinoma. The OLGA/OLGIM staging systems for gastric atrophy and intestinal metaplasia are used to assess neoplasia risk, particularly for the intestinal subtype. We aimed to evaluate whether this is also true for other, rarer types of adenomas in a large cohort from two centres.
Methods: A total of 1,253 GA collected from two centres were retrospectively analysed for subtypes (intestinal type-INT; foveolar type-FOV; pyloric gland adenoma-PGA, oxyntic gland adenoma-OGA and others) in relation to background mucosal changes including H. Pylori (HP), intestinal metaplasia (IM), and atrophy.
Results: INT (80.7%) was the most common adenoma type, followed by PGA (9.2%), FOV (4.2%), and OGA (0.3%). INT was predominantly antral (58.3%), while PGA (73.3%), FOV (77.4%), and OGA (50%) were located in corpus. INT exhibited the highest prior/active HP exposure (antrum: 82.3%, corpus: 83.2%) together with IM in the entire stomach (94.6% antrum, 85.9% corpus), and atrophy (95.7% antrum, 87.3% corpus). While IM and atrophy were much lower in PGA 12.5% and 10.6, respectively for antrum and 35.8% and 30.6, respectively for corpus, FOV exhibited the lowest frequency of IM (8%, 11.5%) and atrophy rates (4%, 6%) in corpus and antrum, respectively compared to other subtypes ($p<0.001$). HP exposure was higher in Turkey (85.1%) compared to Germany (73%) in contrast to IM which was slightly more common in Germany (56.7% vs. 49.7%), while atrophy was similarly distributed (55.9% vs. 56.1%).
Conclusion: IM and atrophy as indicators of higher risk for neoplastic transformation in intestinal adenomas do not seem to be in play in FOV or OGA. Though at a lower rate, PGAs also arise in a background of atrophic mucosa. Taken together, these findings suggest that OLGA and OLGIM are useful only in intestinal adenomas.

E-PS-06-078
Dome carcinoma arising in a colonic tubular adenoma with high-grade dysplasia: a case report
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Background & Objectives: Dome carcinoma is a rare variant of colorectal carcinoma, characterized by a distinctive morphological pattern with expansive growth, lymphoid-rich stroma, and cystic glands with eosinophilic debris. We present a case of dome carcinoma arising in a colonic tubular adenoma with high-grade dysplasia, emphasizing diagnostic challenges and clinical management.
Methods: A 50-year-old woman was referred for evaluation of a colonic polyp detected during a colonoscopy. The exam revealed a Paris 0-IIa flat, stellate lesion (25 mm) in the cecum, resected via piecemeal diathermic loop.
The patient had no significant personal history or associated symptoms.
Results: Histopathological examination of the fragments showed a tubular adenoma with high-grade dysplasia and, in deeper sections, an

infiltrative neoplasm within the submucosa surrounded by lymphoid tissue. The tumour consisted of cystically dilated glands with eosinophilic necrotic debris, pushing borders, and a dense lymphoid stroma with germinal centres, consistent with dome carcinoma.
Due to incomplete resection margins, the patient underwent right hemicolectomy, which revealed no residual tumour or lymph node metastases.
The patient remains under surveillance and disease free.
Conclusion: This case highlights the unique clinicopathological features of dome carcinoma, including its association with precursor adenomatous lesions and prominent lymphoid stroma. The characteristic histomorphology—expansile growth, cystic glandular dilatation, and lack of desmoplasia— can pose a diagnostic challenge to differentiate from pseudoinvasion of lymphoglandular complexes of the submucosa. While complete endoscopic resection may be curative for early lesions, surgical management remains essential for cases with incomplete excision or deeper invasion. Further studies are needed to better characterize the biological behaviour and long-term outcomes of this uncommon entity.

E-PS-06-079
Colorectal carcinoma with sarcomatoid components and focal mucinous differentiation: a rare case of isolated BRM (SMARCA2) loss
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Background & Objectives: Colorectal Carcinoma with Sarcomatoid Components is a rare, aggressive WHO-recognized subtype. While SWI/SNF alterations are documented, isolated BRM (SMARCA2) loss remains poorly characterized. We report a novel case with focal mucinous differentiation, adenoma origin, and isolated BRM loss to explore its clinicopathological implications.
Methods: An 86-year-old female presented with perforated rectosigmoid carcinoma. Histopathological analysis included morphology, SWI/SNF complex proteins (SMARCB1/INI1, SMARCA4/BRG, SMARCA2/BRM), and mismatch repair (MMR) status. Intraoperative findings revealed liver metastasis and peritoneal implants. R2 resection was performed due to critical status.
Results: A 9 cm perforated tumour arose from a high-grade tubulovillous adenoma. Biphasic morphology included mostly sarcomatoid (80%) (rhabdoid and spindle cells) and focal adenocarcinoma (20%) including (5%) mucinous components. IHC revealed intact MMR proteins (MLH1, MSH2, MSH6, PMS2) and retained INI1, BRG, while BRM was lost. OSCAR keratin was negative in sarcomatoid regions. The patient succumbed to rapid disease progression two months postoperatively.
Conclusion: This case highlights isolated BRM loss as a rare, underreported molecular event in sarcomatoid CRC—distinct from the more commonly observed co-alterations involving SMARCA4/INI1. Our findings advocate for systematic evaluation of SWI/SNF proteins in CRC to refine prognostic stratification and to expand the molecular spectrum of sarcomatoid CRC as reported in recent literature.

E-PS-06-080
Interaction of Desmin and mast cells in colorectal cancer
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Background & Objectives: Mast Cells (MC) are one of the most common types of cells in tumour microenvironment. They have many different well-studied functions, but their exact role in tumour oncogenesis is still understudied. Desmin is a protein of intermediate filaments that is usually expressed in muscle cells. Sometimes, Desmin expression is detected in tumour cells that were not originally muscular, including colorectal cancer cells. The role of Desmin in tumour morphogenesis is unclear.
Methods: Histological examination of surgical material obtained from 45 patients was performed. MC and Desmin were detected by immunohistochemical method using monoclonal mouse antibodies to Tryptase and Chymase (for MC) and monoclonal mouse antibodies to Desmin. Also, double immunolabeling was used to visualize the colocalization of MC and Desmin. To evaluate the level of functional activity of MC, the degranulation index was calculated using special formula.
Results: Expression of Tryptase-positive and Chymase-positive MC and Desmin was observed almost in all studied samples. The amounts of MC and Desmin in tumour were counted. MC degranulation index was calculated and compared to the amount of Desmin. Cases were divided into two groups: the first one – patients with a high degranulation index of MC, and the second – patients with a low degranulation index of MC. The amount of Desmin in tumour was higher in the group of cases with low degranulation index of MC ($p<0.01$, Mann-Whitney test). Using double immunolabeling, the result obtained was visualized. MC were more active in cases where the expression of Desmin was low.
Conclusion: Expression of MC and Desmin was detected almost in all studied samples. MC degranulated more in the group with low Desmin expression. It is necessary to continue studying their role in the morphogenesis of colorectal cancer.

E-PS-06-082
YAP expression in sporadic and inflammatory bowel disease-associated colorectal cancer
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Background & Objectives: Yes-associated protein (YAP) plays a critical role in the development and progression of various tumours, demonstrating its potential as a prognostic and therapeutic target. However, there is considerable debate regarding whether YAP acts as an oncogene or tumour suppressor during the tumorigenesis of colorectal cancer (CRC).
Methods: This study collected tumour tissue microarrays from two distinct types of CRC: sporadic CRC and inflammatory bowel disease (IBD)-associated CRC. We assessed YAP expression using immunohistochemical analysis, and its correlation with the clinicopathologic features and the expression pattern of other biomarkers.
Results: In sporadic CRC, YAP expression in tumour was not significantly associated with age, gender, tumour site, and tumour differentiation ($P > 0.05$). CRCs with positive YAP expression frequently demonstrated deep invasion with serosal involvement (20.7%), as compared with the YAP negative cases (3.4%) ($P = 0.041$). CRCs with positive YAP expression were less likely to have nodal metastasis (pN1-2: 44.8%), as compared with the YAP negative cases (65.5%) ($P = 0.105$). YAP expression was not associated with immunoreactivity of other biomarkers including Claudin 18.2, p53, AMACR, and nuclear beta-catenin. In IBD-associated CRC,

the YAP positive expression rate was significantly higher (50.0%, 32/64) compared to the sporadic CRC cohort (33.3%, 29/87) (P = 0.045). However, in IBD-associated CRC, YAP expression was not correlated with the clinicopathological parameters, including depth of invasion and lymph node metastasis, and histological features of IBD-associated CRC, including signet-ring cell features, medullary features, Crohn-like reactions, or dirty necrosis.
Conclusion: YAP expression is associated with deep invasion and serosal involvement in sporadic CRC, supporting its role as an oncogenic factor in the tumorigenesis of sporadic CRC. Its positive expression rate is higher in IBD-associated CRC. However, our study suggest that YAP may involve different pathways between sporadic and IBD-associated CRC.

E-PS-06-083
Colitis cystica profunda mistaken for mucinous adenocarcinoma in a patient with ulcerative colitis - a case report
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Background & Objectives: Colitis cystica profunda (CCP) is a rare benign lesion of the gastrointestinal tract characterized by submucosal mucin-filled cysts. Depending on the localization, it is called colitis, gastritis, or enteritis cystica profunda. Predominantly polypoid lesions involve the entire colon, mainly in the anterior wall of the rectosigmoid tract . They vary in size, depth, and localization, while the surrounding tissue may show changes consistent with chronic inflammation and fibrosis.
Methods: We present a case of a 56-year-old woman with CCP as a complication of chronic ulcerative colitis.
Results: A 56-year-old female patient with UC was admitted to the hospital with signs and symptoms of pancolitis. An abdominal CT showed a large cecal infiltrative mass, narrowing the colon's lumen. A colonoscopy was performed and a diagnosis of colonic adenocarcinoma was suspected. Total colectomy was performed, and the samples were sent to the pathohistological analysis. Submucosal cystically dilated mucin-filled glands, lined with a single-layered cylindrical epithelium with the nuclei in the basal layer were seen histopathologically. Surrounding these glands there was no connective tissue, apart from small focuses where the gland wall ruptured and a reaction to the spilled mucus was present. The lack of cellular atypia and desmoplastic stroma surrounding the glands dismissed the diagnosis of a neoplastic process. Immunohistochemistry was negative for proliferation (Ki67, p53) and microsatellite instability (MLH-1, MSH-2, MSH-6, and PMS-2). The diagnosis of colitis cystica profunda in background of ulcerative colitis was made.
Conclusion: Clinicians and pathologists must maintain a high index of suspicion and consider a broad differential diagnosis when interpreting biopsies from patients with UC, particularly those with unusual or complex clinical features.

Funding: This research was supported by the Science Fund of the Republic of Serbia, Grant No 9802, Activated Charcoal as a Carrier of Probiotics: A New Approach for Pathogen Elimination in Wounds-ProHealingAC

E-PS-06-086
Role of E-cadherin as a surrogate prognostic marker in Colorectal carcinoma and its correlation with stage, grade and other important parameters determining aggressiveness
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Background & Objectives: Colorectal carcinoma (CRC) is the second commonest cause of cancer-related deaths worldwide, and its 5-year survival rate ranges from 90% for early stage cancers to 10% for metastatic cancers. Epithelial (E)-cadherin (CDH1 gene) represents the prime mediator of intercellular adhesion. Its downregulation promotes cell dyscohesiveness, migration and invasion which facilitates invasive growth and metastasis. While some researches have shown that CRC cases with loss of E-cadherin expression had lower survival time and suggested ecadherin as a significant independent predictor for poor prognosis, other researches found no significant association. In this study we analysed the expression of E-cadherin in tumour tissue (surface and deeper) of CRC in relation to other clinicopathological features such as cancer stage, grade, permeation into the lymphatics and venous channels and tumour location.
Methods: A total of 124 CRC cases were evaluated with haematoxylin & eosin stain and immunohistochemistry using Student's unpaired t test, Mann Whitney U test, Fisher Exact Probability test and Chi square test, post ethical committee approval.
Results: The cases were ranging from 28 years to 91 years with mean age 61 years. 81 were males and 43 females. 33% were located in rectosigmoid colon, while, 27% in the right-sided colon. Loss of ecadherin expression was seen nearly twice in the deeper portions of the tumour as compared to superficial. Majority of the early stage and low grade tumours (70%-100%) showed moderate to strong ecadherin expression but did not show a significant pattern in higher stage/ grade tumours or with permeation into the lymphovascular channels.
Conclusion: Our study was unable to demonstrate a significant positive correlation between loss of ecadherin and tumour aggressiveness, but found some interesting results in various related domains. However, this association remains largely unexplored and necessitates greater attention with a larger sample size to identify a significant surrogate prognostic marker in CRC.

E-PS-06-087
Endoscopic submucosal dissection for upper gastrointestinal tract lesions: a single centre experience
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Background & Objectives: Endoscopic submucosal dissections (ESD) are increasingly performed for the removal of superficial lesions of the gastrointestinal (GI) tract as an alternative to surgical resection. This poster summarizes a single centre's experience in the diagnostic workup of 15 cases of ESD for GI tract lesions received from October 2024 to March 2025.
Methods: ESD specimens (n=15, 4 colonic, 6 rectal, 5 gastric) were received in our Department pinned on styrofoam sheets in a 4% neutral buffered formalin solution, fixed for a minimum of 12 hours, inked in the lateral (mucosal) and deep (submucosal/muscularis propria) margins and submitted for histological examination. Histopathological characteristics of the tumours and margin status were analysed.
Results: Specimens from 15 patients (7 female, 8 male) with median age 67.5 years (range: 41-78 years) were processed. Mean maximum diameter of ESD specimens was 57.6 mm (range: 30-110 mm), while the lesion size averaged 38.6 mm (range: 12-80 mm). Specimens included ESD of 8 invasive (4 gastric adenocarcinomas, tubular subtype, 4 colorectal adenocarcinomas NOS) and 7 of non-invasive tumours (3 colonic adenomas with high-grade dysplasia without

lamina propria invasion and 1 with low-grade dysplasia, 2 traditional serrated adenoma of colon (TSA) and 1 gastric inflammatory fibroid polyp). The lateral margin was involved in 1 case of colonic adenoma with low-grade dysplasia and the deep margin in 2 cases (1 rectal adenocarcinoma and 1 gastric inflammatory fibroid polyp).
Conclusion: ESD is a satisfactory method of invasive treatment for superficial GI tract lesions. Histopathological specimen handling and microscopic examination are of paramount importance in the accurate diagnosis of the resected lesions and margin status assessment, as well as identifying characteristics of prognostic and predictive value, guiding subsequent treatment decisions.

E-PS-06-088

Clear cell features in Colorectal adenocarcinoma: a case series with histopathological and molecular characterization

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Background & Objectives: Colorectal cancer (CRC) is the most common gastrointestinal malignancy, with an annual incidence of 1.9 million cases and over 930,000 deaths. Prognostic factors include histological subtype, differentiation grade, invasion depth, lymphovascular invasion, perineural growth, tumour budding, and metastatic spread. Among adenocarcinomas, clear cell modifications are rare and associated with enteroblastic differentiation, resembling foetal gut epithelium and expressing markers such as Alpfa-fetoprotein (AFP), Sal-like protein 4 (SALL4), and Glypican-3. This study aims to compare a case series of CRCs with clear cell features to existing literature and evaluate whether a percentage cutoff can define a distinct histotype, similar to gastric adenocarcinoma with enteroblastic differentiation.
Methods: Eleven cases of CRC with clear cell features were analysed. Histological examination was conducted on formalin-fixed, paraffin-embedded samples using PAS and Alcian Blue staining. Immunohistochemical analysis was performed for AFP, SALL4 and Glypican-3. Molecular testing assessed microsatellite status and mutations in KRAS, BRAF, PIK3CA, HER2, and NTRK.
Results: The cohort included six males and five females (M:F ratio = 1.2:1), with a mean age of 69.8 years. Tumours were located in the cecum (1), ascending colon (3), sigmoid colon (3), and rectum (4). Ten cases were low-grade, while one was high-grade. Most tumours extended beyond the muscularis propria (pT2: 2 cases, pT3: 7 cases, pT4: 2 cases). Lymph node involvement was observed in 9 cases (pN1: 5, pN2: 4), and distant metastases were present in 2 cases. All tumours were microsatellite stable. AFP was positive in 5 cases, Glypican-3 in 2, and SALL4 in 1. KRAS mutations were identified in 3 cases and PIK3CA mutations in 2.
Conclusion: Clear cell modifications in CRCs are rare but potentially aggressive. Their identification and classification are crucial for accurate prognosis and management. Standardized criteria should be developed to enhance recognition, stratification, and treatment approaches tailored to these tumours.

E-PS-06-089

Clinicopathological analysis of appendiceal neoplasms: a single institution study

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Background & Objectives: Appendiceal neoplasms are rare with an incidence of 0.9-1.4%. They present unique diagnostic and therapeutic challenges due to the varied histological subtypes and common clinical presentation as acute appendicitis. The objective of this study was to analyse the clinicopathological characteristics of the spectrum of appendiceal neoplasms.
Methods: A retrospective and prospective study of appendiceal neoplasms, both primary and secondary, was conducted. Cases diagnosed between January 2017 and December 2023 at the Department of Pathology, Kasturba Medical College, Mangalore were included. Cases were analysed for demographics, presenting symptoms, radiological features, type of surgical interventions, and histopathology.
Results: Out of 3529 appendectomy specimens, 58 (1.07%) were identified as neoplastic. Of these, 26 were appendiceal mucinous neoplasms (AMNs), 10 neuroendocrine tumours (NETs), 2 goblet cell adenocarcinomas, and 20 secondary tumours. Age ranged from 13 to 86 years, with a mean of 51.4 years. Women (63.79%) were more often affected than men. The majority (63.79%) presented with right iliac fossa pain, mimicking acute appendicitis.
Conclusion: Appendiceal neoplasms are rare and often present diagnostic challenges, as most present as acute appendicitis. They are incidentally identified on radiology, intra-operatively or histopathologically. Currently, mucinous neoplasms, especially low-grade AMNs, are the commonest primary tumours, followed by NETs. In adult patients undergoing appendicectomy for acute appendicitis, a high index of suspicion for neoplasms is required. Meticulous grossing of the appendix clinches the diagnosis.

E-PS-06-090

Medullary carcinoma of the colon: an uncommon subtype of colorectal cancer. Clinical, histopathological and molecular profile of 19 cases

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Background & Objectives: Medullary carcinoma of the colon is a rare subtype of colorectal adenocarcinoma, accounting for approximately 0.03% of cases. It is frequently associated with microsatellite instability (MSI) and BRAF mutations. Despite its high-grade morphology, most series report a favourable prognosis. We aimed to describe the clinical, histopathological and molecular features of a series of cases diagnosed in our institution.
Methods: A retrospective review was performed on cases diagnosed between 2000 and 2024. Inclusion criteria were the availability of a surgical specimen and a medullary pattern representing >50% of the tumour, according to the 5th WHO criteria (solid/trabecular growth, expansive borders, and dense intraepithelial lymphocytic infiltrate). Clinical data and histological parameters were collected. MSI was analysed by immunohistochemistry, while BRAF and KRAS mutations by PCR.
Results: We identified 19 cases: 11 females (57.9%) and 8 males (42.1%), mean age of 70 years (range, 45–91). Symptoms were present in 17/19 patients (89.5%), including abdominal pain (47.4%), altered bowel habits (21.1%), rectal bleeding (21.1%), and constitutional syndrome (31.6%). Most tumours were located in the right colon (89.5%) with a mean size of 6.62 cm. Fourteen cases (73.7%) were pure medullary carcinomas. The majority were locally advanced (pT3: 57.9%; pT4: 26.3%) with low budding (68.4%) and frequent extramural venous invasion (52.6%). Lymph node metastases were encountered in 31.6%, and distant metastases in 11.5%. MSI was confirmed in all cases, with loss of MLH1 and PMS2. BRAF mutations were detected in 42.1%, and no KRAS mutations were identified. The mean follow-up was 45.8 months, with 31.6% mortality, half of which occurred within the first 7 months.
Conclusion: Medullary carcinoma is an infrequent subtype of colorectal carcinoma, predominantly affecting women and located in the right colon. Despite high-grade morphology, its prognosis is relatively

favourable. Recognition of this entity is essential, and MSI evaluation is helpful for its diagnosis.

E-PS-06-091

Mesenchymal tumours of the stomach after endoscopic resection

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Background & Objectives: Mesenchymal tumours (MT) are not typical for the GIT and range from reactive tumour lesions and benign neoplasms to aggressive sarcomas. The most typical mesenchymal tumour of the stomach is GIST, followed in descending order by smooth muscle and neurogenic tumours. The main problem is the differential diagnosis of these neoplasms both at the preoperative stage and during further morphological examination. On the other hand, the problem of benign tumours is the correct terminology, which will help to avoid diagnostic ambiguity and prognostic uncertainty, and therefore the need for subsequent treatment.
Aim: correct differential diagnostic criteria for gastric MT after endoscopic resection (EFTR, STER,ESD).
Methods: The study based on material obtained after endoscopic resection in MONIKI, and the group was 20 patients (age range 45-80) during 2021-2024yy.
Results: MT were presented: 4/20 – leiomyoma, 10/20 – GIST, 3/20 – inflammatory fibrous polyp (IFP); 1/20 – schwannoma (ScW); 2/20 – calcifying fibromatous pseudotumor (CFP). It should be noted that only GISTs had a clear picture during EUS, in other cases the final diagnosis was made only after morphological examination with IHC. Gross, the tumour size varied from 0.5 to 7.0 cm. With the exception of ScW and CFP, the tumours were whitish in colour, fibrous, homogeneous in appearance, and dense-elastic consistency. ScW had a yellowish tint, soft-elastic consistency; CFP - with areas of microcalcifications. Microscopically, MT are localized in the submucosal layer and represented by multidirectional spindle-shaped, stellate cells with ovoid hyperchromatic nuclei and noticeable nucleoli. The stromal component varies depending on the MT. The minimal IHC panel - CD34, CD117, S-100, DOG-1, Vim, PanCK, SMA.
Conclusion: GISTs remain the most common mesenchymal tumours of the stomach, but other rare mesenchymal neoplasms should be remembered. Currently, endoscopic methods of tumour resection are increasingly used as a minimally invasive intervention and replace open surgery.

E-PS-06-092

Clinical and morphological features of patients with autoimmune gastritis for diagnosis approach in advance

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Background & Objectives: Autoimmune gastritis (AIG) associates with a high risk of gastric atrophy, stomach cancer and neuroendocrine tumours. To improve the diagnosis of AIG in individuals with different H. pylori infection status, an open, cross-sectional cohort study was conducted to identify the most informative clinical, endoscopic, and morphologic features of the disease.
Methods: 124 patients with chronic gastritis were examined. The main group included 35 patients with AIG, comparison group 1 - 38 patients with H. pylori-associated and AIG, comparison group 2 - 51 patients with H. pylori-associated gastritis. The examination included clinical and laboratory tests, endoscopy with histopathological examination.
Results: In 40% patients with AIG without H. pylori infection, endoscopic signs of atrophy in the antral region were observed, but only in 11.4% patients there was evidence of weak atrophy and focal complete intestinal metaplasia according to pathomorphological investigation. In the group of AIG patients associated with H. pylori, the prevalence of endoscopic signs of multifocal atrophic gastritis was statistically significantly higher (p=0.007) when compared to the main group, and without statistical significance when compared to the group of patients with H. pylori associated gastritis (p=0.064). Pseudopyloric metaplasia (p=0.001) and complete intestinal intestinal metaplasia (p=0.001) were statistically significantly more frequent in the gastric corpus. Additionally, with the involvement of the stomach body in the pathologic process, changes in the antral region were also found in patients with AIG in combination with H. pylori infection.
Conclusion: Diagnosis of AIG in patients with different H. pylori infection status requires a comprehensive approach, assessing the presence and severity of inflammation and atrophy, mainly in the body. In patients with AIG and absence of H. pylori infection in anamnesis, it is possible to detect signs of inflammation and atrophy of the antral region, probably due to the modulation of gastric microbiota on the background of hypochlorhydria.

E-PS-06-093

Cronkhite-Canada syndrome: a rare cause of diffuse gastrointestinal polyposis

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Background & Objectives: Cronkhite-Canada Syndrome (CCS) is a rare, non-hereditary, gastrointestinal disorder first described in 1955. It is characterised by diffuse gastrointestinal polyposis, protein-losing enteropathy, and ectodermal abnormalities, including alopecia, onychodystrophy, skin hyperpigmentation, and a fissured tongue. CCS primarily affects adults in their sixties and has no clear aetiology. Fewer than 500 cases have been reported, predominantly in Japan. The disease is relentlessly progressive, leading to severe malnutrition, gastrointestinal bleeding, and infections. Historically, mortality reached 50%, but advancements in treatment—including corticosteroids, immunosuppressants, and nutritional support—have significantly improved outcomes, with 5-year survival now exceeding 90%.
We report a case of CCS in which diagnosis was delayed due to non-specific early endoscopic and histological findings, highlighting the importance of multidisciplinary discussion in rare disease diagnosis.
Methods:.
Results: A 61-year-old man with no prior medical history developed severe digestive symptoms following a Covid-19 infection. He experienced fatigue, ageusia, nausea, and persistent diarrhoea, resulting in a 35 kg weight loss. Endoscopy revealed giant gastric folds, numerous gastric polyps, and few inflammatory polyps in the duodenum and colon. Gastric biopsies showed foveolar hyperplasia and lamina propria oedema, initially suggesting Ménétrier's disease.
The patient deteriorated with severe protein-losing enteropathy, recurrent gastrointestinal bleeding requiring transfusions, and skin and nail abnormalities. Subtotal colectomy was performed for uncontrolled colonic bleeding, revealing hundreds of polyps.
Microscopically, the polyps resembled inflammatory juvenile-type polyps. The glands were hyperplastic, sometimes dilated and cystic,

overlying a prominent oedematous stroma with a dense inflammatory infiltrate of plasmocytes and eosinophils. The inter-polypoid mucosa exhibited glandular dilation and inflammation.
Conclusion: Diagnosing Cronkhite-Canada syndrome requires a multidisciplinary approach and cannot rely on biopsies alone, given the non-specific nature of the lesions. Clinical suspicion should be high when abnormal inter-polypoid mucosa is present, particularly in the colon. Ectodermal manifestations may have a delayed onset and should not be misattributed solely to malnutrition.

E-PS-06-094
Comprehensive evaluation of PD-L1, MMR and HER2 Status in gastroesophageal cancer biopsies: a 15-month consecutive cohort study
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Background & Objectives: PD-L1 expression is a key biomarker in gastroesophageal cancers, guiding decisions around immunotherapy. This study aimed to evaluate the frequency of PD-L1 positivity in biopsy samples and investigate its association with mismatch repair (MMR) status, HER2 expression, and various clinicopathological features.
Methods: A retrospective analysis was conducted on 33 consecutive gastric and oesophageal biopsy specimens over a 15-month period. PD-L1 expression was assessed using the Combined Positive Score (CPS), with a CPS >1 considered positive. MMR status and HER2 expression were evaluated via immunohistochemistry. Associations were analysed using Fisher's exact test or chi-square test, and the PD-L1 positivity rate was compared with published data using a z-test for proportions.
Results: PD-L1 positivity (CPS >1) was observed in 48.5% of cases. Although not statistically significant, PD-L1 positivity was more frequent in dMMR cases (37.5% vs. 12.5% in MSS, $p = 0.217$), in patients over 70 years old ($p = 0.139$), and in HER2-positive tumours (18.8% vs. 12.5%, $p = 0.793$). No significant associations were found with sex, histological subtype, nodal status, or metastatic status. A statistically significant association was identified between MMR status and age ($p = 0.012$), with dMMR more common in older patients. A non-significant trend was also observed between HER2 expression and age ($p = 0.084$). Compared to the KEYNOTE-059 trial (PD-L1 positivity: 57.1%), the difference was not statistically significant ($p = 0.388$), indicating good concordance with published international data.
Conclusion: Nearly half of the gastroesophageal biopsy specimens demonstrated PD-L1 expression above the therapeutic threshold. While most associations were not statistically significant, trends suggested higher PD-L1 expression in dMMR cases and older patients. The significant association between MMR status and age, along with alignment with international studies, underscores the importance of PD-L1 testing in gastric and oesophageal cancer biopsies.

E-PS-06-095
Sevelamer-induced gastrointestinal injury: a hidden threat in chronic kidney disease patients
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Background & Objectives: Sevelamer is a widely used phosphate binder in patients with chronic kidney disease (CKD), but it may be associated with gastrointestinal (GI) mucosal injury, often presenting as crystal deposition and ulceration. Diagnosing sevelamer-induced injury can be challenging due to similarities with other medication-induced injuries.
Methods: A 71-year-old male with chronic kidney disease (CKD) on long-term hemodialysis underwent a routine colonoscopy. Incidentally, a sessile polyp was detected in the distal rectum and removed for histopathological examination. Routine haematoxylin and eosin (H&E) staining, along with special stains, were performed to assess mucosal changes and characterize the crystal deposits.
Results: Histological analysis revealed ulceration and granulation tissue proliferation, accompanied by amorphous, basophilic crystal deposits with "fish scales" like stripes. The differential diagnosis included injuries associated with sevelamer, kayexalate, bile acid sequestrants, and iron supplementation. Special stains such as PAS diastase resistant (PAS-D), Ziel-Nissen, and Perl's were used to characterize the deposits, revealing PAS-D positivity. These histological findings were most consistent with sevelamer-associated mucosal injury. The diagnosis was further supported by the confirmation of the patient´s use of sevelamer for hyperphosphatemia management.
Conclusion: Sevelamer-induced GI injury should be considered in CKD patients who present with gastrointestinal symptoms. In this case, the findings were incidental, but this is not always the case, as sevelamer-associated lesions can include ulceration, erosions, inflammation (such as colitis, gastritis, and duodenitis), and in more severe cases, intestinal necrosis. Recognizing the characteristic histopathological features is essential for accurate diagnosis, preventing unnecessary interventions, and ensuring appropriate treatment. Importantly, sevelamer crystal deposition can extend throughout the entire gastrointestinal tract, highlighting the need for increased clinical and histopathological awareness to prevent misdiagnosis and optimize patient care.

E-PS-06-096
Resection margins in colorectal cancer carry clinical significance with regard to disease
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Background & Objectives: Resection margins in colorectal cancer carry clinical significance with regard to disease recurrence risk and selection for multimodal adjuvant therapy. Specimen shrinkage during tissue fixation and its retractile properties is well known. However, few studies support this for colorectal specimen. However, the effects of shrinkage have not traditionally been taken into account when analysing tumour-free margins. In this study, the evaluation of the amount of shrinkage in excised colorectal cancer specimens and determination of the relation between surgical margins and tumour diameters were aimed.
Methods: In this prospective study, 35 colorectal cancer specimens were measured in the fresh state and subsequently after 24 hours of formalin fixation for total specimen length, tumour size, proximal and distal resection margin for colorectal cancer. Additional information such as age, gender, stage of the disease, type of surgery, and type and grade of tumour were recorded.
Tumour specimens were measured immediate post-resection and at 15 minutes and 24 hours after formalin fixation. Tumour was measured in two dimensions and proximal and distal margins was measured.
Results: Eleven of the patients are women. 24 were male. Their ages ranged between 42 and 80 years. After formalin fixation, we found 23.5% reduction in proximal surgical margins, 29.5% reduction in distal surgical margins and 17% reduction in tumour size. In 14 cases, there was no change in tumour size before and after fixation. No variation in shrinkage was noted owing to patient or tumour related factors.
Conclusion: Considerable shrinkage of tumour-free surgical margins of colorectal cancer specimen was noted after formalin fixation, whilst the tumour itself does not shrink substantially. It demonstrates that

shrinkage from formalin fixation should be a consideration in decision making where the magnitude of tumour-free margins is small. This inference can have implications on the postoperative management plan.

E-PS-06-097

Prevalence and distribution of KRAS, NRAS and BRAF mutations in metastatic colorectal cancer: a single-centre study

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Background & Objectives: KRAS, NRAS, and BRAF are well-established biomarkers for metastatic colorectal cancer (mCRC). Various techniques are used to identify mutations in these oncogenes. This study aims to analyse the mutational profile of a cohort of mCRC patients over a one-year period at a single centre.
Methods: The oncogenes KRAS, NRAS, and BRAF were investigated in 255 mCRC patients. Molecular testing was performed using the Idylla automated system (Biocartis) with the KRAS and NRAS-BRAF cartridges (IVD).
Results: Among the 255 metastatic CRC patients (107 female, 148 male; median age: 58 years, range: 20–84), 127 (49.8%) samples were biopsy specimens, and 128 (50.2%) were surgical specimens, with an average tumour cell percentage of 46%. The Idylla system provided results in an average time of 5.2 days. KRAS mutations were identified in 127 patients (50%), NRAS mutations in 6 patients (2.3%), and BRAF mutations in 11 patients (4.3%). The distribution of KRAS mutations was as follows: codon 12 (74.0%), codon 13 (14.2%), codon 61 (6.3%), codon 146 (4.7%), and codon 59 (0.8%). NRAS mutations were distributed as follows : codon 12 (33.3%), codon 61 (50.0%), and codon 146 (16.7%).
Patients with mutations had a mean age of 57 years (range: 27–84). Mutations were more frequent in men (53.5%) than in women (46.5%), but this difference was not statistically significant ($p \geq 0.05$).
Conclusion: Our results highlight the high prevalence of KRAS mutations in mCRC patients, consistent with findings in the literature.

E-PS-06-098

Crawling to a diagnosis: a case of gastric adenocarcinoma

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Background & Objectives: We present the case of a 34-year-old woman with a recent history of nonsteroidal anti-inflammatory drug (NSAID) use, who presented to the emergency department with melena and asthenia.
Methods: The patient's clinical history was thoroughly reviewed, encompassing personal and familial background, gastroendoscopic examinations, and anatomopathological findings.
Results: An urgent gastroscopy was performed, which revealed a 6 mm bleeding ulcer on the posterior aspect of the lower gastric body. The ulcer was treated endoscopically and proton pump inhibitors (PPIs) were prescribed. A follow-up gastroscopy performed several weeks later to re-evaluate the ulcer revealed progressive healing without any signs of bleeding, and biopsies were obtained. Microscopy showed very focal, irregularly anastomosed glands and isolated cells with PAS-positive eosinophilic cytoplasm, embedded in an inflammatory stroma. CKAE1/AE3 immunohistochemistry yielded inconclusive results, whereas CDX2 staining was positive. These findings were highly suggestive of malignancy, but were insufficient for a definitive diagnosis, so new biopsies were recommended. Subsequent gastroscopy identified two benign looking 2-3 mm raised mucosal areas. Histological analysis confirmed a diagnosis of diffuse/poorly cohesive adenocarcinoma with a crawling-type pattern.
Conclusion: Crawling-type gastric adenocarcinoma is characterized by irregularly fused glands that recreate the shapes of the letters W, H, Y and X, often with a poorly cohesive component that leads to more aggressive behaviour. It commonly occurs in the middle third of the stomach and typically presents as a superficial depressed or flat type lesion on endoscopy. Some studies suggest it is a distinct adenocarcinoma subtype characterized by RHOA mutations and CLDN18-ARHGAP fusions, which may underlie its unique morphology and frequent progression to poorly differentiated adenocarcinoma. However, it remains unrecognized in the WHO classification. Identifying this pattern in small biopsies is crucial to avoid misdiagnosis with a benign lesion such as intestinal metaplasia. In cases of doubt, repeat biopsy is recommended to confirm or exclude adenocarcinoma infiltration.

E-PS-06-099

Inflammatory fibroid polyp: a series of 99 cases and a systematic review of the literature

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Background & Objectives: Inflammatory fibroid polyp is a rare benign mesenchymal lesion of the gastrointestinal tract, primarily located in the stomach, and originates from the submucosa. The onion-skin-shaped arrangement of spindle-shaped cells around the vessels and inflammatory infiltrate dominated by eosinophil leukocytes is typical. In this study, the clinicopathologic features of the inflammatory fibroid polyps are evaluated in light of the literature.
Methods: The patients with inflammatory fibroid polyps included in the study were examined in addition to age, gender, and location, histopathologically, for growth pattern, fascicular and onion-skin pattern, cellularity, collagenization, eosinophil leukocyte infiltration, lymphoid aggregates, and giant cells.
Results: Of the 99 patients included in the study, 40 were male and 59 were female. The mean age was 58.2 years (28-84 years). Eghty-three of the cases were located in the stomach, 8 in the small intestine, 7 in the colon, and 1 in the gallbladder. Sixty-five of the cases were below 1 cm (0.1-5.5 cm). Most cases were of submucosal origin, and 65 showed infiltrative growth. Fascicular pattern was observed in 65 and onion-skin pattern in 60 cases. Collagenization was observed in 75, and lymphoid aggregates in 61 cases. Eosinophil leukocytes were ≥30 in one high-power field in 70 cases. Floret-like giant cells were detected in 15 cases, mostly with gastric localization.
Conclusion: Infiltrative growth pattern, fascicular pattern, collagenization, and lymphoid aggregates were among the common findings, in addition to onion-skin appearance and eosinophil leukocyte infiltration. Floret-like giant cells were especially remarkable in cases with the onion-skin pattern. One of the cases was detected in the gallbladder, a rather rare location. As a conclusion, besides immunohistochemical studies, infiltrative growth pattern, fascicular pattern, collagenization, and presence of lymphoid aggregates can be used as supportive findings in the differential diagnosis of inflammatory fibroid polyp.

E-PS-06-101

Clinicopathological features of Russell Body-associated gastrointestinal lesions

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Background & Objectives: Russell body (RB)-associated gastrointestinal lesions are rare plasma cell-rich inflammatory conditions characterized by the accumulation of eosinophilic immunoglobulin inclusions within Mott cells. While often associated with *Helicobacter pylori* (HP) infection, their biological behaviour and potential association with neoplastic processes remain poorly understood. This study aims to describe the clinicopathological features of ten RB-containing lesions and to compare findings with existing literature.
Methods: We retrospectively analysed ten patients with histologically confirmed RB-associated lesions in the gastrointestinal tract. Clinical parameters, localization, immune status, HP presence, clonality status, and accompanying neoplasms were recorded. Follow-up endoscopic and histological evaluations following HP eradication were documented when available. Observations were interpreted in light of current literature.
Results: The patients (mean age: 55.4 years) presented with lesions predominantly located in the stomach (n=9) and rectum (n=1). All patients were initially HP-positive. Immunohistochemistry revealed polyclonal light chain expression in nine cases and monoclonal kappa restriction in one. Three patients had synchronous adenocarcinoma (two gastric, one rectal). In six patients who underwent post-treatment endoscopy, complete histological resolution of RBs was observed following HP eradication. No hematologic malignancy developed during follow-up, including the monoclonal case.
Conclusion: RB-associated gastrointestinal lesions are typically benign and strongly linked to HP infection, with significant regression following eradication therapy. However, their potential coexistence with malignancies and occasional monoclonal light chain expression necessitate careful histopathological assessment. Awareness of this entity is crucial to avoid misdiagnosis, particularly in cases mimicking signet ring carcinoma or plasma cell neoplasia.

E-PS-06-102
The prognostic role of systemic inflammatory markers in gastric cancer
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Background & Objectives: Despite the new therapeutic approaches, gastric cancer (GC) remains in the first places of cancer-related deaths. In a large cohort a patients, the inflammatory markers were tested, to check if their supposed prognostic value is indeed valuable.
Methods: In 197 consecutive cases of patients with GC, without prior chemotehrapy, the neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte (PLR) ratio, neutrophil to monocyte (NMR) and lymphocyte to monocyte ratio (LMR) were checked and correlated with the classic clinic-pathological parameters. In all patients the above-mentioned markers were checked one day before surgery. In all the cases emergency surgery was done for hematemesis or occlusion.
Results: The cutoff values for NLR, PLR, LMR, and NMR were 3.95,136.98, 1.33, and 6.2, respectively. The tumour stage was associated with the NLR value (p=0.01); a higher ratio was seen in patients diagnosed in T3/4 stage. PLR was correlated with the depth of tumour infiltration (n=0.04). All of the examined markers proved to have independent prognsotic value. A shorter survival rate was proved for patients with high NLR ($p = 0.002$), PLR ($p = 0.014$), and NMR ($p = 0.009$), respectively low LMR ($p = 0.001$).
Conclusion: In clinical practice, the inflammatory profile of the patient might be checked and be therapeutically modulated, for prognostic purposes. As the geographic-related differences might be seen, an internal validation of the cut-off values is necessary.

E-PS-06-103
Prognostic significance of tumour budding Bd0 category in pT1 colorectal carcinoma with immunohistochemistry confirmation
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Background & Objectives: pT1 colorectal carcinoma (CRC) can be treated locally by endoscopy. The decision on additional surgery is based on the presence of histological features that confer risk of lymph node metastasis (LNM), including tumour budding (TB). A new scoring category with zero buds, namely Bd0, has recently been described, in which immunohistochemistry (IHC) may be a useful tool to determine the absence of TB. The aim of this study is to identify Bd0 pT1 CRC, explore the need of IHC and evaluate its implication in patient prognosis.
Methods: A retrospective multicentre study was designed including 1,543 endoscopically treated pT1 CRCs, of which 714 underwent subsequent surgery. Haematoxylin-eosin (H&E) slides were scanned and twenty gastrointestinal pathologists assessed TB on H&E. Additionally, cytokeratin IHC was performed on Bd0 cases.
Results: On H&E, 60.3% (931 cases) had zero buds (Bd0); 28.5% (440 cases) had 1-4 buds (Bd1); 7.3% (112 cases) had 5-9 buds (Bd2); and 3.9% (60 cases) had ≥10 buds (Bd3). Cases classified as Bd0 using H&E were significantly associated to a lower risk of LNM ($p = 0.001$), while no association was found with the risk of recurrence ($p = 0.549$). IHC was performed on 800 Bd0 cases (86%), of which, 50.25% (402 cases) were confirmed Bd0 by IHC, and 398 tumours (49.75%) had any grade of TB. Only 5 Bd0 cases by IHC had LNM (3%), while 8.2% of Bd0 on H&E but presence of TB on IHC had LNM, although the difference was not significant ($p = 0.097$). IHC analysis was neither associated with the risk of recurrence ($p = 0.641$).
Conclusion: The presence of any grade of TB is associated with an increased risk of LNM in pT1 stage CRC. The addition of IHC to confirm Bd0 grading enables to identify patients with better outcomes.

E-PS-06-105
A retrospective analysis of gastrointestinal malignant melanoma, with special emphasis on anorectal malignant melanoma

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Background & Objectives: Malignant melanoma (MM) of the gastrointestinal system (GIS) is divided into primary mucosal MM and metastatic MM, with or without a detectable primary tumour. Both forms are linked to high morbidity and substantial disease burden. This study focused on GIS MMs, placing particular emphasis on the molecular characteristics of the cases.
Methods: Sixty-three cases diagnosed between 2000 and 2024 at Ege University Pathology Department were analysed, comprising 81 biopsies and resection specimens. Histopathological evaluation included tumour localization, size, pTNM staging, immunohistochemical profiles, molecular studies, presence of primary or metastatic disease, and patient survival. Statistical analyses were conducted using SPSS 20.0, with variables summarized by mean and median values. Associations and age correlations were examined using Chi-square and ANOVA analyses.
Results: Among the 63 cases, 35 were male (55.6%) and 28 female (44.4%), with a median age of 62 years (range: 26–89 years). Tumours were localized to anorectal (AMM) (n=26), colon (n=10), small intestine (n=12), stomach (n=11), and multiple GIS sites (n=4). Mucosal involvement was significantly more common in anorectal and colon tumours compared to stomach and small intestine tumours (21 versus 9 cases, p=0.020). The median age was higher in anorectal MM cases compared to other sites (65 versus 58 years, p=0.031). Known primary MM was frequently observed in cases involving the small intestine (41.7%), stomach (36.4%), and colon (20%), but not in anorectal cases (p=0.007), indicating AMM as possible primary mucosal MM.
BRAF PCR assessment was performed in 29 cases, with no positive results among AMM cases (p=0.01). Eight of 15 tumours showed CD117 positivity, with C-KIT exon 11 mutation in two cases.
Conclusion: AMM's biology and behavioural patterns differ from non-AMM GIS MMs, and the genomic landscape of GIS MM might differ from cutaneous MM. Therefore, a comprehensive molecular assessment is recommended for these cases.

E-PS-06-107
Multiple gastrointestinal stromal tumours: a series of 27 patients
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Background & Objectives: Multiple gastrointestinal stromal tumours (GIST) are rare. They can be sporadic or assocciated to neurofibromatosis. Most of gastrointestinal stromal tumours (GIST) arise in the gastrointestinal tract (GIT) mainly in the stomach and small intestine but ocasionally they are found outside the GIT, in the mesentery and omentun (extraGIST). Our objective is investigate the clinicopathologic features and prognosis of multiple GIST patients, taking into account their location.
Methods: Between 2000 and 2025, patients who underwent surgery for multiple GIST at Hospital Universitario de Navarra were selected for the study and their clinicopathological features were analysed. Molecular test to detect KIT/PDGFRA mutations were performed in some of them.
Results: A total of 27 patients with multiple GIST were enrolled, 16 males and 11 females. Patients age ranged from 24 to 78 years old. Twenty-six cases were sporadic and one patient was associated with neurofibromatosis type 1. Seventeen cases were synchronous tumours and 10 metachronous (the interval between the primary tumour and subsequent tumours ranged from 1 to 10 years). Sixteen patients have all the tumours within the gastrointestinal tract whereas 11 have at least one ExtraGIST. The follow-up period varied between 4 months and 20 years. Overall survival was worse in the ExtraGIST cases, were 61% expired due to disease whereas only 31% of GIST gastrointestinal tract associated expired. The follow-up period oscillated from 4 months to 20 years.
Conclusion: There is no criteria to differenciate primary versus metastatic cases in the setting of multiple synchronous or metachronic GIST. The prognosis of Extra-GIST patients is worse than gastrointestinal GIST.
Molecular analysis is recomended in multiple GIST to evaluate the presence and type of mutation and therefore the different sensitivity to imatinib

E-PS-06-108
The number of Langerhans cells is unchanged in untreated and treated eosinophilic oesophagitis
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Background & Objectives: Eosinophilic oesophagitis (EoE) is a relatively rare, chronic, immune-mediated disease of the oesophagus characterised by eosinophil-dominant inflammation, morphological changes to the epithelium and oesophageal dysfunction. Langerhans cells are antigen-presenting cells (APCs) found in the oesophageal epithelium and may have a role in EoE pathogenesis by stimulating an antigen-driven T-cell mediated hypersensitivity reaction.
Methods: We performed immunohistochemistry using an antibody against the CD1a antigen, a specific marker for Langerhans cells, on formalin-fixed paraffin-embedded sections of oesophageal biopsies obtained from patients (n=11) diagnosed with EoE, based on clinical and histological criteria. For four of EoE patients, we compared CD1a staining in tissue sections obtained pre- and post-treatment. We used as normal controls tissue sections of patients (n=5) with suspected EoE that was not confirmed histologically. In each tissue section, we identified the five high power fields (HPF-objective x400) with the higher density of CD1a-positive cells, and we counted the average number of immunopositive cells per HPF. Statistical analysis was performed by GraphPad Prism 10, using unpaired and paired t-test.
Results: We observed CD1a-positive cells with the typical morphology of dendritic cells, mainly in the suprabasal area of the oesophageal epithelium. We found an increased number of CD1a-positive cells in EoE patients (11.56/HPF) compared to normal controls (10.2/HPF); however, this increase was not statistically significant. Similarly, we observed a non-significant increase of CD1a-positive cells in EoE patients pre-treatment (13.25/HPF) compared to post-treatment biopsies (10/HPF).
Conclusion: Our analysis suggests that the number of oesophageal APCs remains unchanged in normal controls and adults with EoE, treated or untreated. Our data agree with prior studies in adult patients that revealed a stable number of oesophageal Langerhans cells in health and disease and are in contrast with reports of an increased population of Langerhans cells, that decreased significantly after treatment, in children with EoE.

E-PS-06-109

Clinicopathological study of squamoid morules in colorectal neoplasms

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Background & Objectives: Colorectal adenomas with squamoid morules (SM) are rare; however, colorectal adenocarcinomas are even rarer. The aim was to study the clinicopathological features and immunohistochemical analysis of SM in colorectal neoplasms.
Methods: This was a multicentre retrospective study. We identified 25 colorectal neoplasms with SM and collected clinicopathological data. For IHC, the expression of CDX2, p40, CK5/6, CK20, beta-catenin, LEF1, CD10, synaptophysin, chromogranin, and Ki-67 were examined.
Results: We identified 25 colorectal neoplasms with SM in twenty-three patients: eighteen males (72%) and seven females (28%) ranging from 35 to 88 years (average: 61,8 years). Fourteen neoplasms were found in the rectosigmoid, 3 in the descending, and 8 in the right colon. Fifteen tumours were removed by endoscopic, and ten by surgical resection. The type of colorectal tumours with SM were tubulovillous adenomas (n=17; six with adenocarcinoma), tubular adenoma (n=5), and intestinal adenocarcinoma (n=3). The average size of the adenomas was 3,7 cm (range: 0,8-10 cm). The number of SM in each tumour varied ranging from a few foci (52% cases) to extensive foci (48%). Three neoplasms showed foci of SM not only in adenoma but also in adenocarcinoma. All cases showed CDX2, CK5/6, beta-catenin (nuclear and cytoplasmic), LEF1 and CD10 positivity. SM were focally positive for p40 and synaptophysin in six cases respectively (24%), and in four cases (16%) CK20 was focally positive. SM from all 25 neoplasms were completely negative for Ki-67.
Conclusion: To our knowledge, our study reports the highest number of cases of colorectal neoplasia with SM. SM are a rare but problematic finding in colorectal tumours. SM are characterized by male predominance, large adenoma size, beta-catenin and CK5/6 positivity, and no Ki-67 expression. Pathologists should be aware of rare occurrence of SM in colorectal adenomas to prevent a misinterpretation as foci of invasive carcinoma.

E-PS-06-111

Study of the mutational profile of KRAS and BRAF status in non-metastatic versus metastatic colorectal adenocarcinomas

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Background & Objectives: Colorectal cancer ranks third in Tunisia in terms of cancer incidence and mortality, whose dominant histological subtype is adenocarcinoma (ADK). Its treatment has been recently revolutionized with the introduction of immunotherapy. It is therefore essential to study the mutational profile of the RAS and BRAF genes today to elucidate on one hand their interference with the response to immunotherapy and on the other hand their prognostic value, in particular the progression of the disease and the occurrence of distant metastases.
Methods: Our study was retrospective, about 496 cases of metastatic and non-metastatic colorectal adenocarcinomas collected at the Pathology Department A of the Salah Azaïez Institute between April 2021 and December 2022. The molecular study was performed using Biocartis' IdyllaTM.
Results: Our series included 299 men and 197 women with a gender ratio of 1.52. Patients presented with colonic tumours in 73.3% of cases and rectal tumours in 26.7% of cases. Histologically, 92.7% of tumours corresponded to common-shaped ADKs. The other subtypes noted were, in order of frequency, mucinous ADKs (5%), signet-ring ADKs (1.5%), scalloped ADKs (0.6%), and micropapillary ADKs (0.2%). ADKs were moderately differentiated in 45% of cases, well differentiated in 38.5% of cases, and poorly differentiated in 6.5% of cases.
Vascular emboli were found in 13.7% of cases. Perineural sheathing was observed in 10.3% of cases. Distant metastases were confirmed in 25,2 % of cases. A KRAS mutation was found in 48.8% and 49.4% of cases with and without metastases respectively (p=0.999). A BRAF mutation was found in 5.6% and 3.4% of cases with and without metastases respectively (p=0.360).
Conclusion: Our study did not demonstrate a significant association between KRAS BRAF status and the occurrence of distant metastasis. However, to highlight the prognostic value of KRAS and BRAF mutations, it would also be essential to elucidate their association with overall survival.

E-PS-06-112

Three-in-one: a curious case of intra-ampullary adenocarcinoma

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Background & Objectives: Ampullary adenocarcinomas constitute 6-9% of all periampullary malignancies, representing approximately 15% of pancreaticoduodenectomies. Likewise, adenomyomatous hyperplasia is a rare cause of biliary obstruction and common bile duct dilation, mimicking malignancy and posing a diagnostic challenge prior to surgical intervention. We present a curious synchronous intra-ampullary adenocarcinoma arising from intra-ampullary papillary-tubular neoplasm and adenomyomatous hyperplasia.
Methods: A 78-year-old male with a previous laparoscopic cholecystectomy presented with acute pancreatitis and associated acute cholangitis. Follow-up imaging studies and upper endoscopy showing an oedematous papilla raised a suspicion for ampullary carcinoma and consequent bile duct ectasia, and the patient underwent cephalic duodenopancreatectomy.
Results: Grossing revealed the main lesion to be a subepithelial nodular lesion with well-defined borders confined to the ampulla of Vater. Additionally, there was another subepithelial lesion which, when cut, did not appear to be related. Microscopically, the main lesion was consistent with intra-ampullary adenocarcinoma of pancreatic-biliary type, developed in an intra-ampullary papillary-tubular neoplasm with both low- and high-grade dysplasia. The additional lesion was histologically consistent with adenomyomatous hyperplasia.
Conclusion: Ampullary lesions can cause exuberant clinical manifestations whether of a benign or malignant nature and thus motivate surgical intervention. The synchronicity of entities in this case may have contributed to a more florid clinical presentation leading to an earlier diagnosis and management. This case also highlights the diagnostic difficulties associated with ampullary lesions which can be surpassed by a thorough gross examination.

E-PS-06-113

Mutational status of KRAS, NRAS and BRAF in metastatic colorectal cancer: correlation with metastatic sites

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Background & Objectives: Metastatic colorectal cancer (CRC) represents an advanced stage of the disease with a poor prognosis. KRAS, NRAS, and BRAF gene mutations are routinely analysed to

guide treatment decisions, but their association with distant metastases and metastatic sites remains unclear. This study aimed to evaluate the mutational profiles of these genes and analyse the distribution of metastatic sites in CRC patients with distant spread.
Methods: We conducted a monocentric, longitudinal, and retrospective study in the Department of Pathology and Cytology at the Salah Azaïez Institute in Tunis. It included colorectal adenocarcinomas referred for RAS (KRAS and NRAS) and BRAF mutation testing between April 1, 2023, and December 31, 2024. Only patients classified as M1 according to the TNM system were included in the analysis.
Results: Among 496 CRC cases, 125 (25.2%) had distant metastases. These included 89 M1a cases (71.2%), 25 M1c (20%), 9 M1x (7.2%), and 2 M1b (1.6%). The most frequent metastatic sites were the liver (49.6%), peritoneum (15.2%), and lungs (9.6%). Other sites included unspecified locations (8.8%), ovaries (5.6%), dual sites (5.6%), vagina (1.6%), and miscellaneous (4.0%). KRAS mutations were found in 48.8% of M1 patients, NRAS in 4.8%, and BRAF in 5.6%. Compared to non-metastatic patients, there was no statistically significant difference: KRAS (49.4%, p=0.999), NRAS (5.7%, p=0.800), and BRAF (3.4%, p=0.360).
Conclusion: Liver metastases were the most common, followed by peritoneal and pulmonary sites. Most patients were classified M1a, indicating single-organ involvement. The lack of significant association between RAS/BRAF mutations and the presence or location of metastases suggests these mutations may not predict metastatic spread. Further studies are needed to identify novel biomarkers involved in metastatic behaviour in CRC.

E-PS-06-114
On the issue of clinical and epidemiological features of oesophageal cancer in pre-pandemic conditions at the regional level
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Background & Objectives: According to world statistics, oesophageal cancer (EC) is an aggressive tumour and ranks 8th in the structure of tumour diseases in the world. The aim of the study was to study the dynamic changes in some indicators of the incidence of EC in the Voronezh region of Russia.
Methods: Cases of histologically verified diagnosis of EC from 2008 to 2018 were selected. The annual rates of EC verification, age of patients, gender, stage of the disease, number of deaths from this disease (including under 1 year), as well as the division into urban and rural populations were taken into account.
Results: 827 cases of histologically verified EC were registered. The highest incidence rates were observed in the age group of 40-50 years. Over the years, EC has been diagnosed in 735 men (88.8%), and 92 women (11.2%). The share of the urban population was 39.9%, while the share of the rural population was 60.1%. The most common stage of the disease is stage II, which is 657 people (79.4%). The total death rate from EC 589 people (71.2%), while 121 people died within a year of diagnosis (20.5%), which is lower than the national annual mortality rate. There has been a decrease in mortality from EC from 85 people in 2008 to 53 people in 2018.
Conclusion: There is a decrease in mortality from EDC in the Voronezh region and the detection of the disease at an early stage, which reflects a policy aimed at preventive measures. At the same time, more than half of the patients died from the EC, a quarter of whom died within the first year after diagnosis. Obviously, further development of new morphological criteria for predicting the course of this disease is necessary, based not on the relationship between the stage of the disease and the clinical prognosis.

E-PS-06-115
Primary mucosal melanoma of the gastrointestinal tract: a rare case with multisite metastasis
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Background & Objectives: Primary mucosal melanoma of the gastrointestinal (GI) tract is rare, constituting <1% of GI malignancies and 25-50% of melanomas in dark-skinned populations. Despite multimodal therapies, survival remains poor due to delayed diagnosis. This case highlights clinicopathological features to underscore diagnostic challenges and aggressive behaviour.
Methods: A 63-year-old male presented with abdominal pain. Imaging revealed a 6x6.5 cm contrast-enhancing ileal mass. Surgical resection (segmental small bowel resection, right hemicolectomy, cholecystectomy) was performed. Specimens underwent macroscopic evaluation, histopathological analysis including immunohistochemistry.
Results: Gross examination revealed an 8.6x6.2 cm polypoid tumour penetrating to serosa, multifocal brown lesions in the small intestine and distal colon. The gallbladder exhibited a 1.8 cm pigmented fundal lesion with adjacent 'cat's tongue' mucosal changes, while the cystic duct contained a 0.3 cm brown intraluminal lesion contiguous with a 1 cm serosal pigmented focus. Microscopy revealed pleomorphic epithelioid/spindle melanocytic cells with vesicular nuclei, prominent nucleoli, and heavy pigmentation. Immunohistochemistry confirmed melanocytic differentiation (MelanA+, S100+, HMB45+). Tumour foci involved mucosa, submucosa, and subserosa of the small intestine, colon, and gallbladder, with lymphovascular invasion and nodal metastasis. The largest lesion (8.6 cm polypoid mass) originated in the small intestine. Since no other primary focus was found in the patient's dermatological examination and whole body scan, the largest polypoid mass in the small intestine was accepted as the primary lesion.
Conclusion: This case exemplifies the aggressive nature of GI mucosal melanomas, often diagnosed at advanced stages due to nonspecific symptoms and occult anatomical sites. Histopathological and immunohistochemical confirmation is critical, as seen in this multifocal, metastatic presentation. Early detection remains challenging, contributing to poor prognosis. Increased clinical suspicion and recognition of morphological diversity, including pigmented lesions and spindle-cell morphology, may facilitate timely intervention. Further research into molecular drivers (e.g., NRAS mutations) and targeted therapies is essential to improve outcomes in this lethal malignancy.

E-PS-06-117
Crohn's disease-a mycobacterial infection
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Background & Objectives: Demonstration of cell wall deficient mycobacteria (CWDM) in resected tissue from patients with Crohn's disease.
Methods: Wellington Hospital archives (2015-2019) were searched for resections for Crohn's disease (18 cases).
Tissue blocks were stained with the standard Ziehl-Neelsen stain (optimised for Mycobacterium tuberculosis) but with a change in the decolourising step, substituting 30% HCl in isopropyl alcohol for 3% HCl in 97% ethanol.
15 controls (noninflammatory colon) were similarly analysed.
Results: All 18 Crohn's cases contained spherical brightly staining red structures 6-10 microns in diameter, located deep in the intestine wall, in areas of chronic inflammation and fibrosis, not consistently

related to granulomata, some associated with macrophages. Multiple or loosely grouped forms were present. A thin blue halo, possibly biofilm, surrounded some.
We believe these to be CWDM, in particular Mycobacterium avium paratuberculosis (MAP). Loss of the outer membrane/cell wall permits osmotic swelling of the normally bacillary organism, and reduces its antigenicity. The bacillary form of MAP is readily seen with conventional stains in ruminants with Johne's disease, which has otherwise similar clinical and pathological features to Crohn's disease (wasting enteritis, lymphadenopathy, granulomatous tissue reactions).
None of 15 control cases contained the organisms.
Conclusion: Our findings require independent confirmation. The study fulfils Koch's first postulate for causation. In one unrelated case we were able to cultivate CWDM from ileocaecal tissue of a Crohn's patient, but were unable to maintain growth. One author (JA) has regularly cultured CWDM from blood of Crohn's disease patients.
Mycobacteria are difficult to eradicate. The effects of absence of the cell wall are poorly understood. Novel theories of pathogenesis arise, such as direct chemical toxicity (mycolic acid), rather than antigenically driven.
These organisms may cause other systemic disorders, particularly sarcoidosis. The author (AT) has seen them in tissue biopsies from such patients.

E-PS-06-118
Small bowel, small bacilli, big stenosis – *Mycobacterium genavense* in the origin of jejunal stenosis
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Background & Objectives: Small bowel obstruction is a fairly common cause of ED admissions, especially due to adhesions (in patients with previous abdominal surgery or abdominal trauma), hernias and neoplasms. However, there are other aetiologies of stenosis and obstruction that should be kept in mind. In patients with immunosuppression infectious agents should always be remembered. In this case report we relate a clinical case with an unusual cause of jejunal obstruction.
Methods: We report a case of a 40 year old woman recipient of kidney transplantation 23 years prior, with four episodes of gastroenteritis with no causative agent identified in the previous 6 months, who was admitted to the emergency department with abdominal pain, fever, vomiting and weight loss. Laboratory results showed increased inflammatory parameters; cultures were negative. The CT scan revealed circumferential thickening of the jejunum in a length of 70mm, with mesenteric adenopathy and ascites. An enteroscopy was performed, permitting visualization of a jejunal stenosis, with small mucosal ulcers. Biopsies were obtained.
Results: The fragments obtained consisted of intestinal mucosa with multiple foamy histiocytes in the lamina propria. The Ziehl-Neelsen stain revealed multiple intracytoplasmic acid-fast bacilli within the histiocytes. No granulomas were observed. These findings were consistent with infection by nontuberculous mycobacteria. The patient started a multidrug regimen, with clinical improvement. Three months later the PCR assay done in the formalin-fixed, paraffin-embedded biopsy samples was positive for *Mycobacterium genavense.*
Conclusion: *M. genavense* a nontuberculous mycobacteria that in rare cases can infect immunocompromised patients, with poor prognosis. The treatment is similar to other nontuberculous mycobacteria, with a prolonged multidrug regimen and close monitoring. *M. genavense* is difficult to culture, and most cases require molecular assays for diagnosis. This case highlights the importance of surgical pathologists in the timely diagnosis and treatment of infectious diseases.

E-PS-06-119
Mucinous neoplasms of the vermiform appendix: a clinicopathological study of 95 cases
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Background & Objectives: Appendiceal mucinous neoplasms are rare lesions that range from low-grade neoplasms to invasive mucinous carcinoma. Even low-grade lesions can exhibit aggressive behaviour. The recent World Health Organization (WHO) classification has provided a consensus on the nomenclature, facilitating communication between pathologists and clinicians and improving patient care. This study aims to describe these lesions in a large sample and reclassify older cases according to the updated WHO classification.
Methods: Patient records from two tertiary care centres were reviewed for cases diagnosed with a mucinous appendiceal tumour over a 25-year period (2000–2024). Discordant cases were reclassified according to the latest WHO classification of tumours of the appendix.
Results: Ninety-five cases were identified. The mean age of the patients was 57 years [13-89], with a male-to-female ratio of 0.48. Upon gross examination, mucocele was identified in 51 cases (53.6%). Lesions were classified as low-grade appendiceal mucinous neoplasm (LAMN) in 83 cases (87.3%), high-grade appendiceal mucinous neoplasm (HAMN) in 2 cases (2.1%), and invasive mucinous adenocarcinoma in 10 cases (10.5%). Associated pseudomyxoma peritonei (PMP) was found in 5 cases (5.2%), of which 4 were low-grade and 1 was high-grade. Pseudomyxoma peritonei was associated with ruptured LAMN in 4 cases and mucinous adenocarcinoma in one case.
Conclusion: Mucinous neoplasms of the appendix are rare, and recognizing the histological patterns of these lesions is crucial for diagnosis and management. LAMNs have relatively bland histological features but can be associated with pseudomyxoma peritonei, which worsens prognosis. This series represents the largest Tunisian cohort of theses uncommon neoplasms.

E-PS-06-120
MMR deficiency in chronic gastritis as gastric cancer prediction marker
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Background & Objectives: The DNA mismatch repair (MMR) system deficiency causing microsatellite instability (MSI) is common in cancers including gastric adenocarcinoma. There is controversy about whether MSI occurs in established gastric tumours or precancerous lesions, particularly intestinal metaplasia.
Methods: The MMR status was assessed in gastric mucosa specimens with chronic gastritis (n=150) and mucosa specimens of stomachs resected for cancer (≥1 cm from a border of tumour growth, distant zone group, n=155) using immunohistochemical (IHC) staining with anti-MSH2, DBM15.82; anti-MSH6, 44; anti-MLH-1, G168-15; anti-PMS2, A16-4 (Diagnostic BioSystems, USA). Fisher's exact test was used for comparing groups, p<0,05 considered significant.
Results: All cases of the first group (gastric mucosa specimens with chronic gastritis) turned out to be MMR-proficient, regaining MLH1, MSH2, MSH6, PMS2 proteins IHC expression. In the distant zone specimens there were 8 MMR-deficient cases. In five of them loss in the MSH2/MSH6 pair was noted, one case each accounted for a loss in the MLH1/PMS2 pair, an isolated loss of MSH6 protein expression in a focus of intestinal metaplasia, and a combined loss of expression

in the MLH1/PMS2 pair and MSH6 protein. The presence of MMR deficiency cases in the distant zone group demonstrated statistically significant differences compared to the gastric mucosa specimens with chronic gastritis group, p=0.007).
Conclusion: The presence of MMR deficiency in the distant tumour growth zone associated with gastric cancer according to the field cancerization theory and its absence in morphologically similar gastric mucosa specimens with chronic gastritis may indicate that the MSI develops in the early stages of carcinogenesis. It indicates the potential use of the MMR status as a component of a decision support system for assessing the MSI-associated gastric cancer development risk.

E-PS-06-121
Concept of immunohistochemical markers panel in differential diagnostics of dysplasia and gastric cancer
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Background & Objectives: According to the GLOBOCAN data for 2022, gastric cancer (GC) is among the top ten leading causes of cancer morbidity and mortality, ranking seventh and sixth, respectively. There are inconsistent suggestions that marker panels can be useful tools for early/differential diagnostics at the stage of early, severe precancerous lesions.
Methods: Immunohistochemical staining using anti-Ki-67 (monoclonal antibody, clone SP6, Cell Marque, USA), anti-p53, (monoclonal antibody, clone DO7, Cell Marque, USA), anti-β-catenin, (monoclonal antibody, clone 14, Cell Marque, USA), were performed in gastric cancer specimens (n=150), gastric mucosa biopsy indefinite for dysplasia (n=75) and gastric mucosa biopsy with low/high grade dysplasia (n=75).
Results: Immunohistochemical verification of the proliferative compartment and generative zone orientation loss, vertical and horizontal gradient violation using Ki-67 indicate presence of low/high grade dysplasia and allow to exclude indefinite dysplasia. P53 protein expression exceeding first threshold level 30% indicated presence of low/high grade dysplasia, level <30% suggest reactive nature of the process and label case as indefinite for dysplasia. Exceeding the second threshold of 70%, or complete absence of P53 protein expression indicate gastric carcinoma. Disappearance of the membrane mark and aberrant nuclear expression of the β-catenin protein indicate gastric carcinoma with high specificity, which, despite low sensitivity, can be used in differential diagnosis with dysplasia.
Conclusion: The proposed concept of immunohistochemical markers panel, that include Ki-67, P53, β-catenin, potentially can be useful tool as a component of a decision support system by complement each other's capabilities in the differential diagnosis in cases of indefinite for dysplasia, low/high grade dysplasia and intramucosal gastric cancer.

E-PS-07 E-Posters Digestive Diseases Pathology (Liver/Pancreas)

E-PS-07-001
The expression spectrum of Claudins and Carbonic Anhydrase IX in neoplastic and pre-neoplastic lesions of the gallbladder: new diagnostic horizons
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Background & Objectives: The use of immunohistochemical markers such as Claudin-4, Claudin-18.2, Carbonic Anhydrase IX (CA-IX), markers of intestinal, pancreatico-biliary and both, respectively, is gaining momentum in refining the diagnoses of pancreatico-biliary and gastro-enteric tract lesions; especially Claudin18.2 has major therapeutic implications. This study aims to understand how the change in differentiation of pre-neoplastic and neoplastic lesions also changes the immunohistochemical expression of Claudins and CA-IX.
Methods: Twenty-five gallbladder lesions from 12 resected patients (8 females, 4 males; mean age 73.25±7.3 years) were selected: 8 low-grade BilIN (LG-BilIN), 8 high-grade BilIN (HG-BilIN), 2 intestinal-type IPMN, and 7 infiltrative adenocarcinomas. Immunohistochemistry (IHC) for CA-IX (clone NCL-L), CLDN4 (clone 3E2C1) and CLDN18.2 (clone 43-14A) was automatically performed.
Results: CA-IX was positive in 20 (80.0%) lesions, 6 LG-BilIN, 7 HG-BilIN, 1 IPMN, and 6 adenocarcinomas. CLDN4 was positive in 22 (88.0%) lesions, 7 LG-BilIN, 7 HG-BilIN, 2 IPMN, and 6 adenocarcinomas. CLDN18.2 was performed in 15 cases so far, and it was positive in 8 (53.3%) lesions, 2/5 LG-BilIN, 3/5 HG-BilIN, 1 IPMN, and 2/4 adenocarcinomas.
Furthermore, the concomitant positivity of CA-IX and CLDN4 was the commonest, being observed in the 72.0% of all lesions. The concomitant expression of CA-IX and CLDN18.2 was observed in 40.0% of lesions. The expression of both CLDN4 and CLDN18.2 was observed in 60.0%.
Conclusion: In gallbladder pre-invasive and invasive neoplastic lesions, CLDN4 is the most positive marker, regardless the presence of intestinal differentiation, and often together with CA-IX positivity. CLDN18.2, as expected, seems to be more related to gastric differentiation. The expression of all examined markers is observed across all types of lesions, regardless the dysplasia grade.
It is appropriate, to confirm this study, to expand the number of cases and to perform multicentre studies, including mutational analyses to understand any biological changes in pre-neoplastic and neoplastic gallbladder lesions.

E-PS-07-002
Cancer's journey to the pancreas: a case series of metastatic disease
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Background & Objectives: The pancreas is a rare target for metastatic lesions, accounting for approximately 2% of pancreatic malignancies, so therefore, whenever a formation in the pancreas is detected, usually a primary tumour is suspected. But we have encountered a series of secondary tumours to this location which remind us to think twice.
Methods: A case study is made in which 16 cases of pancreatic lesions with proven origin from other primaries are examined with regard to the diagnostic methods used, incidence of the different tumours of origin, synchronous or metachronous manifestation of the metastases, disease-free interval for the latter, as well as the pathological aspects of histology and much needed differential diagnosis with the help of immunohistochemistry.
Results: We present 16 cases: 1 is from a malignant melanoma, 1 from high grade ovarian carcinoma, 2 from colorectal carcinoma, 2 from invasive ductal breast carcinoma, 3 with lung origins and 7 from a renal cell carcinoma. 10 diagnosed on small biopsy specimens and 6 on surgical specimens.
Conclusion: In case of abnormal morphology of a primary pancreatic tumour, it is necessary to discuss the likelihood of metastatic disease and actively seek clinical information about a previous oncological

disease. Because as we have demonstrated there is a diversity of neoplastic malignancies which do show such prospects, some more than others.

E-PS-07-003

Radiofrequency ablation for inoperable cholangiocarcinoma: unraveling the CD4/CD8 ratio and its link to survival outcomes

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Background & Objectives: Cholangiocarcinoma is a rare and aggressive bile duct malignancy often advanced at diagnosis. In inoperable cases, palliative treatments like radiofrequency ablation (RFA) help control tumour growth and improve quality of life. Recent studies suggest that the CD4/CD8 T-cell ratio may influence cancer outcomes, but the effect of RFA on this ratio and its link to survival in cholangiocarcinoma is unclear. This study aims to explore how RFA impacts the CD4/CD8 ratio and its correlation with survival in these patients.
Methods: We retrospectively examined available data in 27 cases of cholangiocarcinoma diagnosed by endoscopic retrograde cholangiopancreatography (ERCP) followed by biopsy, in our department. All patients received palliative treatment through RFA. Biopsies were performed both before and after the RFA procedure, and the following elements were analysed: histopathological diagnosis, specimen volume, percentage of CD3 positive T cells, CD4+ T cell/HPF and CD8+ T-cell/HPF.
Results: The results showed a survival rate of 18.51%, with 10 cases of patients who survived for more than one year, of which only 5 cases of long-term survivors (LTS). The average duration of survival was 7 months. All LTS patients experienced a decrease in CD4/CD8 ratio after RFA and 55% of the analysed cases showed an increase in the percentage of CD3 positive T cells.
Conclusion: Even though it is a malignant pathology with a low survival rate, inoperable cholangiocarcinoma palliatively treated by RFA may show cases of LTS patients who have a decrease in the CD4/CD8 ratio at repeated pre- and post-procedural biopsies. Although the cohort studied was small, these findings could serve as a foundation for future research into immune responses and survival outcomes.

E-PS-07-004

Long survivors versus short survivors in inoperable cholangiocarcinoma – is there the key in the lymph cells?

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Background & Objectives: Extrahepatic cholangiocarcinoma (eCCA) is an aggressive tumour, frequently diagnosed in advanced stages, that rarely beneficiates of proper biopsies. Multiple lines of chemotherapy and immunotherapy are studied in these patients with insufficient data about histologic parameters and their evolution under therapy. Radiofrequency ablation (RFA) is a palliative method of treatment that can induce changes in tumoral microenvironment, changes that are involved in modulating therapeutical response (especially at immunotherapy) and overall survival.
Methods: This study is part of o pilot prospective study including patients with inoperable eCCA that underwent a diagnosis biopsy followed by RFA and clinical surveillance with repeated biopsies at each stenting endoscopic intervention. We comparatively evaluated the proportion of T cells and their subtypes in tumoral microenvironment on pre-RFA and post-RFA biopsies.
Results: We included in this study 22 patients that had at least two biopsies (one at diagnosis, before RFA, and the second after approximately 6-8 weeks). Patients were separated in two sub-groups: long survivors (over one year from diagnosis, 10 patients, median survival minimum 21 months, since 5 patient are still alive) and short survivors (less than an year, 12 patients median survival 5 months).
While long survivors registered a significant decrease (two-tailed P=0.0388) in T cell ratio in intratumoral lymph cells (43 versus 54%), short survivors had an increase of the T cell ratio (63 versus 51%).
Conclusion: A strong T cell-based immune response after RFA seems to corelate with a poor survival. Although the study included a small number of cases, these data are important since there are very few studies including repeated biopsies in eCCA. Since conventional chemotherapy has limited results, there is an increased need for studies about the immune local response in CCA evolution.

E-PS-07-005

Intestinal Metaplasia of the gallbladder: when is additional sampling justified?

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Background & Objectives: Intestinal metaplasia (IM) is a complication of chronic cholecystitis and thought to be a precursor of neoplasia. Since gallbladder neoplasias are often unrecognizable macroscopically, data on sampling gallbladders with IM is conflicting. In this study, we aimed to evaluate whether additional sampling is necessary in each IM case.
Methods: A total of 1,720 cholecystectomy cases were sampled by taking longitudinal full-thickness slices, including the fundus, corpus, neck, and cystic duct margin. IM was identified in 314 cases (18.3%). Cases with incidental invasive carcinoma, convincing/extensive high-grade dysplasia (HGD), or those in which the "roll method" could not be applied methodologically (e.g., thick gallbladder wall, acute cholecystitis) were excluded. The remaining 211 cases underwent total sampling (TS) using the "roll method."
Results: Cases with IM in the initial/standard sample (IS) were categorized as:
(i) no atypia (n=145),
(ii) reactive/regenerative atypia (RA) (n=22),
(iii) suspicious for dysplasia (n=14), and (iv) dysplasia (low-grade dysplasia (LGD) or focal HGD suspicion) (n=30).
After TS, the final diagnoses were: no atypia (n=125), RA (n=31), LGD (n=48), and HGD (n=7).
Among IM cases without atypia at IS, 86.2% (125/145) remained without atypia, 10.3% (15/145) had RA, 3.4% (5/145) had LGD, and none had HGD after TS.
IM cases with RA in IS showed 72.7% (16/22) RA and 27.3% (6/22) LGD after TS.
The final diagnosis of all IM cases suspected of dysplasia in IS was interpreted as LGD.
Among IM cases with dysplasia at IS, 76.7% (23/30) were diagnosed as LGD, while 23.3% (7/30) had HGD.
Conclusion: According to our results, if there was "no atypia" or "RA" with IM in the initial samples, the worst final diagnosis was LGD (7% of cases). Hence, our findings indicate that additional sampling should only be considered when dysplasia is suspected or confirmed in IS.

E-PS-07-006

CD4+ and CD8 + T cells in cholangiocarcinoma - radiofrequency ablation induced changes with prognosis significance

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Background & Objectives: Radiofrequency ablation (RFA) has emerged as a minimally invasive treatment option for unresectable extrahepatic colangiocarcinoma (CCA). RFA also induces stromal and cellular changes with prognosis significance.
This study aims to evaluate the relationship between CD4+ and CD8+ T cells in biopsies from patients with cholangiocarcinoma before and after RFA.
Methods: This prospective cohort study enrolled 27 patients diagnosed with cholangiocarcinoma who underwent radiofrequency ablation (RFA) with a least one biopsy before RFA and another one after minimum 4 weeks from RFA. 21 cases had complete data to assess outcome following RFA treatment.
The presence and number of CD4+ and CD8+ T lymph cell were evaluated in tissue samples harvested before and after RFA (numbered on high power fiels in hot-spot).
Results: Post-RFA biopsies showed an increased medium number of CD4+ and CD8+ cells, comparing with their pre-RFA counterparts. Regardless of this trend, there are some cases with lower level of CD4+ cells and CD8+ cells on the biopsy performed after RFA (6 cases for each marker, 4 of them having concomitant decrease of both subtypes). The median survival was 7 months, with a significant higher survival in the subgroup that underwent decrease of CD4+ cells (19 vs 7.8 months, two-tailed P value 0,0079). Also, the number of CD4+ cells was significant lower on pre-RFA biopsies of long survivors.
Conclusion: RFA induces changes in the composition of inflammatory infiltrate, some of them influencing the outcome of patients with advanced cholangiocarcinoma. T helper lymph cells are especially correlated with survival.

E-PS-07-007
Retrospective analysis of frozen section and permanent diagnosis concordance in hepatobiliary system pathology: a single-centre experience
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Background & Objectives: Intraoperative consultations play an important role in hepato-pancreatobiliary surgeries and they are often difficult and challenging. Therefore evaluating the diagnostic accuracy of intraoperative frozen section analysis is essential.
Methods: A total of 200 frozen section samples from 166 patients were analysed, including 37 bile duct margins (BDM), 47 pancreatic neck/retroperitoneal margins (PRM), 21 liver parenchymal margins (LPM), and 95 cases with suspected malignancy. The concordance between intraoperative frozen section and permanent diagnoses was statistically analysed based on parameters such as localization (liver, pancreas, gallbladder), malignancy status, age, gender, and pathologist experience.
Results: The study cohort comprised 91 male and 75 female patients, with a median age of 50 years. The permanent diagnosis was concordant in 191 cases, while discrepancies were observed in 9 cases. In all but one of these discrepancies, the FS results were negative, but carcinoma was detected in the permanent sections. Among these, in two cases of PRM, no tumour was observed in FS slides, but malignancy was detected in deeper sections of the permanent samples. In one gallbladder case, a polyp within the debris was overlooked during macroscopic examination. The other cases with discrepancy were 1 BDM, 1 LPM, 1 PRM and 3 focal carcinoma focus which missed in FS. The only case with a false-positive FS result was due to misdiagnosis of reactive ductal structures in chronic pancreatitis.
When evaluated based on tissue type, the accuracy rates were 94.87% for liver specimens, 97.22% for gallbladder specimens, 94.64% for pancreas specimens, and 96.67% for ductal specimens, with an overall accuracy of 95.5%. Additionally, frozen sections evaluated by gastrointestinal pathologists had an accuracy rate of 96.03% (121/126), whereas those assessed by non-GI pathologists had an accuracy rate of 94.59% (70/74).
Conclusion: Frozen section permanent section incompatibility was mostly found as false negativity.

E-PS-07-008
Liver explants: histological experience in end stage liver disease
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Background & Objectives: Histology of liver explants is a field of Pathology which needs further enrichment with the experience from different geographical regions. The present study aims to explore common and distinct histological features in liver explants from the transplantation centre in "Laiko" Athens General Hospital. The investigation focuses on the modifications of primary liver diseases in late-stage cirrhosis.
Methods: Thirty-two explants received between 2022 and 2024 were re-evaluated histologically on histochemical stains H&E, Masson-trichrome, Gomori, Orcein Shikata and Perls and on K7 immunostain regarding Laennec stage, disease-related features (DRF), necroinflammatory activity, cholestasis, steatosis, siderosis, and vein thrombosis/obstruction (VTHR/OBSTR). Twenty-two patients were men and 10 women with a mean age 51.5 years (range 21 to 67 years). Histological and/or clinical diagnosis were steatohepatitis-related cirrhosis (SRC) (ALD, Metabolic Dysfunction or both) (11 cases), chronic hepatitis (CH) (5) [HBV (2), HBV/HDV (2), autoimmune (1)], primary sclerosing cholangitis (PSC) (10), primary biliary cholangitis (PBC) (3), cystic fibrosis (1), fibropolycystic (1) and Wolman disease (1). Hepatocellular carcinoma (HCC) was found in 3 cases and combined HCC-Cholangiocarcinoma in 1.
Results: VTHR/OBSTR was found in 16 and venous stasis in 16 cases. DRF loss was observed in 10 SRC and attenuation of necroinflammatory activity in 2 HBV, 1 HBV/HDV, 1 autoimmune hepatitis-related cirrhosis and in one PBC case. Fibrosis regression was encountered in 4 SRC cases. Moderate and severe siderosis was detected in 3 SRC cases and 1 PSC. Steatosis ranged between 0 and 10% in the examined explants. In all biliary cholestatic cases copper-binding protein was conspicuous and K7-expression extensive. In 3 PSC explants segmental cirrhosis was diagnosed.
Conclusion: Common findings, irrespective of aetiology, were vascular complications and absent or mild steatosis. Attenuation of inflammatory activity in CH-cirrhosis and loss of DRF in SRC may be ascribed to progressive exhaustion of the immune system, alcohol abstinence and malnutrition.

E-PS-07-009
High cellular prion protein expression in cholangiocarcinoma: a marker for early postoperative recurrence and unfavourable prognosis
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Background & Objectives: The cellular prion protein (PrP^C), traditionally associated with neurodegenerative disorders, plays an

important role in cancer progression and metastasis by inhibiting apoptosis. To investigate the influence of PrP^C expression in cholangiocarcinoma (CCA) on patient outcomes following surgical resection.
Methods: Patients who underwent curative surgical resection for either intrahepatic or hilar CCA were enrolled in this retrospective study. Based on the immunohistochemical staining results of the surgical specimens, patients were categorized into two groups: The low PrP^C group (negative or 1+) and the high PrP^C group (2+ or 3+). Survival analyses, including overall survival and recurrence-free survival, were conducted using the Kaplan-Meier method and compared using the log-rank test.
Results: In total, seventy-six patients diagnosed with CCA (39 with intrahepatic and 37 with hilar CCA) underwent curative hepatectomy from January 2011 to November 2021. Among these patients, 38 (50%) demonstrated high PrP^C expression, whereas the remaining 38 (50%) showed low expression of PrP^C. During a median follow-up period of 31.2 months (range: 1 to 137 months), the high PrP^C group had a significantly shorter median overall survival than the low PrP^C group (40.4 months *vs* 137.9 months, respectively; $P = 0.041$). Moreover, the high PrP^C group had a significantly shorter median recurrence-free survival than the low PrP^C group (13.3 months *vs* 23.8 months, respectively; $P = 0.026$).
Conclusion: PrP^C expression is significantly associated with early recurrence and decreased survival period in CCA patients following surgical resection. Thus, PrP^C may be used as a prognostic factor in treatment planning.

E-PS-07-010

Immune-related pathologic response (irPR) features and immunotherapeutic response score (ITRS) predict survival following neoadjuvant combined immunotherapy in intrahepatic cholangiocarcinoma

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Background & Objectives: Immune checkpoint inhibitor (ICI) based combined neoadjuvant therapy (NAT) is increasingly utilized in the management of initially unresectable intrahepatic cholangiocarcinoma (iCCA). However, immune-related pathologic response (irPR) features and immunotherapeutic response score (ITRS) remain poorly understood in iCCA.
Methods: This study enrolled 147 iCCA patients who received NAT. irPR features (tumour infiltrating lymphocyte, tertiary lymphoid structure, lymphoid aggregate, plasma cell infiltration, granuloma, neutrophil, foamy macrophage, cholesterol cleft, hemosiderin macrophage, giant cell, neovascularization and mature fibrosis) were accessed on routinely processed haematoxylin-eosin stained post-NAT surgical resection specimen tumour bed slides. Kaplan-Meier and Cox regression analyses were used to investigate irPR features and ITRS correlations with recurrence-free survival (RFS) and overall survival (OS).
Results: The irPR features were identified in the post-NAT surgical resection specimen of iCCA. Six selected irPR features (tumour infiltrating lymphocyte, lymphoid aggregate, cholesterol cleft, tertiary lymphoid structure and neutrophil) were included in ITRS. A binary ITRS scheme was developed, wherein patients classified as ITRS-low exhibited significantly better OS (hazard ratio [HR]:3.03; 95% confidence interval [CI]: 1.55-5.89, P<0.01) and RFS (HR:1.94; CI: 1.24-3.03, P=0.03) compared to those in the ITRS-high group, based on univariate analysis. In a multivariate analysis including lymphovascular invasion, perineural invasion and major pathologic response. ITRS scheme was also found to be an independent prognostic factor for OS (HR: 1.95; 95% CI: 1.02-4.27, P = 0.04).
Conclusion: This study proposed an irPR features-based ITRS scheme that significantly predicts OS and RFS in iCCA patients receiving ICI-based combined NAT. The ITRS is feasible for implementation in routine diagnostic pathology practice and offers novel insights into resistance mechanisms associated with immunotherapy. Further validation in future prospective multicentre clinical trials is warranted.

Funding: This work was supported by the Original Discovery Program of National Natural Science of China (82150004), the Shanghai Municipal Science and Technology Major Project, the National Municipal Key Clinical Specialty, and the start-up fund of Southeast University

E-PS-07-011

The histopathological diagnosis of hepatic graft-versus-host disease: insights toward an improved diagnostic workup

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Background & Objectives: The histopathological diagnosis of hepatic graft-versus-host disease (hGVHD) is challenging due to the broad differentials, subtle features, and significant implications on patient therapeutic management and clinical outcomes. A histopathological algorithm (HA) has been published to facilitate hGVHD diagnostic workup on liver biopsy (Stueck AE et al. Mod Pathol. 2018), but focused on differentiating hGVHD from hepatic disease of non-transplanted patients and has yet to be fully validated. In this study, we aimed to critically evaluate the diagnostic performance of the HA, as well as additional histopathological features, in a series of adult and paediatric patients with a clinical suspicion of hGVHD.
Methods: Thirty-four liver biopsies, performed for clinically suspected hGVHD in adult (n=24) and paediatric (n=10) patients who underwent hematopoietic stem cell transplant (January 2000 - January 2024), were retrieved together with corresponding clinical, therapeutic, and follow-up data. Three pathologists, blinded to clinical data and original diagnosis, independently assessed several histopathological features and applied the HA. Diagnostic performances and interobserver concordance rates of histopathological features and HA were then analysed and compared with post-biopsy clinico-therapeutic management.
Results: Clinico-serological data collection is ongoing, but preliminary findings from 26/34 cases – 21/26 with clinically confirmed hGVHD (cc-hGVHD) – align with the literature and were used for this preliminary study. HA-based diagnosis did not identify 8/14 and 2/7 of adult and paediatric cc-hGVHD, respectively. Implementing granular histopathological characterization – such as detailed portal tract distribution of bile duct injury – improved these metrics, reducing misdiagnosed adult (3/14) and paediatric (0/7) cc-hGVHD, and associated with a correct clinical diagnosis of adult hGVHD (p=0.020). Excellent agreement among pathologists (ICC, range: 0.79-1) was observed for all histopathological variables, including HA.
Conclusion: Our preliminary study revealed critical aspects of the HA and identified new features that may improve hGVHD histopathological diagnosis. We endeavor to validate our findings with complete data collection and multi-institutional cohorts.

E-PS-07-012

Coexisting hepatic actinomycosis and IgG4-related disease mimicry: a diagnostic challenge

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Background & Objectives: Hepatic actinomycosis is a rare condition usually secondary to abdominal or pelvic infections, while IgG4-related disease (IgG4-RD) of the liver is also uncommon. The overlap of these two conditions can complicate diagnosis, as IgG4-positive plasma cells may be a reactive response to infection rather than indicative of true IgG4-RD.
Methods: We present the case of a 71-year-old Hispanic male who was admitted multiple times over six months due to weight loss, nausea, and poor oral intake. His past medical history includes hypothyroidism, iron deficiency anaemia, and right hepatic vein thrombosis. Imaging consistently revealed multiple hepatic lesions, raising concerns of abscesses or malignancy.
Results: A liver biopsy revealed mixed inflammation, with a predominant presence of plasma cells, hepatic necrosis, extensive fibrosis, and sulfur granules. Microbial sequencing from the FFPE block confirmed the presence of *Actinomyces israelii* and *Fusobacterium nucleatum*. *A. israelii* is an anaerobic Gram-positive branching rod, while *F. nucleatum* is an anaerobic, Gram-negative bacillus that can both colonize various human environments. Prior published case reports indicate that coaggregation of bacterial species in the actinomycosis microenvironment conditions can facilitate anaerobic bacterial growth.
Additionally, immunohistochemistry showed an elevated number of IgG4-positive plasma cells (>50/HPF), suggesting the possibility of concomitant IgG4-RD. Despite elevated serum IgG4 and IgG, clinical and imaging findings did not align with typical IgG4-RD. A multidisciplinary team agreed to treat the patient with amoxicillin/clavulanate.
Conclusion: This unique case highlights the diagnostic complexity of hepatic lesions with IgG4 positivity in the context of infection and emphasizes the importance of differentiating between IgG4-RD and conditions that mimic it. Although persistent IgG4 elevation may be misleading, microbiological studies confirmed *Actinomyces* and *Fusobacterium* co-infection, allowing appropriate treatment without unnecessary intervention for IgG4-RD. At the most recent follow-up, there was a marked clinical improvement and a significant reduction in the size of the liver mass.

E-PS-07-013

Morphometric analysis in metabolic dysfunction-associated steatotic liver disease: toward augmented biopsy in type 2 diabetes

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Background & Objectives: Although liver biopsy remains the reference standard for the diagnosis of steato-hepatitis with metabolic dysfunction-associated steatotic liver disease (MASLD), its utility is challenged by limitations, particularly inter-observer variability. Morphometric analysis of biopsy and imaging techniques that provide continuous and objective assessment of steatosis and fibrosis, may overcome this limitation.
Methods: This study compared the performance of morphometric analysis of steatosis and fibrosis to non-invasive imaging in patients with type 2 diabetes mellitus (T2DM) enrolled in the QUID-NASH project. Among 223 T2DM patients with MASLD, steatosis was assessed by MRI–proton-density fat fraction (MRI-PDFF), for fibrosis, liver stiffness measurement (LSM) by magnetic resonance elastography (MRE) and vibration-controlled transient elastography (VCTE). Morphometric analysis examine steatosis and fibrosis in biopsy slides, assessing steatosis proportionate area (SPA) and collagen proportionate area (CPA), respectively. We assessed the relationship between semiquantitative histological grading and morphometry, as well as the correlation between quantitative morphometric data and non invasive techniques.
Results: Steatosis grade was related to SPA ($p<0.0001$), which was significantly correlated with %PDFF (rho: 0.88 [95% CI: 0.84 to 0.92],). Fibrosis stage was related to CPA and weakly correlated with LSM by MRE (rho: 0.26 [0.12 to 0.39]), and moderately with LSM by VCTE (rho: 0.52 [0.42 to 0.61]).
Conclusion: Our study demonstrates the relevance of quantitative morphometric assessment of steatosis and fibrosis in T2DM patients with MASLD. Such an easily applicable approach could be used in routine practice to better characterize two cardinal features of the disease and to improve monitoring.

E-PS-07-015

Clinicopathological and immunprofiles of three cases of SMARCA4-deficient tumour of different presentation

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Background & Objectives: SMARCA4-deficient tumours are aggressive malignancies characterized by inactivation of the SMARCA4 gene, leading to the loss of BRG1 protein expression. These tumours exhibit diverse morphologies and can present in various anatomical locations, often mimicking other malignancies. Due to their rarity and aggressive nature, accurate diagnosis is crucial for clinical management. This study presents three cases of SMARCA4-deficient tumours with distinct clinicopathological and immunohistochemical profiles, illustrating the heterogeneous nature of this entity.
Methods: Three patients diagnosed with SMARCA4-deficient tumours were analysed retrospectively. Clinical history, imaging findings, histopathology, and immunohistochemical markers were evaluated to establish a comprehensive clinicopathological correlation. SMARCA4 (BRG1) loss was confirmed in all cases by immunohistochemistry (IHC).The broad immunohistochemical panel used reveals similarities and differences.
Results: Case 1: 70-year-old man with Horner's Syndrome and lung mass, supraclavicular lymph node biopsy performed.
Case 2: 62-year-old man with lung parenchymal mass and inguinal lymph node metastasis, both biopsied.
Case 3: The most challenging clinical presentation with symptoms including cholecystitis and ascites. A 72-year-old woman with a mass in the liver and mesothelioma-like involvement of the peritoneal cavity was noted in imaging studies. Histopathologically, the first tumour, like the third one, exhibited plasmacytoid morphology consisting of loosely cohesive round cells with eccentric nuclei and abundant eosinophilic cytoplasm, latter showed a more myxoid stroma. CK, claudin 4, and EMA were focally expressed and both were CD138 positive. Case 2 showed spindle cell morphology arranged in fascicles resembling sarcomatoid carcinoma and unlike the others, claudin 4 was significantly positive
Conclusion: SMARCA4-deficient tumours can exhibit diverse morphologies and occur in multiple anatomical sites, making diagnosis challenging. These cases illustrate the varied histological appearances, from plasmacytoid to spindle cell and myxoid stroma with discohesive

cells. Immunohistochemical analysis, including SMARCA4 loss, is crucial for accurate diagnosis. The prognosis remains poor, highlighting the need for further research into potential targeted therapies.

E-PS-07-016

Prognostic impact of T cell markers, expression of immune checkpoint proteins and microsatellite instability in pancreatic ductal adenocarcinoma

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Background & Objectives: Pancreatic ductal adenocarcinoma (PDAC) has low survival rate. The importance of immune checkpoint markers mediating immune tolerance,such as programmed cell death-1 (PD-1) and programmed cell death ligand-1 (PD-L1) is increasingly recognized in PDAC. Additionally,the investigation of microsatellite instability (MSI), which occurs at a low rate (1%) in PDAC,is necessary for the development of future treatments.
Methods: In this study, the association between the expression of following markers:PD-1, PD-L1, CTLA-4, CD3, CD4, MLH1, MSH6, MSH2 and PMS2,along with clinicopathologic characteristics such as age, gender, tumour grade, tumour T stage, tumour size, tumour N stage, number of metastatic lymph nodes, retroperitoneal surgical margin, pancreatic surgical margin, perineural and lymphovascular invasion and also their relation to overall and disease-free survival were examined in PDAC.
Results: The study included 98 patients who underwent proximal pancreaticoduodenectomy due to PDAC. 57% of the patients were male. The incidence of MMR defficiency was very low(1.02%), consistent with the literature. The estimated 1,3 and 5-year disease-free survival (DFS) was 47.6%,3.7% and 3.7% in the PD-1 negative/+ <1% positive group and 68.4%,34.0% and 22.7% in the positive group. In the analysis based on the cut-off value of 7.5 for the CPS of PD-L1,DFS was statistically significantly higher in patients with CPS>7.5 compared to patients with CPS≤7.5. Patients with both PD-1 and PD-L1 positivity had longer overall and disease-free survival. The Cox Regression Analysis showed that PD-1 positivity increased overall survival by 2.409 times while PD-1 positivity increased DFS by 2.88 times.
Conclusion: The positive impact of high PD-1 and PD-L1 levels on survival suggests that additional mechanisms affecting survival in PDAC,such as LAG-3,TIM-3 and TIGIT,require further investigation. This information may also contribute to explaining why immune checkpoint inhibitors are less effective in PDAC. In this context,developing combination strategies,inducing PD-1+ tumour-specific T cells could be a promising approach to enhancing antitumor responses.

E-PS-07-017

Clear views, intact tissue: a non-destructive nano-CT pipeline for liver histology

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Background & Objectives: Nanotomography (nano-CT) is a type of non-destructive 3D x-ray microscopy that enables is a non-destructive imaging technique that enables high-resolution visualisation of tissue microarchitecture. Conventional contrast-enhancing stains used in radiology often compromise tissue integrity, limiting subsequent histological evaluation. Liver fibrosis, characterised by an intricate fibrous network, is particularly challenging to assess at the 3D cellular level. Current approaches are labour-intensive and require a complete assessment and sectioning of the whole tissue block.
Methods: We developed an optimised preparation workflow for high-resolution nano CT imaging using the Xradia Versa 620 (Zeiss, Germany), which achieves from micron to sub-micron resolution through geometric and optical magnification. Healthy and cirrhotic liver tissue samples (0.5 cm cubes) were fixed in formaldehyde/acetic acid, washed, stirred in water, stepwise ethanol-dehydrated, snap-frozen in liquid nitrogen, and freeze-dried. Nano-CT imaging was performed using 4x and 20x objectives. After nano-CT imaging, samples were rehydrated in formaldehyde, paraffin-embedded, and stained (H&E, Sirius Red, and Hepar immunohistochemistry) to evaluate antigenic and morphological integrity. qPCR was conducted to assess genetic stability, and morphological measurements were analysed using the 3D visualization and analysis software Dragonfly (Object Research Systems, Canada).
Results: The nano-CT protocol provided excellent structural contrast and allowed detailed volumetric measurements of liver fibrosis in 3D. Importantly, tissue integrity was preserved, enabling high-quality histological evaluation comparable to conventional methods even after rehydration. Furthermore, RNA levels and housekeeping gene expression were detected in all samples. The combined results reveal a novel approach to tissue reuse and visualization.
Conclusion: This non-destructive nano-CT workflow allows detailed 3D visualisation of liver microarchitecture, including fibrosis, while preserving tissue for downstream analysis on a morphological and molecular level. It offers a robust preclinical and translational research tool, facilitating integrated morphological and molecular assessment of liver disease.

E-PS-07-018

First case of primary pancreatic gastrointestinal stromal tumour in our Pathology Department: a rare diagnostic encounter

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Background & Objectives: Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours of the gastrointestinal tract; however, primary GISTs arising outside the gastrointestinal system, such as in the pancreas, are extremely rare. We present the case of a 66-year-old Caucasian male diagnosed with a primary GIST of the pancreas, highlighting the rarity of this condition.
Methods: Initial examination of the patient revealed tenderness in the epigastric and left hypochondrial regions. Preoperative imaging identified a tumour located in the tail of the pancreas with no other visceral lesions. Therefore, a splenopancreatectomy was performed, and the resection specimen was sent to the Department of Pathology. Histological and immunohistochemical analyses were performed to characterize the tumour.
Results: Gross examination of the specimen revealed a 17×15×8 cm tumour in the tail of the pancreas with both cystic and solid components. Histologically, the tumour was a well-circumscribed, multinodular mesenchymal proliferation composed of predominantly spindle cells. The immunohistochemistry panel included S100, desmin, CD34 and CD117. There have been fewer than 70 cases reported in literature, therefore, a primary gastrointestinal stromal tumour of the pancreas was unlikely, and CD117 was performed for exclusion purposes only. The tumour cells were diffusely and intensely positive for CD117 and

CD34, negative for S100 and desmin, thus confirming the diagnosis of a gastrointestinal stromal tumour. The patient had no other tumours involving the gastrointestinal system, so the final diagnosis was a primary gastrointestinal stromal tumour of the pancreas.
Conclusion: This case represents the first reported primary pancreatic GIST diagnosed in our department. The rarity of extragastrointestinal GISTs, particularly in the pancreas, underscores the importance of considering such entities in the differential diagnosis of abdominal masses. The distinct histopathological and immunohistochemical features were crucial in establishing the diagnosis, and this case contributes valuable insight to the growing body of knowledge on primary pancreatic GISTs.

E-PS-07-019
RhoV is a basal-like pancreatic cancer marker and is associated with poor prognosis
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Background & Objectives: Pancreatic ductal adenocarcinoma (PDAC) is the third leading cause of cancer-related mortality, with a dismal five-year survival rate of just 11.5%. Genomic profiling has categorized PDAC into two principal subtypes—basal-like and classical—of which the basal-like subtype is associated with significantly worse clinical outcomes. It is critical to identify therapeutic targets for the basal-like PDACs. We have identified RhoV as a tissue-specific Rho GTPase promoting PDAC progression, particularly within the basal-like subtype. However, a systemic evaluation of RhoV expression in PDACs and its association with other putative basal markers is still lacking.
Methods: A total of 160 PDAC specimens resulting from the Whipple procedure were collected from Brown University Health's pathology archive. RhoV, p63, and CK5/6 were stained in sequential tumour resection slides. H-scores were obtained by multiplying staining intensity (0, 1, 2, or 3) and the percentage of stained tumour cells (0-300). Positivity was defined as an H-score of 5 or greater. The patient's recurrent and overall survival data and relevant tumour information were extracted from the medical chart and pathology report.
Results: RhoV, p63, and CK5/6 were positive in 60.3%, 31.3%, and 64.9% of PDACs, respectively. 70.8% of RhoV-positive and 94.5% of p63-positive tumours were also CK5/6-positive. The expression of three markers was not associated with tumour cellularity or small/large duct types. RhoV expression was related to poor histologic grade (P=0.0029), while p63 and CK5/6 were not. RhoV expression was associated with significantly worse overall and recurrent survival (P=0.0324 and P=0.0410, respectively), while there was no significant association between p63 and CK5/6 expression and prognosis.
Conclusion: RhoV is a basal-like marker that coexpresses with putative basal markers p63 and CK5/6. While p63 and CK5/6 have limited prognostic implications, RhoV is confirmed as a useful prognostic marker for PDAC and can be a potential therapeutic target.

E-PS-07-020
Insights in the epidemiological trend of hepatic tumours: a single-centre, 5-year retrospective analysis
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Background & Objectives: Hepatic tumours(HTs) are heterogenous neoplasms that cover a wide spectrum of histologic lesions. The liver is a common site for metastasis due to its dual vascular supply and fenestrated sinusoidal endothelium, which create a favourable microenvironment for metastatic cell infiltration. The aim of our study was to assess the epidemiological trends by clinicopathological factors of HTs, with a special focus on liver metastases(LM), diagnosed over the last 5 years in an university hospital in Romania.
Methods: A retrospective observational study was performed, including all pathological reports of patients with HTs registered in our Department of Pathology, between 2020-2024. Patients were divided into three groups: G1-metastases, G2-primary malignancies and G3-benign tumours. We assessed the frequency of diagnoses throughout the study period, patients' demographic characteristics and primary site of origin in LM.
Results: This retrospective study included 142 patients (92 males;50 females) diagnosed with HTs between 2020-2024 in our Department of Pathology. Out of these, 99 were positive for a diagnosis of LM. The median age(MA) was comparable between G1 and G2, however patients in G3 had a significantly lower MA compared to G1 and G2 patients (59.50 years-old vs. 67.58 years-old vs. 66.76 years-old; p=0,014/p=0,015). During the study period we observed a 13.79% increase in HTs cases number in 2022 which was followed by a descending trend in the subsequent years. The most common primary site of origin among our patients was the gastrointestinal tract(n=26), followed by pancreato-biliary tract(n=16), lung(n=7), genito-urinary system(n=4), skin(n=4) and breast(n=1), while in 43 cases the primary origin remained undetermined.
Conclusion: In our study, patients with benign HTs had a significant lower MA, while LM remained the most diagnosed HT overall, with gastrointestinal tract being the most frequent primary site of origin. LM carry a very poor prognosis in oncologic patients, due to increased treatment resistance and impaired organ function.

E-PS-07-021
Characterising the nature of intraparenchymal lesions identified in liver explants - a study of macroscopic, microscopic, an dradiological correlation
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Background & Objectives: Accurate liver explant assessment is key for characterising known and identifying unsuspected solid lesions.
Methods: A single-centre retrospective evaluation of intraparenchymal lesions identified in consecutive liver explants from first-time recipients with chronic liver disease over 18 months, and correlated with pre-transplant radiological findings.
Results: 48/134 (36%) explants had ≥1 lesion on histological examination; of these15 (31%) had >1 lesion type. 18% of explants contained hepatocellular carcinoma(s) (HCC) (median size 14mm, range 3-55mm); 18% macroregenerative nodule(s) (MRN) (8mm, 1-36mm); 6% necrotic nodule(s) (26mm, 6-58mm); 1.5% haemangioma (10 and 25mm); 1.5% dysplastic nodule(s) (9 and 12mm); 1.5% a bile duct adenoma (7 and 13mm), and 0.7% intrahepatic cholangiocarcinoma (45mm).
≥1 lesion was identified in 33/75 (44%) explants with steatotic liver disease (SLD) including 18/33 (55%) HCCs; 6/16 (38%) explants with alpha-1-antitrypsin deficiency including 3/6 (50%) HCCs; 10/13

(77%) with viral hepatitis including 6/10 (60%) HCCs; and 4/7 (57%) containing siderosis including 2/4 (50%) HCCs. No HCCs were identified in explants with cholangiopathy, vascular abnormalities, autoimmune hepatitis, or acute necrosis.
26/134 (19%) explants had ≥1 solid radiological observation pre-transplant and ≥1 histological lesion. In 24, microscopic assessment confirmed the most significant radiological diagnosis: 19 HCCs, 2 necrotic nodules, 1 MRNs, 1 haemangioma, and 1 intrahepatic cholangiocarcinoma. 9/134 (6.7%) had a radiological observation pre-transplant, comprising 7 LI-RADS-3 observations, 1 suspected cyst/haemangioma, and 1 porto-systemic fistula, without a histological correlate in the explant. 22/134 (16%) had ≥1 histological lesion, although no concerning pre-transplant radiological observation; most were MRNs, however, 15 HCCs, size range 4-17mm, including one with lymphovascular invasion, were identified across 5 explants, all with SLD. Three were stage pT2N0, and 2 pT1a.
Conclusion: HCCs in liver explant can be small and unsuspected from pre-transplant imaging, highlighting the need for thin slicing and detailed assessment. Reviewing the radiological findings before histological evaluation facilitates macroscopic assessment.

E-PS-07-022
Hepatic carcinossarcoma versus collision tumour: a challenging diagnosis
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Background & Objectives: Primary hepatic carcinossarcoma is extremely rare and contains a mixture of carcinomatous and sarcomatous components, described in literature with possible extrahepatic exophitic growth. Due to its rarity, there is no known aetiology or estabilished treatment protocols. Collision tumours are lesions with two or more distinct cell populations that maintain distinct borders.
Methods: We present a case of a sixty year old man previously diagnosed with two renal cell carcinomas, one in each kidney that underwent surgery. The patient was further submitted to liver transplantation due to multiple hepatocellular carcinomas, one of which was treated with chemoembolization, one cholangiocarcinoma and one combined hepatocellular-cholangiocarcinoma, developed in cirrhotic alcoholic liver disease. One year after transplant, on CT-scan, there was evidence of a 34 mm nodule adjacent to the liver/right nephrectomy loca, which was submitted to biopsy.
Results: On biopsy examination we found a neoplasm with two admixed components, one with spindle-to-ovoid mesenchymal cells and another with epithelial tubular pattern. Both components had marked pleomorphism, with bizarre nuclei and a high mitotic rate. On immuno-histochemistry the epithelial component had expression of CK7, CK19, MNF16, EMA and BerEP4, while the mesenchymal component had expression of ERG and CD31, with negativity for CAMTA-1 and a mutated p53 phenotype. There was negativity in both components for PAX8, HepPar-1, Desmin and Calretinin. Separated by bland connective tissue there was evidence of hepatic tissue on the periphery of one fragment.
Conclusion: Hepatic carcinossarcomas are rare, usually without differentiation of the sarcomatous component, however there are cases described with osteosarcoma, fibrosarcoma and chondrosarcoma, while none with angiosarcoma. In our case the sarcomatous component has vascular differentiation, but the presence of an intermixed epithelial and sarcomatous components abides with the diagnosis of a carcinossarcoma, as collision tumours are characterized by having distinct borders. Definite diagnosis is only possible on resection specimen.

E-PS-07-023
Hepatic epithelioid haemangioendothelioma: a rare vascular tumour revealed by liver biopsy- pathological insights and diagnostic challenges
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Background & Objectives: Hepatic epithelioid haemangioendothelioma (HEHE) is a rare, low-to-intermediate-grade malignant vascular tumour of the liver with a variable clinical course. Due to its nonspecific presentation and imaging findings, histopathological examination remains the gold standard for diagnosis. This case report aims to describe the histopathological and immunohistochemical features of HEHE in a biopsy specimen, contributing to the diagnostic approach of this rare entity.
Methods: A percutaneous liver biopsy was performed on a 55-year-old woman presenting with abdominal discomfort and multiple hepatic lesions on imaging. Haematoxylin-eosin (H&E) staining was used for histpathological assessment, and immunohistochemistry (IHC) was performed to confirm vascular differentiation and rule out other hepatic neoplasms.
Results: Histopathological examination revealed scattered cords and nests of epithelioid endothelial cells within a myxohyaline stroma, accompanied by mild cellular atypia. Occasional intracytoplasmic vacuoles suggesting primitive vascular lumina were observed. Immunohistochemical staining showed strong positivity for endothelial markers CD31, CD34, and Factor VIII, supporting the vascular origin of the neoplasm. Tumour cells were also positive for vimentin, while negative for hepatocellular markers (HepPar-1, glypican-3) and biliary markers (CK7, CK19), ruling out hepatocellular carcinoma and cholangiocarcinoma.
Conclusion: HEHE remains a diagnostic challenge due to its rarity and overlapping histological features with other hepatic tumours. The combination of histopathological evaluation and a specific IHC panel is crucial for accurate diagnosis. Given the unpredictable clinical course of HEHE, histopathological confirmation is essential for guiding patient management, including consideration of surgical resection, liver transplantation, or targeted therapies.

E-PS-07-024
Unveiling the potential role of SATB2 as a diagnostic biomarker in a cohort study of patients diagnosed with cholangiocarcinoma
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Background & Objectives: SATB2, a transcriptional co-factor and gene regulator, involved in stem cell pluripotency and tumorigenesis, is a specific biomarker in colorectal adenocarcinomas. Although research on SATB2 in cholangiocarcinoma, the second most common liver tumour, is limited, this study aims at evaluating the potential utility of SATB2 in cholangiocarcinoma diagnosis beyond cytokeratin 7 and 19.
Methods: Archival formalin-fixed and paraffin-embedded tissue from 34 patients, comprising 19 women and 15 men, aged 49 to 85 years, with cholangiocarcinomas resected between 2020 and 2025 were retrieved. Immunohistochemical staining was performed and SATB2 nuclear expression was evaluated using an h-score system. The h-score (0-5) was calculated using the sum of the staining intensity

(0=negative, 1=weak, 2=moderate, 3=strong) and the percentage of positive cells (<5%=0, 5-49%=1, >50%=2).
Cases were categorized into groups based on histomorphological and immunohistochemical features, including WHO histological subtype of cholangiocarcinomas, degree of differentiation, histological pattern, presence of necrosis, perineural and vascular/lymphatic invasion, intratumoral inflammatory cell infiltrations and coexpression with cytokeratin 20 and CDX2.
Results: The vast majority of patients (73.53%) was immunohistochemically negative (h-score 0) whereas positive nuclear expression of SATB2 was detected in only 9 cases (26.47%). Among the positive cases, h-scores were: 1 (14.71%), 3 (5.88%), 4 (2.94%) and 5 (2.94%). No cases had an h-score of 2.
Statistical analysis showed no significant correlation between SATB2 immnunohistochemical expression (h-score) and any of the histomorphological and immunohistochemical parameters examined (Pearson chi-square test, p>0.05).
Conclusion: Further studies are required to clarify the potential role of SATB2 and other molecules as diagnostic, prognostic and predictive biomarkers in cholangiocarcinomas. These studies may offer promising targeted treatment options.

E-PS-07-025
Molecular classification of neuroendocrine neoplasms in small biopsies
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Background & Objectives: To evaluate the role of molecular genetic analysis using next generation sequencing (NGS) in small biopsies, e.g. core biopsies (CB) and fine needle biopsies (FNB) to differentiate between neuroendocrine tumour grade 3 (G3 NET) and neuroendocrine carcinoma (NEC), to determine the origin of NEC in liver metastases and to provide information on potential molecular targets for therapy.
Methods: In the period from 2019 and 2024 a total of six cases met the entry criteria: 3 pancreatic neuroendocrine neoplasms (NEN) (two CB, one FNB) and three liver NEN metastases (two CB, one FNB). NGS was performed with Oncomine Comprehensive Assay v3 (Thermo Fisher Scientific) on tissue blocks in four cases and on cell suspension in two cases.
Results: In two of three pancreatic NENs, the presence of TP53 and RB1 mutations confirmed NEC, since these genetic aberrations are generally lacking in G3 NET. Both tumours also harboured KRAS gene mutations, confirming their pancreatic origin. In the remaining pancreatic tumour, mutations in KRAS, TP53 and RNF43 genes, but not in RB1 gene suggested the possibility of mixed endocrine non-endocrine tumour or a precursor cystic neoplasm of pancreas.
Two of three metastatic NEN in the liver harboured mutations in TP53, RB1 and TERT (promoter region) genes confirming the metastatic NEC from known bladder primaries. In the remaining liver NEN metastasis no mutations in the tested genes were confirmed, including TP53 and RB1. The tumour was, therefore regarded as a metastatic G3 NET of unknown primary.
No therapeutically relevant genetic alterations were found in any of the cases.
Conclusion: NGS can be successfully performed on small biopsies and on cell suspension obtained by FNB, thus enabling clear distinction between G3 NET and NEC, providing information on potentially targetable genetic aberrations and establishing the origin of metastatic liver NEC.

E-PS-07-026
EBV-related adenocarcinoma of the ampulla of Vater: a rare tumour or an underrecognized entity?
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Background & Objectives: Molecular classification for ampullary tumours is not as well established as it is for gastric carcinoma. However, genetic alterations like Kras mutations and MSI status are linked to ampullary neoplasia and have some correlation with prognosis and therapy. In gastric carcinoma, EBV detection is associated with a better prognosis, but it remains uncertain whether this applies to ampullary adenocarcinoma. Our case report suggests that routine detection of medullary morphology and EBV should be considered in the diagnosis of ampullary adenocarcinoma.
Methods: We present the case of a 72-year-old female patient diagnosed with ampullary carcinoma after the onset of jaundice, who subsequently underwent pancreaticoduodenectomy. Histopathological analysis of the surgical specimen revealed a neoplasia with mixed features, including a predominantly solid-syncytial pattern interspersed with inflammatory cells at the tumour base, along with a superficial tubular morphology.
Results: Given the morphological findings, we investigated the presence of Epstein-Barr virus (EBV) antigens using EBER-1 probe in situ hybridization (ISH), which demonstrated strong and diffuse positivity. Immunohistochemical analysis disclosed proficient mismatch repair (pMMR) protein expression and complete loss of CK7 expression. The stromal tumour infiltrating-lymphocytes was evaluated in 10%.
Conclusion: Ampullary adenocarcinoma lacks a well-defined molecular classification, and only a few cases of EBV-positive tumours have been previously reported. Recognizing medullary morphology in ampullary carcinoma and assessing EBV status may have significant clinical implications, as it could be associated with improved survival and an increased likelihood of response to PD-1 blockade therapy.

E-PS-07-027
Clinicopathological and immunohistochemical characteristics of solid pseudopapillary neoplasms of the pancreas
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Background & Objectives: Solid pseudopapillary tumours (SPTs) of the pancreas are rare, low-grade malignant neoplasms that primarily affect young women. While their clinicopathological features are well-defined, the underlying molecular mechanisms and prognostic factors remain insufficiently elucidated. This study aims to analyse the clinicopathological and immunohistochemical characteristics of SPTs to refine diagnostic criteria and improve prognostic stratification in the anatomic pathology department of CLCC Batna in 2024.
Methods: We conducted a retrospective descriptive study of eight cases of SPT diagnosed at the anatomic pathology department of CLCC Batna in 2024. Data collected included patient demographics, tumour location and size, histological architecture (proportion of papillary and solid components), presence of necrosis, capsule status, invasion,

metastatic potential, surgical margin status, and immunohistochemical markers (β-catenin, CD10, progesterone receptor [PR], synaptophysin [SYNAPTO], and chromogranin [CHROM]). Statistical analysis was performed to correlate histopathological characteristics with clinical outcomes.

Results: The study included eight female patients with a median age of 28 years. Tumour size ranged from 4.5 to 8 cm, with a predominantly papillary architecture (60–90%). Necrosis was observed in only one case. Capsular invasion was identified in 5/6 resected cases, but no metastases were reported. All tumours showed strong nuclear positivity for β-catenin and were also positive for CD10, PR, and SYNAPTO, while CHROM was consistently negative. Surgical margins were clear in 5/6 cases, whereas one case exhibited tumour infiltration, requiring adjuvant chemotherapy.

Conclusion: Our findings confirm the low malignant potential of SPTs, characterized by a distinctive immunohistochemical profile (β-catenin+, CD10+, PR+, SYNAPTO+) and favourable clinical outcomes despite frequent capsular invasion. The consistent expression of PR may be associated with a less aggressive phenotype, highlighting its potential role as a prognostic marker. Furthermore, although surgical resection is generally curative, the tumour infiltration observed in one case necessitated adjuvant treatment, emphasizing the importance of complete tumour excision.

E-PS-07-028

A rare case of cholangiocarcinoma developing from a biliary adenofibroma

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Background & Objectives: Biliary adenofibroma is a rarely described entity with even rarer reports of malignant transformation. Its recognition, as well as the aspects that might suggest malignancy, is of extreme importance, as it can alter patient follow-up.

Methods: We report a case of a female patient in her 70's, with prior history of left hepatectomy for hepatocellular carcinoma, recurrence and subsequent thermoablation. A 5.6 cm hepatic lesion was discovered during follow-up, biopsied and the patient underwent hepatic segmentectomy.

Results: Macroscopically, the lesion had well-defined, lobulated borders and a biphasic appearance, with a solid, yellowish area and another translucent multicystic component.

Histologically, the tumour was composed of dilated, irregular tubular structures, lined by bland-looking cells and embedded in a fibrous, smooth muscle actin-positive stroma. The macroscopically solid areas corresponded to a denser architectural pattern, with cribriform and back to back tubuloacinar structures lined by cuboidal cells, with eosinophilic cytoplasm, round nuclei and occasional small nucleoli, sometimes with luminal, PAS-D positive secretion. This area had minimal to no intervening stroma and showed atypical mitoses.

All epithelial cells throughout the lesion were CK7 and CK19 positive with SMAD4 and BAP1 retention. The cystically dilated areas also showed EMA positivity. Most neuroendocrine markers (except synaptophysin) were negative, as were hepatocellular markers, GATA3, PAX8, TTF1 and thyroglobulin. P53 had a wild-type staining pattern. Ki67 was about 10%.

Due to the architectural pattern, we considered the tumour to be a malignant transformation of a biliary adenofibroma into a cholangiocarcinoma with a microcystic/cribriform pattern. The patient eventually developed lung metastasis.

Conclusion: Although rare, the malignant transformation of biliary adenofibromas, as reported in the literature and in our case, highlights the preneoplastic nature of this entity and the importance of close follow-up.

E-PS-07-029

Hepatocellular carcinoma: when morphology and immunohistochemistry reveal the keys to prognosis

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Background & Objectives: Hepatocellular carcinoma (HCC) is a malignant liver tumour characterized by diverse morphological and clinical features, which complicate its diagnosis and management. The prognosis of HCC is influenced by various factors, including tumour differentiation, vascular invasion, and the presence of cirrhosis. This study aims to investigate the morphological and immunohistochemical characteristics of HCC in patients who underwent hepatectomy, in order to identify key prognostic factors.

Methods: This retrospective study analysed the pathological reports of 10 patients who underwent hepatectomy for HCC at the Cancer Control Centre (CLCC) of Batna in 2024. The parameters examined included tumour differentiation, inflammatory infiltrates, tumour size, vascular invasion, perineural invasion, surgical margins, liver condition, and capsular status. The diagnosis of HCC was confirmed using immunohistochemical markers HepPar-1, Glypican-3, and Arginase-1, while markers CK7, CK19, and CD10 were used to exclude differential diagnoses.

Results: The study population had an equal sex ratio of 1:1. The tumours were predominantly moderately differentiated (Grade II), with sizes ranging from 2 cm to 6 cm. Encapsulation was observed in 70% of cases, while 30% of the tumours were non-encapsulated, potentially indicating more aggressive behaviour. Most tumours developed in a cirrhotic liver background. The immunohistochemical analysis confirmed HCC with positive staining for HepPar-1, Glypican-3, and Arginase-1, and negative staining for CK7, CK19, and CD10. Vascular and perineural invasion, although rare, were associated with a poorer prognosis.

Conclusion: The absence of encapsulation, lower tumour differentiation, and the presence of vascular and perineural invasion are key factors associated with a poor prognosis in HCC. These findings underscore the importance of a comprehensive morphological and immunohistochemical evaluation to improve risk stratification and guide the management of HCC patients.

E-PS-07-030

A rare case of signet ring cell hilar adenocarcinoma of the extrahepatic bile duct

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Background & Objectives: Signet ring cell carcinoma (SRCC) is a rare and aggressive subtype of adenocarcinoma, typically arising in the stomach. Its occurrence in the extrahepatic bile duct is exceptionally rare, with fewer than 20 cases reported in the English literature. Due to its aggressive nature and diagnostic challenges, awareness and reporting of such cases are crucial.

Methods: We present the case of a 71-year-old woman who was admitted with obstructive jaundice and pruritus. Imaging studies revealed a 3 cm hilar mass in the common hepatic duct, obstructing and infiltrating both the left and right hepatic ducts. The patient underwent a right hemihepatectomy. The resected specimen was examined macroscopically and microscopically, and staged according to current TNM guidelines.

Results: Grossly, a 3.7 cm firm, gray-white tumour was identified at the bifurcation of the common hepatic duct, with infiltration into adjacent hepatic tissue. Microscopic examination showed a polymorphous adenocarcinoma with a predominant (>50%) signet ring cell component. Tumour cells exhibited solid and infiltrative growth with abundant intracytoplasmic mucin and eccentrically displaced nuclei. The stroma was desmoplastic with a mixed inflammatory infiltrate. Three of seven lymph nodes showed metastasis with extranodal extension. Infiltration extended to the coagulation zone of the hepatic resection margin. The patient unfortunately died shortly after surgery due to postoperative complications.
Conclusion: This case highlights the importance of recognizing signet ring cell carcinoma in rare anatomical locations such as the extrahepatic bile ducts. Despite surgical resection, prognosis remains poor. Accurate histopathological diagnosis and reporting are essential for improving understanding of this rare malignancy.

E-PS-07-031
CD55 as a potential biomarker for high-grade pancreatic cancer precursor lesions
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Background & Objectives: Pancreatic cancer, a leading cause of cancer-related mortality, arises from precursor lesions such as pancreatic intraepithelial neoplasia (PanIN), intraductal papillary-mucinous neoplasms (IPMN), and mucinous cystic neoplasms (MCN). Detecting microscopic high-grade precursor lesions remains a challenge, with limited biomarkers available. Previous research suggests that CD55, a membrane-bound glycoprotein involved in complement system regulation, may be elevated in high-grade lesions. This study aims to investigate CD55 expression in pancreatic cancer precursor lesions and its potential as a biomarker.
Methods: A cohort of 161 precursor lesions (130 IPMN, 12 MCN, and 72 PanIN) from 85 patients was assessed for CD55 expression using immunohistochemistry (IHC). Of these, 32 IPMN, 3 MCN, and 5 PanIN were classified as high-grade. Additionally, CD55 levels were analysed in cyst fluids from 46 patients using ELISA, including samples from 6 low-grade, 12 high-grade, 5 ungraded neoplastic cysts, and 23 non-neoplastic cysts.
Results: CD55 IHC showed high interrater concordance (Kappa 0.66–0.84) by three observers. The two observed staining patterns, luminal and cytoplasmic, were significantly increased in high-grade lesions compared to low-grade ($p=0.0011$ and $p<0.0001$, respectively). ELISA analysis revealed significantly higher CD55 levels in low-grade mucin-producing neoplasms than in non-neoplastic cysts (1444.7 ng/ml vs. 284.4 ng/ml, $p<0.001$). Although high-grade cystic neoplasms exhibited even higher mean CD55 levels (5044 ng/ml), the difference between high- and low-grade lesions was not statistically significant.
Conclusion: CD55 expression is significantly elevated in high-grade pancreatic precursor lesions, reinforcing its role in pancreatic cancer development. Furthermore, IHC-based CD55 scoring is reproducible. With further validation, CD55 could serve as a biomarker for identifying high-risk pancreatic precursor lesions.

E-PS-07-032
Tumour mimickers in the pancreas and spleen; accessory spleen and perisplenitis cartilaginea
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Background & Objectives: Tumour-mimicking lesions in the pancreas and spleen are of significant importance for both clinicians and pathologists. In this case, two tumour-like conditions occurring simultaneously are presented.
Methods: Our case, 75 year old male patient was clinically investigated for malignancy for a lesion 3 cm in its biggest diameter on computer tomography (CT) and localised in pancreatic tail. Fine Needle Aspiration(FNA) Biopsy revealed acinar cell groups that cannot be distinguished from malignancy and it was reported as "Suspicious for Malignancy". The patient underwent a distal pancreatectomy and splenectomy. During the surgery on the surface of the splenic capsule white solid lesions of variable size resembling metastatic nodules were observed and intraoperative pathology consultation was requested.
Results: In the macroscopic examination, 2 well circumscribed brown lesions were observed in the pancreas parenchyma and spleen hilum fat tissue. On the surface of the splenic capsule largest being 1.5 cm in diameter multiple white coloured solid implant-like lesions were observed. No tumour was detected in the intraoperative pathology consultation for the pancreatic lesion and the nodules on the splenic capsule. After detailed inspection and examination with light microscopy, pancreatic lesion was reported as accessory spleen in the tail and hilus fat tissue. The white solid lesions which encovered spleen capsule revealed thick, dense, hyalinized fibrous tissue; along with cartilage-like areas within the fibrous stroma and occasional foci of dystrophic calcification was observed microscopically and reported as "Perisplenitis Cartilaginea".
Conclusion: Pancreatic accessory spleen may show atypical findings in FNA and mimic malignancy. Perisplenitis cartilaginea (also known as "Hyaline Perisplenitis" or "Icing Sugar Spleen) is an infrequent benign finding that accompanies intraabdominal inflammatory conditions and may raise the suspicion for metastatic nodules. It is important for the clinician and pathologist to be aware of this entity in order to distinguish it from metastatic lesions and its malignant masqueraders.

E-PS-07-033
SEL1L-NTRK1 is a recurrent gene fusion in pancreatic acinar cell carcinoma with potential therapeutic significance
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Background & Objectives: Pancreatic acinar cell carcinoma (PACC) is a rare malignant exocrine epithelial neoplasm. It does not share the common mutations found in pancreatic ductal adenocarcinoma, and it is of clinical relevance to characterize its molecular signature.
Methods: A retrospective search for PACC patients with genomic alterations was performed in our pathology database from 2020 to 2024. The clinicodemographic and histopathologic information were collected. The findings were analysed in conjunction with a review of the current literature.
Results: We identified one case of PACC with SEL1L-NTRK1 gene fusion through database search and two additional such cases through literature review (published in 2021 and 2024). These 3 patients were all male with age of 65, 71, and 81 years old. The patients' medical history included hypertension, hyperlipidemia, chronic kidney disease, and ulcerative colitis. Radiographically, the PACCs measured 2.0 cm, 2.2 cm, and 4.2 cm, respectively. The tumour involved pancreatic head, neck, and body. All PACC cases demonstrated distant metastasis including liver (3/3) and lymph nodes (3/3). Two patients underwent surgical resection. These patients received gemcitabine-based adjuvant treatment, and the treatment were all discontinued due to further disease progression or adverse effects. The genomic analysis revealed all 3 cases had SEL1L-NTRK1 gene fusion (which has not been reported in any other tumour types), a low tumour mutational

burden and microsatellite-stable status. Additional somatic mutations were found in MEN1, NBN, RB1, ASXL1, and PBRM1 genes. Two patients subsequently received NTRK inhibitors (entrectinib and larotrectinib). One patient demonstrated exceptional radiographic response with near complete liver lesions disappearance. However, another patient discontinued Larotrectinib treatment because of rapid disease progression.
Conclusion: Our study suggests that the SEL1L-NTRK1 gene fusion is a unique and recurrent genomic alteration in PACC. Further study is warranted to determine its frequency and routine testing for such fusion in PACC may provide potential therapeutic benefits.

E-PS-07-034
Neonatal giant cell hepatitis (NGCH) associated to a currently rare cause: haemolysis
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Background & Objectives: Neonatal giant cell hepatitis (NGCH) is a common histologic finding to a wide variety of liver insults, therefore, the differential diagnosis is broad. The most common causes are perinatal infections, congenital malformations, metabolic disorders and hepatobiliary abnormalities. Identification of aetiology is essential because some of these causes need early treatment or even surgery.
We present an infrequent case of severe neonatal cholestasis associated with morphological findings of NGCH caused by haemolytic disease (HDN).
With improving of prenatal care and the use of anti-D prophylaxis the frequency of liver injury in haemolytic disease has become rare. Currently there is small knowledge about patterns of presentation. Traditionally it was associated to "inspissated bile syndrome" which may need surgical intervention. NGCH is another possible finding that could be caused by neonatal haemolysis. This association has to be known and has some special characteristics and clues.
Methods: Four-month girl, born at 33+1 due to Rh (anti-D, anti-E) incompatibility. Appropriate prenatal care included 3 Red Blood Cell transfusions.Liver enzymes were elevated with higher AST elevation, **AST 235 U/L,** GPT 66 U/L, GGT 70 U/L, ALP 568U/L.Bilirubin 10,2 with high direct Bb.Ferritin 8474ng/m.
Ultrasound showed hepatosplenomegaly. Cholangiography excluded biliary tree abnormalities.
Results: Biopsy showed a diffuse, **panlobular multinucleated giant cell transformation and ballooning of hepatocytes**. Inflammation was scarce and mixed with haematopoiesis. There´s mild ductular reaction, that excluded obstruction and moderate canalicular cholestasis. Characteristically,there´s **hemosiderosis** in giant cell hepatocytes and reticuloendothelial cells. Other diseases were excluded (normal BSEP, TJP2 expression, c5b-9 negative, no infections, etc).
Conclusion: Up to 13% of neonates with alloimmune HDN develop cholestasis which needs biopsy. In the past most cases were attributed to "inspissated bile syndrome".
NGCH has been documented in cases of HDN with cholestasis rarely, but its clinicopathologic features have not been sufficiently described. We present a characteristic case.

E-PS-07-035
Chromophobe variant of hepatocellular carcinoma: a rare histopathological entity with diagnostic challenges – a case report
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Background & Objectives: The chromophobe variant of Hepatocellular carcinoma (HCC) is a rare histological subtype of HCC. Due to its distinct morphological features, this variant poses significant diagnostic challenges, potentially leading to misclassification. Increased awareness among pathologists is essential for accurate identification and differentiation from other hepatic neoplasms and metastasis.
Methods: A 69-year-old woman with acute renal failure who was found to have elevated liver function tests on blood tests. Ultrasonographic evaluation revealed a 12 cm mass in the liver. MRI showed a lobulated-contoured lesion measuring 12,5 cm, with no evidence of a solid lesion infiltrating the vena cava. Elevated levels of alpha-fetoprotein (AFP) and CA 19-9 were noted.
Results: Histopathological examination of the liver core biopsy demonstrated tumour cells with chromophobic (clear) cytoplasm and abrupt, marked nuclear pleomorphism against a background of otherwise bland cytology. Scattered microscopic pseudocysts were also observed. Immunohistochemical analysis revealed positive staining for Glypican-3, HSP70, and polyclonal carcinoembryonic antigen (CEA), supporting the diagnosis of hepatocellular carcinoma.
Conclusion: We report a rare histological variant of hepatocellular carcinoma (HCC) characterized by neoplastic cells exhibiting chromophobic (clear) cytoplasm and focal areas of abrupt, severe nuclear atypia, set against a background of predominantly bland morphology. This case highlights the diagnostic challenges and histopathological uniqueness of this underrecognized HCC subtype.

E-PS-07-036
Delayed-onset hepatotoxicity after CFTR modulator therapy in a paediatric patient
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Background & Objectives: Elexacaftor/tezacaftor/ivacaftor (ETI, Kaftrio) is a highly effective CFTR modulator that has significantly improved outcomes in cystic fibrosis (CF). While generally well tolerated, ETI is associated with mild and transient elevations in liver enzymes in approximately 10–15% of patients. However, rare cases of severe drug-induced liver injury (DILI) have been reported, including delayed acute liver failure even after discontinuation. This suggest a possible idiosyncratic or immune-mediated mechanism raising concern for serious hepatic events, particularly in paediatric populations.
Methods: We report the case of a 12-year-old girl with cystic fibrosis (CF) who developed severe liver injury despite the discontinuation of Kaftrio therapy, ultimately requiring liver transplantation. On day(D) 158 after starting therapy, she presented with elevated aminotransferases (AST/ALT: 150/297 U/L), which progressed to AST/ALT: 700/1354 U/L by day 178, prompting the suspension of ETI. On D192, she developed fever, anorexia, odynophagia, headache, abdominal pain and worsening of AST/ALT: 889/2015 U/L. On D206 a transjugular liver biopsy was performed and due to clinical and hepatic deterioation with evolution to acute liver failure she was prompt submitted to liver transplantation (D207).
Results: In both liver specimens a severe pattern of acute hepatitis with centro-central necro-inflamattory bridges leading to massive hepatocellular necrosis and parenchymal collapse was observed. There was mild to moderate portal and lobular mixed inflammatory infiltrate, predominantly neutrophilic, associated with marked periportal ductular reaction. No plasma cells, eosinophils or granulomas were identified and there were no signs of chronic liver disease. In the absence of other causes of severe acute liver damage the diagnosis of kaftrio induced severe acute hepatitis was considered.
Conclusion: This case underscores the potential severity of DILI in paediatric CF patients using CFTR modulators. Even short-term exposure can lead to progressive and life-threatening acute liver failure, reinforcing the need for close biochemical monitoring, early recognition of injury, and long-term hepatologic follow-up.

E-PS-07-037

Next-generation sequencing profile of pancreatic ductal adenocarcinoma after implementation of a dual grossing protocol in pancreatectomy specimens

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Background & Objectives: Pancreatic ductal adenocarcinoma (PDAC) is characterized by its late-stage diagnosis and poor prognosis (only 10–20% of patients have resectable tumours). In light of new therapeutic targets in the field of precision medicine, the study of the molecular biology of PDAC has become essential. In this study, we evaluated the next-generation sequencing profile of PDAC cases and evaluated its correlation with recurrences and survival, considering the application of a dual-grossing protocol which combined the axial and bivalve grossing techniques.

Methods: This observational study includes all resected PDAC specimens diagnosed over the past five years in patients aged >18 at our institution. Next-generation sequencing (NGS) was performed on all samples. Statistical significance was assessed using a two-tailed Chi-square test, with a threshold of $p \leq 0.05$. If expected cell counts were <5, Fisher's exact test was employed. Long-Rank test was performed to analyse the survival differences with a significance level of $p \leq 0.05$. The dual grossing protocol has been developed by combining the axial and bivalve grossing techniques.

Results: 27 cases were analysed: 11 males (40.7%) and 16 females (59.3%), with a mean age of 68. R0 was achieved in 23 cases (85.2%), while R1 was observed in 4 cases (14.8%). *KRAS* mutations were identified in 25.9% of cases, accompanied by *TP53* (25.9%), *FGFR3* (3.7%), and *ATM* (3.7%). Loss of *SMAD4* was detected in 17 cases (53.1%), while *ARID1A* was detected in 1 case (3.7%). *POLE* mutations were not observed. Molecular alterations were associated with age (p=0.01), requirement for neoadjuvant therapy (p=0.046), and N stage (p=0.004), but showed no correlation with recurrences (p=0.47) or survival (p=0.205).

Conclusion: Our findings are comparable to those reported in the literature. Molecular alterations correlate with multiple pathological variables and are the basis for developing new targeted therapies.

E-PS-07-038

Neoplastic findings in cholecystectomy specimens: a 15-year retrospective study

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Background & Objectives: Cholecystectomy is one of the most common surgical procedures performed worldwide. The analysis of cholecystectomy specimens over a prolonged period can provide valuable insights into the prevalence and types of neoplasms encountered. This retrospective study aimed to evaluate the frequency and types of neoplasms found in cholecystectomy specimens over a 15-year period.

Methods: A retrospective review of cholecystectomy specimens diagnosis from the beginning of 2010 to the end of 2024 was conducted. A total of 11573 cholecystectomy specimen were reviewed. Age, gender and prevalence of primary neoplastic findings were recorded.

Results: Of the total cases 6797 (58,7%) were female and 4776 (41,3%) were male with age range 2-105 (mean: 59.1; median 60) and 78 cases (0.67%) exhibited neoplasms. The types of neoplasms identified included: 14 adenomas, 6 billiary intraepithelial neoplasia, 7 intracholecystic papillary neoplasm (IPN), 42 adenocarcinomas, 2 adenosquamous carcinomas, 1 squamous cell carcinoma, 3 undifferentiated carcinomas, 1 neuroendocrine carcinoma, 1 mixed neuroendocrine-non-endocrine neoplasm, and 1 inflammatory myofibroblastic tumour. 9 carcinomas were associated with IPN.

27/78 patients had non-invasive neoplasia and a mean age of 64.6 (39-81) while 51/78 had invasive neoplasia and a mean age of 72.3 (39-96). There was no gender or age diference between IPN (7/78) and IPN associated invasive carcinoma (9/78) patients. Between patients with adenocarcinoma (42/51) and patients with other invasive neoplasia (9/51) there was no age difference but while in the first group 57% of patients were female, in the second group females made up 78% of the total.

Conclusion: Neoplasms in cholecystectomy specimens are rare and varied, with adenocarcinomas being the most common. Non-invasive neoplasia presents in younger patients but no age difference was seen between IPN and IPN associated carcinoma. Non-adenocarcinoma invasive neoplasia are more common in females.

E-PS-07-040

Implication of Syndecan-1 during Extracellular Vesicles uptake in Pancreatic ductal adenocarcinoma cases

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Background & Objectives: The field of Extracellular Vesicles (EVs) has been receiving increased attention, as they are considered important for cell communication. Tetraspanins including CD9, are among their major membrane constituents and therefore representing an often used surface markers. The mechanism underlying EVs uptake is not well defined although evidence suggest that it can be mediated by heparan sulfate proteoglycans such as Syndecan-1 (SDC1) that normally reside on the surface of recipient cells. Thus, the aim of the present study is to investigate the involvement of SDC1 during EVs uptake in cases of pancreatic cancer adenocarcinoma (PDAC).

Methods: Previously published data demonstrated that immunohistochemical identification of EVs using CD9 as a marker is feasible. Thus, the current study applies this methodology to sketch the presence of EVs either in normal adjacent (NA) or cancerous epithelium and stroma by analysing 75 patients with PDAC. Respectively, SDC1 expression was also inspected. Both percentage of positive cells and intensity were scored.

Results: NA epithelium was positive in 66.1% and 14.5% for SDC1 and CD9 while tumour's epithelium was positive in 42.7% and 23.7% of patients respectively. SDC1 intratumoral expression was not restricted on the cell membrane, as a translocation to the cytoplasm was observed in 25.3% of cases. A significant gain of expression compared to NA epithelium was apparent ($p \leq 0.001$) including both membranous and cytoplasmic expression ($p<0.001$ and p=0.009 respectively). Upon translocation of SDC1 to the cytoplasm in tumour's epithelium the supporting stroma was significantly enriched in CD9 expression (p=0.03). NA stroma was negative for both SDC1 and CD9 immunostaining.

Conclusion: The NA stroma profile as well as the accumulation of CD9 in PDAC supporting stroma upon SDC1 translocation to the cytoplasm in tumours epithelium favour the implication of SDC1 in the uptake of CD9 decorated EVs.

E-PS-07-041

Intracholecystic papillary neoplasm: histopathological, immunohistochemical, and molecular study of six cases

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Background & Objectives: Intracholecystic papillary neoplasm (ICPN) is a non-invasive epithelial tumour of the gallbladder that was recently recognized as a distinct entity by the World Health Organization (WHO) and accounts for less than 1% of cholecystectomies. Four histological subtypes have been described: biliary, gastric, intestinal, and oncocytic, often with overlapping features. Its characterization remains limited compared to other hepatobiliary precursor lesions.
Methods: We retrospectively analysed six ICPN cases diagnosed at the University Hospital of Navarra between 2021 and 2024. Histological features (growth pattern, subtype, dysplasia grade, and presence of invasive carcinoma), immunohistochemical expression, and KRAS, NRAS, and BRAF mutation status were analysed.
Results: The mean patient age was 62.7 years, with a predominance of women (71%). Histological evaluation revealed high-grade dysplasia in four cases and invasive adenocarcinoma in one patient. The most frequent histological subtypes were biliary and gastric, followed by intestinal and mixed patterns. Immunohistochemically, CK7 was expressed in most cases and associated with MUC1 in the biliary pattern. CK20 and MUC2 were mostly negative except for the mixed gastric/intestinal subtype. CDX2 was expressed in both the mixed and biliary patterns. MUC5AC was positive in gastric-type lesions, and MUC6 was expressed in the biliary and gastric types. Ki-67 index ranged from 3% to 35%. Molecular analysis revealed that two patients harboured KRAS mutations: c.35G>T (p.Gly12Val) and c.35G>A (p.Gly12Asp).
Conclusion: In our series, most cases were associated with high-grade dysplasia, with only one case associated with invasive carcinoma. Unlike in previous reports, the mixed subtype was not predominant, and the immunohistochemical profiles did not correlate well with histological subtypes. The presence of activating KRAS mutations in two cases suggests a potential role of the RAS pathway in ICPN pathogenesis, consistent with findings in other papillary neoplasms of the pancreatobiliary tract.

E-PS-07-042

SMARCB1/INI1-deficient undifferentiated carcinoma of the ampulla of Vater with microsatellite instability: case report of a very rare and aggressive subtype of ampullary carcinoma

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Background & Objectives: Undifferentiated carcinomas of the gastrointestinal tract are rare, highly aggressive malignant neoplasms, even rarer in the ampullary region. Up to 50% are reported to be SMARCB1/INI1-deficient (SWI/SNF complex subunit), which may or may not have rhabdoid morphology, and these are also frequently associated with microsatellite instability.
Methods: We report the case of a 64-year-old male patient with a twenty-year history of kidney transplant for tubulointerstitial nephritis, with multiple comorbidities. He presented with a cholestatic analytical pattern along with pruritus, abdominal discomfort and nausea. During the diagnostic workup, he developed jaundice, choluria and acholia. Echoendoscopy revealed an ampullo-papillary lesion with dilation of the intrapancreatic common bile duct and the biopsy showed a poorly differentiated/undifferentiated carcinoma.
Results: The pancreatoduodenectomy specimen revealed a 2,5cm, firm, whitish ampullary neoplasm involving both the peri-ampullary and intra-ampullary regions. Histologically, there was a solid proliferation of highly atypical epithelioid cells, with varying amounts of eosinophilic cytoplasm and pleomorphic nuclei with prominent nucleoli. Rhabdoid-like cells were scarcely present. Immunohistochemistry showed reactivity for CAM5.2 and CK7 (multifocal), with absence of SMARCB1/INI1 and preserved expression of SMARCA4. Additionally, there was loss of MLH1 and PMS2 and intact expression of MLH6 and MSH2. This was confirmed by a microsatellite instability-high status by real-time PCR on the Idylla™ platform. Next-Generation Sequencing (NGS) using Oncomine Precision Assay (OPA) panel identified TP53 and GNAS pathogenic variants. The final diagnosis was SMARCB1/INI1-deficient undifferentiated carcinoma of the ampulla of Vater with microsatellite instability. The patient is currently under chemotherapy treatment, four months after initial presentation.
Conclusion: This case illustrates an extremely rare location of SMARCB1/INI1-deficient undifferentiated carcinoma in the gastrointestinal tract. Although it is postulated that loss of one of SWI/SNF complex subunits probably contributes to the arrest of cellular differentiation and consequent aggressive clinical behaviour, further research is needed in order to unravel effective therapeutic approaches.

E-PS-07-043

Clinicopathological perspectives of liver mass biopsies: single centre experience of 406 cases

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Background & Objectives: The increasing use of imaging techniques has led to a rise in the detection of liver masses, making the accurate diagnosis of their nature crucial. While advances in radiology have reduced the need for liver biopsy in hepatocellular carcinoma (HCC), biopsy remains essential for diagnosing various liver lesions, including metastatic tumours. This study aims to evaluate diagnostic role of liver core needle biopsies, with a particular focus on identifying the primary tumour in cases of 9 liver metastases with an unknown primary.
Methods: A total of 406 liver core needle biopsies performed between 2017 and 2022 due to liver masses were reviewed. Clinical, radiological, histopathological and immunohistochemical data for primary and metastatic tumours were evaluated.
Results: Of the 406 liver biopsy cases, a significant portion were diagnosed as metastatic lesions, with common primary sites identified as gastrointestinal, lung, and breast cancers. Immunohistochemical markers showed varying positivity rates across different tumour types, with GATA-3, CDX2, and TTF1 proving particularly useful in distinguishing tumour origin. While some markers were highly specific, others exhibited variable expression, highlighting complexity of diagnosing metastatic tumours with unknown primaries.

Conclusion: Liver biopsy remains a crucial diagnostic tool in the identification of primary and metastatic liver tumours, especially when the primary site is unknown. Immunohistochemical analysis enhances the accuracy of diagnosis, though it should be used in conjunction with clinical and radiological data. This study underscores the importance of a multidisciplinary approach in managing liver masses, with further research needed to optimize diagnostic strategies and improve patient outcomes.

E-PS-07-044

Prognostic value of CD56 in extrahepatic biliary atresia: a retrospective analysis

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Background & Objectives: Biliary atresia (BA) is a progressive fibrosing obstructive paediatric cholangiopathy that causes liver failure. Recent data suggests that CD56 expression may be associated with a worse prognosis in BA. We aimed to evaluate the clinicopathological features of our population, as well as the CD56 expression in ductular reaction of our specimens.
Methods: Our series included all patients with histological confirmation of BA in our department between 2003 and 2024. Clinical information was collected, and all histological findings were reviewed including biliary duct ratio, presence of ductular reaction, duct lesion type, amyloid deposits, presence of inflammation and immunohistochemical expression of CK7 and CD56.
Results: All patients had extrahepatic bile duct BA and 11 cases were included, with a mean diagnostic age of 68 days (σ =27.25), of which 73% were female (n=8) and 27% were male (n=3). Nine per cent (n=1) had died during gestation. Ninety-one percent (n=10) underwent Kasai portoenterostomy followed by liver transplantation. Approximately 36% (n=4) patients had histologically confirmed cirrhosis, 18% (n=2) had amyloid deposits, 91% (n=10) had mixed lobular and portal inflammatory infiltrate, 64% (n=7) had cholestasis and 91% (n=10) had ductular reaction. Fifty-four percent (n=6) of the cases were immunoreactive for CD56, all of them had fibrosis (grades 3-4) and ductal plate malformation. Forty-six percent (n=5) were CD56 negative, of which none had ductal plate malformation.
Conclusion: In our case series, CD56 immunoreactivity was associated with more severe histological features of BA, suggesting a potential role for CD56 as a marker for disease severity.

E-PS-07-045

Expression of some stem cell markers in hepatocellular carcinomas in correlation with clinco-pathological parameters and prognosis

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Background & Objectives: Recently, cancer stem cells (CSCs) have been under focus as one of the determining factors which contribute to intra-tumour heterogeneity. *Cluster of differentiation* (CD) 133 and epithelial cell adhesive molecule (EpCAM) are frequently used markers for identification of CSCs in hepatocellular carcinoma (HCC). This study aimed to assess the relationship between the expression of these two markers in HCC and clinicopathological as well as histopathological parameters. Also, it aimed to evaluate the relation between the expression of these markers and the prognosis of the studied cases.
Methods: The study was conducted on 100 cases of HCC selected randomly from the surgical pathology laboratory at the Gastroenterology Centre, Mansoura University, Mansoura, Egypt, during the period from 2011 to 2014. Seven of these cases showed lost clinical follow-up. Immunohistochemical staining of CD133 and EpCAM for all studied cases was carried out.
Results: The relations between CD133 expression in HCC and the clinicopathological findings of patients revealed high CD133 expression in cases aged above 60 year (p=0.035) and in low grade HCC than high grade (p=0.031). There were no significant relations between EpCAM expression in HCC and the studied clinicopathological findings. Patients with positive CD133 and EpCAM expressions had better overall survival (OS) than those with negative expression (p=0.001 and p=*0.004,* respectively. There was no significant difference between CD133 expression in the disease survival rate (DSR) (p=0.350). Patients with positive EpCAM expression showed a better DSR than those with negative expression (p=0.001).
Conclusion: Immunohistochemical expression of CSC markers can be detected in cells that do not show stemness genes up regulation leading to false over expression of these markers.Also, variables in immunohistochemical staining technique and interpretation as the antibody used and the scoring system can cause wide variability in the obtained results.

E-PS-08 E-Posters Digital & Computational Pathology

E-PS-08-001

Weakly supervised deep learning for worst pattern of infiltration assessment in oral squamous cell carcinoma

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Background & Objectives: The worst pattern of invasion (WPOI) is recognized as a prognostic factor in oral squamous cell carcinoma. Alongside other prognostic factors, its use could be valuable in guiding treatment decisions, particularly in low-stage cases. However, its assessment by pathologists sometimes shows moderate reproducibility. In this context, we developed an algorithm to determine WPOI based on histology slides.
Methods: A total of 173 anonymized digital slides of low-stage (T1, T2) oral squamous cell carcinoma were used to develop different classifiers for WPOI assessment through multiple approaches. The WPOI of these tumours was independently evaluated by two expert head and neck pathologists. The five WPOI classes were grouped into two categories: low-grade (combining grades 1, 2, and 3) and high-grade (combining grades 4 and 5). A deep-learning algorithm was trained to segment tumour areas and generate tumour masks reflecting the tumour shape. First, geometry-based features were extracted from the tumour masks and used to train a classifier with conventional machine learning methods (random forests, support vector machines). Secondly, a deep-learning pipeline incorporating the CLAM workflow was applied for feature extraction and classification. To optimize the results, analyses were conducted using various patch sizes, magnification levels, and different input configurations, including tumour masks, whole slides, or a combination of both.
Results: After testing various deep learning approaches using the CLAM workflow, the best method relied solely on tumour masks at a magnification of 2.5x. This approach achieved an accuracy of 80.2%. Without deep learning, we attained an accuracy of 75.6% using a linear support vector machine.
Conclusion: These results are promising, although the high proportion of low-grade cases (70%) in our dataset should be considered when interpreting them. This algorithm will enable us to improve WPOI assessment and could be further enhanced by incorporating additional prognostic factors.

E-PS-08-002

Algorithm-assisted evaluation improves consistency in mitotic counts, Ki-67 scoring, and grading in gastroenteropancreatic neuroendocrine neoplasms: a comparative study

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Background & Objectives: Grading of gastroenteropancreatic neuroendocrine tumours (GEP-NETs) is based on mitotic count and Ki-67 scoring. Inter-observer variability between pathologists affects one third of cases. Therefore we evaluated whether integrating Virasoft's Ki-67 and mitotic count algorithms into the workflow of pathology residents improves diagnostic consistency and accuracy compared to manual assessment.
Methods: Ground truth (GT) mitotic, Ki-67 counts ang grade were established by 2 senior pathologists. Two pathology residents independently scored mitotic and Ki-67 counts, and grading on 42 WSIs of consecutive NET cases, both manually and with algorithm support. Manual and algorithm-assisted scores were compared with GT using paired t-tests, Pearson correlation coefficients, and Cohen's kappa values.
Results: Mean mitotic count by algorithm and GT were 0.83±1.83 and 0.54±1.41, respectively (p=0.063;Pearson r=0.847). Mean Ki-67 scores by algorithm and GT were 4.0 ± 6.8 and 3.7 ± 6.3, respectively (p=0.058; Pearson r=0.976). The mean manual mitotic counts of the residents were significantly lower than the GT: (Resident 1[R1]:0.29 ±0.81,p=0.023;Resident 2[R2]:0,29±0,93;p=0.04. Algorithm assistance eliminated these discrepancies (0.76±1.92,0.41±1.14,p>0.05). Mean Ki-67 scores of R1 were similar to GT, however R2's scores remained different from GT with some improvements (2.71±5.31,and 3.27± 6.15,p<0.05). NET grading accuracy improved with algorithm assistance, reducing errors for R1 (3 to 1) and R2 (5 to 3) (R1 manual κ=0.81, algorithm-assisted κ=0.86; R2 manual κ=0.75, algorithm-assisted κ=0.85).
Conclusion: The integration of algorithms improved the accuracy and consistency of mitotic count and GEP-NET grading among pathology residents. The role of algorithm support was limited in Ki-67 scoring in this study. Further studies with expanded cohorts and additional residents are needed.

E-PS-08-003

Enhancing diagnostic accuracy for cutaneous drug eruptions: a deep learning approach using whole-slide imaging

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Background & Objectives: Cutaneous drug eruptions represent 1-2% of outpatient dermatology consultations and 5-10% of inpatient dermatological cases worldwide. These reactions exhibit a broad spectrum of clinical and histopathological features, from mild maculopapular rashes to severe, life-threatening conditions like Stevens-Johnson syndrome and toxic epidermal necrolysis. This study aims to evaluate the performance of deep learning algorithms in improving diagnostic accuracy for drug eruptions across diverse patient populations.
Methods: A retrospective analysis was conducted using archived cases diagnosed as drug eruptions in a pathology department between 2014–2024. A control group comprised histologically normal skin tissues from reduction mammoplasty procedures. All slides were digitized using a slide scanner. The patient and control group images were analysed with Vision Transformers (ViTs), specifically the ViT-Large/16 architecture, which utilized pre-trained weights from IMAGENET1K_SWAG_E2E_V1. The model's diagnostic accuracy rates were systematically recorded and compared between the two groups.
Results: The Vision Transformer model achieved a training accuracy of 88.92% (loss: 0.407) and a test accuracy of 86.00% (loss: 0.4801), demonstrating robust performance in classifying biopsy images as normal or abnormal. The study highlights ViTs' effectiveness in analysing subtle histopathological patterns, supported by extensive experimental evaluations. Results indicate that transformer-based architectures may hold advantages over conventional deep learning models for medical image classification tasks, particularly in early detection scenarios requiring high precision.
Conclusion: Deep learning models like Vision Transformers offer a promising tool for improving the detection of cutaneous drug eruptions, which remain diagnostically challenging due to their variable presentations. By enhancing accuracy and enabling personalized risk stratification, these algorithms could support clinical decision-making. The study underscores the importance of standardized AI implementation frameworks that prioritize ethical considerations, algorithmic transparency, and equitable performance across diverse demographic groups to ensure reliability in real-world settings.

E-PS-08-004

Evaluating Large Language Models (LLMs) as a screening tool in breast biopsy diagnosis: a feasibility study

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Background & Objectives: Workloads in pathology have been increasing in volume and complexity. Advances in artificial intelligence (AI) promise increased productivity; adoption remains the exception, however. We investigated the performance of generative algorithms in breast biopsies, using different prompting strategies and retrieval augmented diagnosis (RAG), assessing their potential as screening tools for preliminary review, report pre-filling, and immunohistochemistry (IHC) recommendations.
Methods: Representative images of lesions were extracted from breast biopsies gathered from our archive and fed to GPT4o and o1 large language models (LLMs), alongside clinical information. Two different prompts were tested with each model: a short one, defining only the task – breast biopsy diagnosis – and a longer one detailing common differentials and a diagnostic approach. Each model and prompt were tested with and without RAG.
Results: Our series consisted of 65 cases, all female (ages 18-95). Twenty-three were benign and 42 malignant. Overall diagnostic accuracy varied between 35.38% and 53.85%. For the detection of malignancy, however, this value increased to 73.21-81.54%. Differences between runs did not show statistical significance. The best performing combination was GPT4o with the longer prompt, achieving a sensitivity of 83.33%, a specificity of 78.26%, a PPV of 87.50% and a NPV of 72.00% for the detection of malignancy. IHC studies for oestrogen, progesterone, HER2 and Ki67 were correctly ordered in between 67.69% and 83.07% of cases; when these were ordered, however, they were done so correctly in 92.68-95.07% of cases.

Conclusion: Our results highlight the potential of LLM use in breast biopsy screening and first look. Although the algorithms failed to identify lesions correctly in a significant proportion of cases, they showed good sensitivity and specificity in identifying malignancy and proved accurate in the ordering of additional IHC studies. Therefore, even with current limitations, productivity gains may be possible through screening prior to pathologist evaluation.

E-PS-08-005

Validation of a novel artificial intelligence-based tool for Ki-67 quantification in breast cancer: enhanced accuracy, reproducibility, and efficiency in resource-limited setting

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Background & Objectives: Ki-67 is an important proliferation marker in guiding breast cancer treatment. International Ki-67 Working Group (IKWG) recommends hot-spot, and the Global Scoring (GS) methods to quantify Ki-67 and levels are categorized as low (<5%), intermediate (6–29%), and high(>30%). These manual methods are time-consuming and prone to inter-observer variability and potential sampling bias based on selected microscopic fields.
This study aimed to validate a novel Artificial Intelligence (AI)-based tool, evaluating its accuracy and efficiency compared to manual scoring. The AI tool captures digital images of the entire Ki-67-immunohistochemistry-stained slide in the high-power microscopic field in real-time and automatically calculates the Ki-67 index.
Methods: An AI model was developed using EfficientNetV2 architecture, incorporating distance transformation and watershed algorithms for precise cell segmentation. The model was trained on 350 digital images annotated by pathologists and validated with an additional 350 images. Twenty Ki-67-stained slides from three distinct histopathology units in Sri Lanka were used to minimise variations in slide preparations. AI-derived Ki-67 indices were compared with blinded manual scores by three pathologists using Hot Spot and Global Scoring (GS) methods. Agreement was analysed using Intraclass Correlation Coefficient (ICC) and Bland-Altman plots. Assessment efficiency was compared by measuring evaluation time.
Results: The AI model showed 94.3% accuracy in cell-to-cell identification against pathologist annotations. ICC analysis indicated excellent reproducibility between AI and manual methods for Hot Spot (ICC=0.946, 95% CI:0.672–0.984) and Global Scoring (GS) method(ICC=0.963, 95% CI:0.879–0.987). Bland-Altman analysis confirmed strong agreement without significant systematic bias. The AI method significantly reduced evaluation time (seconds) compared to manual scoring by pathologists (Hot Spot: AI mean=25.5s, Pathologists mean=152.2s, $p<0.01$,t=-7.38; GS:AI mean=250.8s, Pathologist mean=455.1s, $p<0.01$, t=-6.96).
Conclusion: The AI-based tool offers accurate, reproducible, and significantly more efficient Ki-67 quantification, representing a reliable, standardised alternative to manual methods. The AI tool eases workload and reduces diagnostic turnaround times in resource-limited settings. Limitations include dependence on digital microscopy and high-quality slide preparation.

E-PS-08-006

Web application for the automatic segmentation and comprehensive morphometric analysis of arterial cross-sections

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Background & Objectives: Endovascular therapies using balloon catheters and stents are first line treatments of arterial occlusive diseases. In preclinical research, animal models are commonly used to study disease progression and therapeutic interventions. Morphometric analysis of histological cross-sections of stented arteries is an essential tool for these studies. However, manual measurements are subjective and time-consuming (10–15 minutes per cross-section). This study aimed to develop an automated, operator-independent system for comprehensive morphometric analysis to enhance efficiency and accuracy in large-scale data processing.
Methods: A deep learning-based segmentation system was developed to automatically identify arterial structures, including the lumen, internal elastic lamina, external elastic lamina, stent strut voids in histological cross-sections and further quantitative values to characterize the tissue. The neural network architecture nnU-Net v2 was trained and evaluated using a dataset of 820 images annotated by expert histologists. The model's performance was assessed using Dice coefficient, Hausdorff distance, and average surface distance metrics. Additionally, the program was integrated in a web application for free and easy usability for researchers worldwide.
Results: The model achieved a Dice coefficient between 0.892 and 0.996, a median Hausdorff distance between 35 and 104 µm, and a median average surface distance between 4.1 and 10.2 µm. Comparable values were observed for our inter-observer study and therefore demonstrate the excellent system's reliability. The integration of additional features, such as a fibrin quantification and inter-stent distance measurement, further improved the tool's applicability to specific medical research questions.
Conclusion: The developed automatic system enables accurate and efficient morphometric analysis of arterial cross-sections, reducing the processing time to approximately 20 seconds per section. This significantly improves the assessment of disease and therapy progression in preclinical models. The system's scalability allows for future adaptations to additional research applications, supporting further advancements in vascular pathology.

E-PS-08-008

Comparative analysis of ChatGPT models in describing the same histopathology slide

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Background & Objectives: Accurate interpretation of histopathological images is essential in diagnostic pathology. With the rise of AI-based tools like ChatGPT, there is growing interest in evaluating their potential role in medical image description. This study aims to compare the descriptive capabilities of different ChatGPT models when presented with the same histological image of normal brain tissue.
Methods: Five versions of the ChatGPT model (GPT-4, GPT-4o, GPT-3 mini, GPT-3 mini-High, and GPT-4o mini) were presented with the same histopathology slide depicting the normal hippocampus, sourced from the University of Utah WebPath database (https://webpath.med.utah.edu/HISTHTML/NORMAL/NORM058.html). Each model was prompted with two questions:
1) "Describe what you see here" and
2) "From where was this biopsy taken?"
Their responses were analysed in terms of accuracy, anatomical specificity, descriptive detail, and consistency
Results: The models varied in the level of detail and specificity provided. GPT-4o consistently produced the most comprehensive

descriptions, accurately identifying neuronal structures and referencing the cerebral cortex or hippocampus as the likely biopsy site. Earlier or smaller models (such as GPT-3 mini and GPT-4o mini) provided more generalized descriptions, focusing on cellular morphology but with less precise anatomical localization. All models correctly identified the tissue as brain matter but differed in depth and terminology.
Conclusion: This comparative analysis demonstrates the variability in descriptive capabilities among different ChatGPT models when interpreting a standard histopathology image. While newer models like GPT-4o offer enhanced detail and specificity, standardization and further refinement are needed before widespread implementation in pathology practice. This study highlights the potential of AI tools as supplementary aids in histopathological education and diagnostics.

E-PS-08-009
Label- and compute-efficient learning for WSI segmentation: a comparative study of supervised, semi-supervised and self-supervised learning
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Background & Objectives: Whole Slide Images (WSIs) are essential in computational pathology, enabling detailed and high-resolution analysis of tissue structures. However, developing deep learning models for WSI segmentation typically requires extensive pixel-level annotations, which are labor-intensive and costly.
In addition, real-world applications often face challenges such as limited computational resources, long training times, and large-scale data, making scalable and efficient learning essential.
This study systematically compares supervised, semi-supervised, and self-supervised learning approaches for WSI segmentation. We aim to identify strategies balancing segmentation performance with annotation efficiency and computational cost, considering variations in backbone architecture and annotation ratio.
Methods: Tumour segmentation was performed on breast cancer WSIs from the CAMELYON dataset. To improve efficiency, we applied downsampling and ROI-based patch extraction to focus on informative regions.
We adopted widely used backbone models in computational pathology, including ResNet-18, ResNet-50, and Swin Transformer. Supervised models were trained using full annotations, while semi-supervised models used 5% to 50% of labeled data. Self-supervised models were pretrained with SimCLR and fine-tuned with limited annotations.
Segmentation performance was evaluated using Dice Score, mIoU, Precision, and Recall. A custom **Efficiency Index** was defined to jointly assess segmentation performance and computational cost:
Efficiency = Dice / (FLOPs × Training Time)
Results: Semi-supervised learning achieved segmentation performance comparable to fully supervised models with reduced annotations. Self-supervised learning also showed promising performance without annotations, albeit with higher computational costs.
Experiments demonstrated trade-offs between segmentation accuracy and computational efficiency depending on backbone and annotation ratio.
Conclusion: Our findings indicate that semi- and self-supervised learning can serve as practical and label-efficient alternatives to fully supervised learning for WSI-based cancer analysis in computational pathology. These approaches provide a promising direction for scalable and resource-aware AI systems in clinical settings.

Funding: This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: RS-2021-KH113146)

E-PS-08-010
Diagnostic utility of image-based deep learning in the histopathological evaluation of prostatic lesions
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Background & Objectives: Prostate cancer remains a significant global health concern for men, including in Oman. In 2020, it was ranked among the top 10 most prevalent cancers affecting Omani men, accounting for 3.5% of all male cancer cases. The incidence rate of prostate cancer in Oman was estimated at approximately 8.3 per 100,000 individuals. With the growing advancements in artificial intelligence (AI), deep learning techniques have gained widespread attention in computer vision applications, particularly in medical imaging analysis. This study investigates various AI methodologies for the classification of prostate cancer histopathology images.
Methods: This research utilized a prostate cancer histopathological image dataset which comprised a total of 55 images, including 27 benign and 28 malignant tumour samples. The dataset contained cases of prostate adenocarcinoma as well as negative cancer cases. Each image was captured at a magnification of 40x with a resolution of 1360 x 1024 pixels. To facilitate deep learning model processing, all images were resized to 224 x 224 pixels. The dataset was divided into training and testing sets, with 70% (38 images) used for training and 30% (17 images) for testing. The models were evaluated based on key performance metrics, including accuracy, precision, recall, F1-score, and Area Under the Curve (AUC), which assesses the model's ability to distinguish between malignant and benign cases.
Results: Traditional machine learning techniques were applied to the SQUH dataset. Among them, the Support Vector Machine (SVM) demonstrated the highest performance, achieving an accuracy of 82.35%. Deep learning models, particularly those leveraging transfer learning, exhibited superior classification performance compared to traditional models such as SVM and Random Forest.
Conclusion: Our findings highlight the effectiveness of deep learning models in accurately identifying and classifying prostate cancer tumours. These models, once fully optimized, have the potential to assist pathologists in improving diagnostic precision and patient outcomes.

E-PS-08-011
Comparison of manual IHC and brightfield dual ISH HER-2 status results with automatic AI-based HER-2 membrane analysis and semi-automatic dual ISH detection application in gastric adenocarcinoma cases
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Background & Objectives: HER-2 testing is recommended for patients with inoperable, locally advanced, recurrent, or metastatic gastric adenocarcinoma to determine eligibility for trastuzumab therapy. HER-2 status is evaluated based on a membranous stain scoring from 0 to 3+ for Immunohistochemistry (IHC) and counting HER-2 and CEP17 signals in at least 20 tumour cells for Brightfield Dual In-Situ Hybridisation (ISH). Reporting HER-2 status is time-consuming

and subject to interobserver variability. Artificial intelligence-based applications help pathologists achieve objectivity and rapid reporting. Our study aimed to introduce HER-2 automated assessment into our routine for adenocarcinoma cases.
Methods: Tweny six cases of gastric adenocarcinoma with HER-2 IHC and Dual ISH results were selected for this study. All glass slides were scanned with NanoZoomer S360 (Hamamatsu Photonics K.K Shizuoka, Japan) at ×40 magnification. Cases were visualized on Virasoft Image Viewer (Virasoft Corporation, USA). HER-2 IHC analysis was performed with the Virasight algorithm, and Dual ISH slides were analysed with AI-based application (Shimaris, in-house application, MSKCC, USA) previously evaluated for breast cancer specimens.[1],[2] Automated analyses were performed using specific Region of Interests (ROI) selected by pathologists based on hotspots.
[1] Journal of Medical Imaging 6.4 (2019): 047501-047501
[2] LABORATORY INVESTIGATION (Vol. 104, No. 3, pp. S115-S117)
Results: The results of automatic IHC, ISH and ASCO/CAP ISH Group classification were in agreement with the manual results in 88.4% (23/26), 82.6% (19/23) and 79% (17/23), respectively. Discordant cases were observed in heterogeneous and borderline tumours. We could not obtain automatic ISH results from 3 cases due to out-of-focus scans, faint ISH staining and small tumour areas.
Conclusion: To our knowledge, this is the first study to explore methods for providing an automated HER2 status based on both IHC and Dual ISH results simultaneously in gastric adenocarcinoma patients. Our next step is to work on other systems, such as gynecology, and to involve more pathologists.

E-PS-08-013
Incorporation of digital pathology in daily practice; Qualitative findings and perceptions from pathologists and technicians
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Background & Objectives: Digital Pathology (DP) is revolutionizing diagnostics by enabling remote access, efficient slide storage, AI-driven image analysis, and enhanced collaboration and research. This study explores DP's qualitative impact on workflows, logistics, and the perspectives of pathologists and technicians in eight major European laboratories in EU4+UK, while addressing implementation challenges.
Methods: The study employed a targeted literature review, semi-structured interviews, and surveys to evaluate DP's impact on workflows and the perceptions of pathologists and technicians regarding changes in their current and future practices.
Results: A total of 45 pathologists and 47 technicians participated in the surveys. Respondents reported significant benefits of DP, including improved workflow, logistics, and laboratory organization. Among them, 34 pathologists and 29 technicians noted "an important positive impact" on workflows, while 36 pathologists expressed that DP had "an important positive impact" on patient case examination. Adaptation was smooth, with 35 pathologists and 28 technicians finding the DP learning curve "not difficult".
DP strengthened multidisciplinary collaboration, training, research, teaching, and remote work. DP-enabled labs were more attractive to pathologists, addressing staffing issues with temporary remote support and flexible work arrangements. Despite occasional challenges in visualizing details like depth perception, pathologists were generally satisfied, as these issues rarely affected diagnoses. Technicians observed shifts in responsibilities, with automation (e.g., data entry, slide triaging) improving efficiency.
Although Computational Pathology (CP) tools were not routinely used, there was strong interest among pathologists. Adoption was hindered by high costs, limited reimbursement, and the need for algorithm validation. In most CP-enabled labs, funding came through grants or vendor partnerships, raising concerns about long-term sustainability.
Conclusion: DP has a transformative impact on workflows and staff perceptions, with minimal adaptation challenges. However, to maximize its benefits, DP implementation must be supported by optimized laboratory processes. Financial constraints remain a major obstacle to its widespread and sustainable adoption.

Funding: This study was funded by AstraZeneca

E-PS-08-014
Stain normalization without information loss or delay
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Background & Objectives: Digital pathology is rapidly advancing, paving the way for AI-assisted diagnostics. Slide stain normalization, an AI-based preprocessing step, ensures consistent performance across institutions but can be confusing. However, given the large data size in pathology the processing speed of AI remains challenging, potentially disrupting workflow throughput.
AI operates by generalizing from training data. This generalization poses a risk, as the patterns learned from common data may not capture the nuances of rare cases, leading to information loss. When AI models attempt to fill these gaps, hallucinations can occur. In pathology, where precise details are crucial, such hallucinations can have serious consequences.
Methods: The proposed model is restricted to a colour mapping with only a few layers to prevent overwriting structures and to preserve all details in the normalized output. During training, an adversarial approach is utilized. A critic is trained in parallel and rates the realism of the normalized outputs. This critic, unlike the actual normalization model, is unrestricted and optimizes the normalized images to match the characteristics of a target set of images.
Results: The results of the method were compared using the public Mitos & Atypia 14 dataset with related deep learning methods, StainNet and StainGAN. The results demonstrated comparable resemblance

to the target set while surpassing the other methods in terms of structure preservation, showing minimal loss. Additionally, on average, StainGAN takes 129 seconds to preprocess a whole slide image (WSI) on an NVIDIA RTX 4090. In contrast, this method completes the same task in 3.8 seconds, allowing ample time for subsequent AI analysis.
Conclusion: The proposed method effectively balances the need for detailed structure preservation with the efficiency required for practical use in digital pathology. By significantly reducing preprocessing time without compromising on quality, it offers a viable solution for integrating into routine AI supported diagnostic workflows.

E-PS-08-016
MammaPrint prediction from haematoxylin-eosin whole-slide images: preliminary interpretability analysis
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Background & Objectives: Artificial intelligence (AI) models from H&E-stained whole-slide images (WSIs) often lack interpretability. We have implemented an attention-based AI algorithm that achieves strong performance (n=380 WSI, AUC=0.86), but its decision-making process remains unclear. This study evaluates attention heatmaps in a subset of correctly classified cases to identify histologic features influencing predictions.
Methods: Using an attention-based multiple instance-learning model (CLAM), we predicted MammaPrint risk (high vs. low risk) in early-stage breast cancer WSIs. Attention heatmaps were generated by colour-coding patches (red: high attention, blue: low attention). We assessed attention distribution across tumour epithelium, stroma, tumour-infiltrating lymphocytes (TILs), normal epithelium, and in situ carcinoma. Differences between MammaPrint risk groups were analysed using Chi-squared/Fisher's exact tests.
Results: We assessed 60 cases (20 high-risk, 40 low-risk) that were correctly classified by the model. Normal epithelium showed significantly higher attention in low-risk cases ($p<0.005$), while in situ carcinoma trended toward significance ($p=0.066$). Tumour epithelium and TILs consistently received high attention, irrespective of risk category. Stroma showed no differential attention.
Conclusion: The model's attention primarily focused on tumour epithelium and TILs in all cases, suggesting that these features drive predictions universally. Normal epithelium, however, was more attended to in low-risk cases, hinting at a potential discriminator. These preliminary findings reveal limited interpretability for MammaPrint prediction, warranting further analysis in additional cases to elucidate underlying patterns.

Funding: Supported by Instituto de Salud Carlos III (ISCIII) through the projects "PI22/01892" and "PMP22/00054", by CIBERONC (grant CB16/12/00316), by the European Development Regional Fund "A way to achieve Europe" (FEDER)

E-PS-08-017
Automated nuclear grading of breast cancer based on the analysis of selected areas of histological slides (ROI) using AI
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Background & Objectives: Breast cancer is the leading oncological pathology among the female population worldwide and in Russia. A key factor in treatment strategy is the histological NGS grade, that includes tubular, nuclear, and mitotic grades. In routine analysis assessment is time-consuming, often subjective, leading to potential errors. The degree of nuclear atypia is scored (1, 2, 3) based on a combination of factors. As per WHO guidelines, the nuclear grade is determined by the highest score within the analysed tumour sections. Tumour heterogeneity may cause discrepancies in grading by pathologists.
The implementation of digital pathology into routine practice opens up the possibility of using AI in morphological diagnostics.
Methods: The research aimed to develop and validate machine learning algorithms to support medical decision-making in routine breast cancer diagnosis. The main task was to create methods for automated determination of nuclear grade based on AI analysis of extracted regions from histological slides (ROI).
The model is tested on regions annotated by two annotating doctors and a validating doctor, then sent for model inference. The results from the machine learning algorithm are compared with those of the doctors and analysed.
For the "Nuclear Grade" algorithm, the target metrics were: kappa score = 0.4 and mean accuracy = 0.6. Internal evaluation on the test dataset yielded kappa = 0.445 and mean accuracy = 0.67.
Results: The algorithm highlights tumour areas with different levels of nuclear atypia, showing the proportion of each class and calculating the weighted average score (with 1-2 decimal places). This helps the pathologist make more informed decisions and improves the reproducibility of grade assessments within and across studies.
Conclusion: The obtained metrics exceed the target values, that allows to make a preliminary conclusion about the successful implementation of the "Nuclear Grade" machine learning algorithm and the readiness of the ML model for clinical validation.

E-PS-08-018
Deep learning-based diagnostic model for papillary thyroid cancer
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Background & Objectives: Diagnosing PTC remains a significant clinical challenge, significantly when differentiating malignant lesions with borderline nuclear features. Manual histopathological examination, although a standard practice, is time-consuming and limited by subjective variability and the increasing volume of cases. The need for more accurate, efficient, and scalable diagnostic tools is growing, particularly in regions with a high incidence of PTC, such as Oman. Artificial intelligence (AI), intense learning, offers a promising avenue for improving diagnostic workflows in pathology. This study aims to develop and evaluate a novel deep learning-based neural network model to assist in the classification of malignant and benign thyroid pathology images. The goal is to support pathologists with an automated system that reduces workload, increases

diagnostic precision, and highlights suspicious regions for further review.
Methods: A team at Sultan Qaboos University is developing an automated, deep learning-based system to classify pathology images and assist pathologists in the diagnostic process. This article presents a compact, two-step neural network model trained on a limited dataset that enhances diagnostic efficiency and precision in PTC cases.
Results: The proposed solution is a lightweight (1.3 MB), two-step neural network model trained using a limited dataset from the Sultan Qaboos University pathology lab. In the first step, the model classifies the image as benign or malignant. If classified as benign with fewer than 2% false detections, it is forwarded to the pathologist with highlighted suspicious regions. Otherwise, it is processed by a second model that provides a detailed segmentation of malignancy.
Conclusion: This approach leverages deep learning to enhance diagnostic accuracy while maintaining model efficiency, offering a practical AI-based tool to support pathology workflows in thyroid cancer diagnosis

E-PS-08-019
Development of machine learning algorithms to improve the accuracy of diagnosis of HER2\ - status in breast cancer
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Background & Objectives: Breast cancer is the leading oncological pathology among female population and has the highest share in the 30-59 age group.
The HER2 status determines the possibility of prescribing targeted therapy (trastuzumab, etc.), which is indicated for HER2 protein overexpression (3+) and undefined expression (2+ with amplification confirmed by ISH testing) according to ASCO/CAP 2023 guidelines. However, with the introduction of medications of immunoconjugates type (trastuzumab deruxtecan), the approach to low levels of HER2 expression is changing, therapeutic effect may be achieved at any level of tumour cell membrane staining (except for an "absolute zero").
Methods: The research aimed to develop and validate ML algorithms for supporting breast cancer diagnosis and automating HER2 status determination using AI.
HER2 status analysis uses classification metrics like Precision, Recall, F1, and Accuracy, averaged across classes.
Despite achieving **0.9+ metrics** in studies, testing on real-world data typically results in significantly lower values. Therefore, it is proposed to adopt the following target metrics:
- Precision=0,8;
- Recall=0,8;
- F1=0,8;
- Accuracy=0,75 (Both for each class individually and for all classes as a whole).
The model is tested on regions annotated by two annotating doctors and a validating doctor, then sent for model inference. The results from the machine learning algorithm are compared with those of the doctors and analysed.
Results: During the **internal validation** of the model on a **test dataset of 516 polygons** from **184 whole slides**, the following metrics were obtained:
- Precision=0,9;
- Recall=0,9;
- F1=0,9;
- Accuracy=0,9
Conclusion: The achieved metric values during the testing of "**HER2-grade"** machine learning algorithm meet the target criteria, allowing for a preliminary conclusion on the successful implementation of the **"HER2-grade"** algorithm and the readiness of the ML model for clinical validation.

E-PS-08-020
Foundation model distillation to develop robust and efficient AI models for MSI testing in endometrial cancer
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Background & Objectives: AI models for predicting microsatellite instability (MSI) from H&E slides require diverse, multi-centre datasets. This is challenging in cancers with lower MSI prevalence, such as endometrial cancer (EC). While recent foundation models (FM) address data scarcity, they often fail to overcome biases in digital pathology and contribute to high computational costs, limiting clinical applicability.
This study demonstrates that a distilled version of a large foundation model can offer an efficient, robust AI-assisted diagnostic tool for MSI testing in EC.
Methods: We developed AI models to predict MSI status in EC using multi-centre cohorts (2 proprietary, N=239 patients; TCGA, N=478). We compared the performance of a large foundation model ("H0") with a 13x smaller version ("H0-mini").
Results:
- **Performance**: The H0-mini model achieved an AUROC of 0.769 (0.738, 0.760, 0.810) and specificity of 0.497 (0.451, 0.393, 0.648) at 0.9 sensitivity across three left-out cohorts, outperforming H0 by 0.027 (p=0.03) and 0.291 (p<0.001), respectively.
- **Computational cost**: The H0-mini model is 9.1 times faster than H0 on a GPU machine. On standard pathology workstation, processing a WSI takes 15.2 minutes with H0-mini, compared to 120.4 minutes for H0, highlighting the intractability of large FMs without dedicated infrastructure.
- **Robustness**: H0-mini achieved an intra-class correlation of 0.725 (95% CI: 0.651-0.793) between paired resections and biopsies, compared to 0.665 (95% CI: 0.573-0.750) for H0 (p<0.01).

Conclusion: Advanced distillation techniques yield an enhanced, efficient AI model for MSI detection in EC, improving detection capabilities while lowering computational costs. These findings highlight the potential for broader implementation of robust MSI testing in routine clinical practice, aiding streamline diagnosis and targeted therapy in this under-researched cancer population.

E-PS-08-022
A shortcut for detecting collagenic fibres on H&E slides
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Background & Objectives: In present state,producing special stains can be rightly thought of as a tedious, labor-intensive, as well as time consuming task.Broad variability such as techniques and formulations has evolved from site to site,and practitioner to practitioner,until the same stain can appear markedly different from one institution to another. While the small nuances of a stain are often a matter of preference and familiarity,they can also be diagnostically significant differentiators.In this study, We tried to find the potential use of a new method in the detection of collagenic fibres which were visualized by special stains.
Methods: Samples were collected,including 20 liver tissues,20 heart tissues,20 lung tissues.Two serial sections (4μm)were cut from each sample by a cryostat microtome. We used multiphoton microscopy (MPM) to label-freely image on one section which was stained with haematoxylin and eosin (H&E). Images were then compared with the corresponding Masson-stained images (prepared from the adjacent section) to confirm experimental results by two experienced histopathologists.
Results: Data showed that multiphoton imaging allows label-free, rapid visualization of collagenic fibres.There were no differences in the detection of collagenic fibres between Masson-stained image and multiphoton image.
Conclusion: Multiphoton imaging would hold a promising future in rapid and label-free detection of collagenic fibres.

E-PS-08-023
Diagnostic accuracy of ChatGPT in thyroid FNA cytology
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Background & Objectives: Thyroid cytology is widely used to evaluate nodules, but interpreting fine needle aspiration (FNA) smears is challenging and requires expert input. Given the shortage of cytopathologists, supportive diagnostic tools are needed. ChatGPT, a large language model (LLM) developed by OpenAI (CA, USA), can analyse static images and has been studied in histopathology. However, its potential in interpreting thyroid cytology, particularly papillary thyroid carcinoma (PTC), the most common malignancy, remains unexplored. This study evaluates the diagnostic accuracy and consistency of ChatGPT 4.5 in interpreting thyroid FNA cytology images.
Methods: A total of 100 thyroid cytology samples were collected, including 50 PTC cases and 50 non-PTC cases, which consisted of 30 benign follicular nodules, 10 follicular neoplasms, 5 medullary thyroid carcinomas (MTCs), and 5 anaplastic thyroid carcinomas (ATCs). The representative images were selected by an expert cytopathologist and captured at 40x magnification with a resolution of 2448 by 1920 pixels. All diagnoses were independently confirmed by three pathologists. Each image was submitted to ChatGPT version 4.5 in five rounds to assess diagnostic accuracy and consistency.
Results: ChatGPT's average overall diagnostic accuracy was 26.2% when assessed by the Bethesda 2023 categories and 39.2% when assessed by specific diagnostic entities. For malignancy detection, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 62.3%, 65.5%, 73.6%, and 53.6%, respectively. On average, ChatGPT made 51.2 malignant diagnoses (SD = 6.3), most classified as PTCs. MTCs and ATCs were rarely recognized, occurring in 1 and 2 instances. For PTC specifically, the sensitivity, specificity, PPV, and NPV were 64%, 62.8%, 63.6%, and 63.6%, respectively.
Conclusion: ChatGPT 4.5 demonstrated limited diagnostic accuracy and consistency in interpreting thyroid FNA cytology images. Despite moderate sensitivity and specificity for PTC screening, its performance reveals current limitations of LLMs for independent cytologic diagnosis. Further improvements are needed before reliable clinical use.

E-PS-08-024
Introductory framework for synthetic medical image assessment: Foundation Blueprint
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Background & Objectives: The adoption of medical image synthesis technology by both industrial and research communities hinges on the development of quality images. Because the accuracy and utility of synthetic images can vary significantly, rigorous validation against real-world data is indispensable. Unlike other fields, such as art and marketing, where creativity and maintaining a high level of visual appeal ensure a successful image-generation process, generating realistic-looking medical images with faulty architectures or features poses significant risks.
Methods: To date, no evaluation approach adequately addresses the aforementioned pressing difficulty in a manner warranted for grounding synthetic medical images with biological priors. To bridge this gap, we designed a purpose-driven dual-tier assessment method to evaluate the quality of synthetic medical images, whereby predefined assessment criteria are aligned with the specific applications for which the images are intended.
Results: In the course of presenting this study, we: a) detail the designed framework and provide recommendations for assessing the value of synthetic histopathology data, with a focus on images; b) introduce an evaluation matrix that examines two critical components: 1) accuracy, to ensure that synthetic images mirror real images, and 2) identifiability, to assess the risk of personal data leakage. Additionally, we aim to initiate the formation of a multinational consortium to standardize the quality assessment of synthetic histopathology images for both research and development and educational purposes. Adhering to this approach—in conjunction with complying with ethical requirements and regulatory processes being formulated—makes the responsible adoption of medical image synthesis technology viable.
Conclusion: As the emphasis on adopting private synthetic data becomes more pronounced compared to other technologies, the presented foundational method will support pathologists and other medical professionals in understanding this new technology and how it can be responsibly approached. This will result in cost savings and the faster emergence of meaningful synthetic image data sets.

E-PS-08-025
AI-powered mitotic rate assessment enhances diagnostic accuracy and prognostic prediction in liposarcoma
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Background & Objectives: Distinguishing between well-differentiated (WD) and dedifferentiated (DD) liposarcoma can be challenging, especially when the low-grade (LG) spindle cell component does not meet the criteria for typical DD liposarcoma. Mitotic rate (MR) is a key prognostic factor, with ≥5 mitotic figures per 10 high-power fields (HPFs) suggested as a diagnostic criterion for DD liposarcoma. However, MR assessment by pathologists may not consistently reflect the

overall MR across the whole slide. Artificial intelligence (AI)-based MR detection models have emerged as supportive tools to enhance diagnostic accuracy. This study investigates whether AI-assisted MR assessment improves accuracy and consistency among pathologists of varying experience levels, reduces inter-rater discrepancies, and provides a more comprehensive MR evaluation across whole-slide images.
Methods: An AI-powered whole-slide image (WSI) analyser (Lunit SCOPE IO) was applied to 89 liposarcoma cases (74 DD, 15 WD) from Seoul National University Bundang Hospital. Three pathologists—a bone and soft tissue expert, a general pathologist, and a fellow—assessed MR without AI assistance, followed by AI-guided re-evaluation of discordant cases. The expert's reading served as the ground truth.
Results: The AI model achieved 89.9% concordance with the ground truth (80/89 cases). Initial agreement rates for the fellow and general pathologists were 85.4% and 84.3% (Cohen's $\kappa = 0.71$ and 0.68). After AI-assisted re-evaluation, agreement improved to 92.1% and 93.2% (Cohen's $\kappa = 0.84$ and 0.86). While the AI model effectively segmented tumour areas, it misclassified some mitotic cells due to incomplete segmentation or apoptotic body misidentification. Despite these limitations, AI-assisted review enhanced diagnostic accuracy.
Conclusion: AI-assisted MR assessment improved diagnostic agreement among pathologists and reduced interobserver variability. These findings highlight its potential to standardize MR evaluation in liposarcoma, enhancing diagnostic consistency and accuracy.

E-PS-08-026
Equivalency of digital Whole Slide Image (WSI) scoring to microscope glass slide scoring for evaluation of Programmed Death-Ligand 1 (PD-L1) expression in colorectal carcinoma
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Background & Objectives: PD-L1 IHC 22C3 pharmDx (SK006) is a qualitative assay used to detect PD-L1 expression in formalin-fixed, paraffin-embedded (FFPE) tissues. This study aimed to demonstrate concordance between glass slide versus whole slide image (WSI) scoring on colorectal carcinoma (CRC) specimens using the combined positive score (CPS) algorithm at a CPS $\geq$ 10 cutoff.
Methods: Thirty unique CRC specimens were immunohistochemically stained with SK006 and scored using a light microscope; corresponding WSIs were generated using the Aperio AT2 Scanner and scored using ImageScope software. These specimens represented a dynamic range of PD-L1 expression.
Three observers scored blinded and randomized glass slides and WSIs with a minimum 14-day washout period between scoring the two modalities. Concordance in PD-L1 binary expression status between observer reads of each modality was assessed by estimating positive percent agreement (PPA), negative percent agreement (NPA), and overall agreement (OA).
Data for CRC specimens was combined with previously generated data from multiple tumour indications at the CPS $\geq$ 10 cutoff; prior to pooling data, the Fisher-Freeman-Halton test was performed to determine if significant heterogeneity in concordance across tumour types was present. Additional analysis was performed for CRC specimens alone. Acceptance criteria (AC) for the pooled analysis required the lower bound (LB) of the bootstrapped 95% confidence interval (CI) for PPA, NPA, and OA be $\geq$ 85%. Analysis conducted on CRC alone was not subject to AC.
Results: The pooled data had CI LB values $\geq$ 85% with point estimates > 92%. While not subjected to AC, all CI LB values for CRC alone were $\geq$ 84.4%, with point estimates > 91%.
Conclusion: These results support equivalency between glass slide and WSI scoring and support their interchangeable use by observers for PD-L1 expression of specimens from the multiple tumour indications stained with SK006, including CRC, that were analysed at the CPS $\geq$ 10 cutoff.

E-PS-08-027
Automated analysis of eosinophils in inflammatory nasal polyps: detection, classification, and quantification in haematoxylin-eosin-stained slides from patients treated with anti-IL5 immunotherapy
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Background & Objectives: Chronic rhinosinusitis with nasal polyps (CRSwNP) is an inflammatory condition in which tissue eosinophilia plays a key role in both pathogenesis and treatment response. Accurate quantification of eosinophils in biopsies is essential for identifying candidates for targeted therapies such as mepolizumab, an anti-IL-5 monoclonal antibody. Manual identification in routine stains is a subjective process, typically involving the selection of three "hotspots" followed by the calculation of an average eosinophil count. This underscores the need for automated tools to improve objectivity and reproducibility in quantification.
Methods: Histological sections of nasal polyps from 18 patients with CRSwNP, stained exclusively with haematoxylin and eosin (H&E), were analysed. A total of 29 slides were collected. Images were digitized using a Leica Aperio CS2 scanner at 40x magnification and stored on a physical server. The dataset was subsequently divided into 15 images for training, 7 for testing, and 7 for validation.
A Random Forest model was used for automated classification. The model was configured with a maximum tree depth of 12 and a minimum of 5 samples per node to balance pattern capture and generalization. To assess model accuracy, a comparative analysis was conducted between manual and automated eosinophil quantification using the annotated H&E slides and corresponding pathology reports as reference standards.
Results: A total of 14 paired samples were analysed to compare manual eosinophil counts ("Manual") with digital quantification ("EOS-Q"). A strong and statistically significant correlation was observed ($r = 0.81$, $p = 0.0005$).
urthermore, the correlation between eosinophilic inflammation (EOS-Q) and symptom severity (SNOT scores) was assessed in 9 paired observations, yielding a weak and non-significant correlation ($r = 0.26$, $p = 0.49$).
Conclusion: This study demonstrates that automated analysis of eosinophils in H&E-stained inflammatory nasal polyps is a reliable and reproducible tool. Its application in clinical settings could optimize patient selection for targeted therapies.

E-PS-08-028
Automated quantification of CD34+ blasts in bone marrow biopsies using deep learning
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Background & Objectives: Quantifying CD34+ blasts in bone marrow is essential for diagnosing and classifying myelodysplastic syndromes (MDS) and acute leukemias. Currently performed manually, this process is prone to interobserver variability, affecting diagnostic accuracy. Digital pathology and deep learning offer a promising solution to improve objectivity and reproducibility.
Objective: To develop a deep learning model for automated quantification of CD34+ blasts in digitized bone marrow biopsies, improving diagnostic precision and efficiency.
Methods: A retrospective review was conducted on clinical cases with suspected MDS or leukaemia from a tertiary hospital between 2021 and 2024. A total of 110 bone marrow biopsy images stained with CD34 immunohistochemistry were collected and digitized. Expert pathologists manually segmented and annotated cellular components to create a training dataset.
A processing pipeline was developed to extract annotations and train multiple deep learning models. A UNet model was initially used as a baseline. Further evaluation included convolutional neural networks (CNNs) and Vision Transformers to identify the best-performing architecture. Data augmentation techniques, such as rotation and translation, were applied to improve generalization.
Results: Preliminary results indicate strong alignment between model predictions and expert assessments. For instance, in a case labeled as having <1% blasts by pathologists, the model predicted 1.6%. In another case assessed as >20%, the model estimated 17.6%. These outcomes demonstrate the model's potential to approximate human evaluation with clinically relevant accuracy.
Conclusion: Deep learning models can significantly enhance the quantification of CD34+ blasts in bone marrow biopsies. By reducing variability and improving consistency, such tools have the potential to support hematopathologists and improve diagnostic workflows in clinical practice.

E-PS-08-029
helloAmyloid: transforming amyloid screening with deep learning on smartphone-derived H&E images
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Background & Objectives: Amyloid deposition in renal biopsies is confirmed by Congo Red staining under polarized light, though H&E remains routine. Over the past 6–7 years, we used Congo Red routinely, and using this data, we developed an almost no-cost, instant approach—helloAmyloid software—to predict amyloid accumulation directly from smartphone photographs of H&E sections as a screening (and eventually diagnostic) test. Images were captured through a microscope at 40× magnification using an iPhone 15, based on the hypothesis that a deep learning model could identify deposits prior to confirmatory staining.
Methods: We collected 1196 positive and 1224 negative H&E photographs (verified by Congo Red under polarized light on the same regions). Negative images were selected from areas morphologically mimicking amyloid in conditions such as diabetes, monoclonal gammopathy, hypertension, and FSGS. The central one-third of each image was cropped to yield 1900×1900 pixel patches, then resized to 950×950. A custom TensorFlow model (~4 million parameters) was trained on Google Colab using A100 and L4 GPUs. Performance metrics and the confusion matrix were determined at an ideal threshold (Youden index: 0.4157).
Results: The model achieved an AUC of 0.910 (DeLong test p=0.0184), with a sensitivity of 0.93 and specificity of 0.77 among 564 test images. These results indicate that our approach reliably distinguishes amyloid deposits from routine H&E preparations, achieving a high true positive rate with acceptable false positives.
Conclusion: HelloAmyloid v0.21 demonstrates high sensitivity and acceptable specificity in detecting amyloid deposits from H&E images. As the dataset expands and the model is refined, further improvements are expected. Moreover, we plan to extend the dataset to include images from other tissue types, exploring the model's potential as a universal screening tool. Ultimately, this approach may streamline early renal amyloid detection and reduce reliance on additional staining in resource and time-limited settings.

E-PS-08-030
The 3D fusion of complex medical image data in virtual reality
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Background & Objectives: In our research, we focus on 3-dimensional (3D) fusion of data from different imaging modalities used in medicine. The main objective of our research was to design and develop a system in which CT/micro-CT images can be combined with their corresponding histological samples in 3D, allowing the user to examine any displayed tomogram from any sectional plane. In addition, in our research we aimed to be able to interactively display different measurement data in 3D to the user.
Methods: We implemented 3D data visualizations using a graphical engine. For our solution to produce the fused 3D image data, the CT image and the corresponding histological serial section are required as input parameters.
Results: We designed and developed a software solution that can simultaneously display 3D information from different imaging modalities to researchers in virtual reality (VR). With our solution, the user can see in 3D space exactly from where in the radiological tomogram the histological sample was taken. Our software is capable of multi-level 3D data visualization, i.e. the display of multiple tomograms embedded in each other. The software solution developed by us provides the user with the possibility to interactively display various diagnostic measurement data in 3D, in addition to the fused display of complex 3D image data structures. This allows us to provide the doctor with more data, reducing the time needed to make a diagnosis and increasing its accuracy.
Conclusion: In our research, we designed and developed a solution that can display complex, embedded 3D data structures to the user. Thanks to the embedded 3D data structures, the user can view different tomograms at the same time, allowing a quick overview along any virtual sectional plane. The VR solution we have developed provides a completely new perspective for doctors/researchers in terms of visualizing complex image data structures.

E-PS-08-031
A MedSAM-based interactive annotation tool for efficient and consistent pathology image segmentation
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Background & Objectives: Accurate and consistent annotation of pathology whole slide images (WSIs) is essential for developing AI models for cancer diagnosis and prognosis.
However, the annotation process is time-consuming and often suffers from inter-observer variability due to the ultra-high resolution and complex tissue structures present in pathology images.

Such variability directly impacts the reliability and generalization of AI models.
To address these challenges, we developed an annotation tool optimized for pathology image segmentation by integrating OpenSlide, PyQt5, and MedSAM, aiming to provide an efficient and consistent annotation workflow.
Methods: The proposed tool extracts region-specific tiles from WSIs using OpenSlide, enabling lightweight handling of large-scale pathology images without memory overload.
Through a PyQt5-based interactive interface, users can intuitively navigate WSIs using pan and zoom, and define regions of interest (ROIs) within each tile using point- or box-based prompts.
These prompts help MedSAM effectively segment ambiguous or complex tissue structures by incorporating expert guidance.
Users can interactively visualize, refine, and correct the generated segmentation masks in real-time.
The annotation results can be exported as binary mask images in either PNG or JPG format, along with annotation metadata in JSON or XML format, supporting practical usage for AI training and pathology analysis.
Results: The tool was evaluated on the Camelyon16 dataset for breast cancer metastasis detection.
The results demonstrated that the proposed tool significantly reduced annotation time while improving the accuracy and consistency of tumour region segmentation.
The combination of prompt-based input and automatic segmentation showed superior performance compared to automatic segmentation alone.
Conclusion: The proposed tool improves the efficiency, accuracy, and consistency of pathology image annotation.
It not only supports AI-based histopathological research but also serves as a practical assistant for pathologists by reducing annotation workload and facilitating consistent and efficient labelling in routine practice.

Funding: This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: RS-2021-KH113146)

E-PS-08-033

Evaluating the concordance between artificial intelligence and traditional histopathology in breast carcinoma grading

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Background & Objectives: Breast carcinoma is the most prevalent malignancy among women, with global incidence rates increasing by 0.5-1% annually. Traditionally, diagnosis relies on histopathological examination of stained haematoxylin and eosin (H&E) slides providing insights into tumour morphology. Advancements in Artificial Intelligence (AI) offer potential to enhance diagnostic accuracy by efficiently analysing datasets, reducing human error, and improving objectivity. This study aims to compare the performance of an AI model in grading breast carcinoma with the conventional H&E-based grading method.
Methods: Conducted at the Department of Pathology, a tertiary care medical college. The study included pathology slides from patients who underwent radical surgeries such as wide local excision (WLE), breast-conserving surgery (BCS), and modified radical mastectomy (MRMS). Cases of invasive ductal carcinoma (IDC) were analysed using routine histopathological methods and an AI model. The AI's grading was compared to the Bloom-Richardson grading system by CAP reporting.
Results: A total of 48 cases were included, with patient ages ranging from 40 to 81 years; all were female. Tumour sizes ranged from 0.5 to 3.5 cm, with 36 left-sided and 12 right-sided tumours. The Bloom-Richardson grading revealed 16 Grade I (34%), 20 Grade II (41%), and 12 Grade III (25%) tumours. In comparison, the AI model classified 40 tumours as Grade I (83.4%), 8 as Grade II (16.6%), and none as Grade III.
Conclusion: The AI model demonstrated a tendency to under-grade tumours, particularly in identifying higher-grade cases. This suggests that the current AI model may not fully capture tumour heterogeneity discernible by pathologists. Therefore, AI alone may not suffice for accurate breast cancer grading. Integrating AI with human expertise is essential for reliable diagnoses. Further validation through larger, multicentric studies is needed to enhance the AI model's accuracy prior to its integration into clinical practice.

E-PS-08-034

LazySlide: efficient whole-slide imaging analysis framework across scales and modalities

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Background & Objectives: Computational pathology is advancing disease detection and classification, yet integrating histopathological images with other data modalities like clinical reports and genomics data remains challenging. Despite technological progress in whole-slide imaging (WSI) analysis, existing software solutions often operate in isolation, creating inefficiencies in data integration and limiting cross-scale analysis capabilities. This complexity presents substantial barriers for researchers seeking to conduct comprehensive multimodal studies. Thus, we propose a new interoperable, scalable framework that enables users of varied experience levels to analyse histopathological data across different scales and modalities.
Methods: We developed LazySlide (https://github.com/rendeirolab/LazySlide), an open-source Python package designed to enhance multimodal WSI analysis in clinical research. LazySlide enables efficient handling of WSIs across formats, providing efficient image processing capabilities across multiple spatial scales—from whole-slide overview, and regions of interest, to cellular features. The framework includes comprehensive functionalities such as quality control, automated segmentation of tissues, microanatomical structures and cells, morphological feature extraction using deep learning models, and integration with multiple data modalities such as clinical text reports and genomics data. Integration with workflow management systems ensures scalability to large cohorts while maintaining the reproducibility of analytical pipelines.
Results: LazySlide demonstrates superior efficiency in cross-scale analysis of gigapixel WSI data compared to existing solutions. The framework enables simultaneous investigation of mesoscopic tissue architecture and microscopic cellular morphology, with seamless integration of additional data modalities such as genomic profiles and clinical parameters. This multi-scale, multimodal approach has been applied in research across multiple pathologies, revealing clinicopathological associations that were previously difficult to detect using traditional single-modality analysis methods.
Conclusion: LazySlide streamlines multimodal, cross-scale analysis of histopathological data, facilitating the discovery of comprehensive insights into disease biology. It supports biomarker discovery and improved patient stratification, offering a practical tool for advancing translational pathology research.

E-PS-08-037

AI-driven pathology and proteasome localization: advancing clinical prognosis in multiple myeloma

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Background & Objectives: Multiple Myeloma (MM) is a plasma cell malignancy characterized by clonal synthesis of immunoglobulins. In accordance, proteasome inhibitors have been used in the treatment of MM, as they aggravate the stress experienced by MM cells, leading to their death. Recent evidence provides further mechanistic insights into the roles of the proteasome in MM, pointing out a link between the subcellular localization of the proteolytic complex and patients' response to treatment. However, extracting this localization information at the single-cell level across whole-slide biopsies remains labor-intensive, expensive, and impractical for clinical translation, motivating the development of automated computational approaches. Current computational pathology methods in MM are limited, typically focusing only on small tissue regions or cell analyses, requiring costly manual annotations with limited scalability. Here, we investigate whether advanced foundation model-based artificial intelligence (AI) approaches, leveraging large-scale pretraining, can accurately detect subcellular proteasome localization, towards prognosis in MM.
Methods: We developed a novel double-staining immunohistochemistry (IHC) protocol enabling simultaneous visualization of malignant cells and proteasome localization across entire biopsy slides from MM patients. Whole-slide biopsies were annotated at the tile level based on proteasome localization. We applied AI models to compare the predictive performance of a pretrained foundation model (GigaPath) with a conventional deep learning baseline for tile-level proteasome localization classification.
Results: The pretrained foundation model (GigaPath) achieved higher accuracy, F1-score, and AUC-ROC (7%,6%,4% improvement respectively) compared to the baseline deep learning model, without fine-tuning, demonstrating superior predictive performance for detecting proteasome subcellular localization, along with the ability to integrate whole slide information.
Conclusion: Our study highlights the feasibility and potential of leveraging pretrained foundation models to automate the detection of proteasome subcellular localization in MM biopsies, towards novel prognostic biomarkers. Ongoing work aims to integrate whole-slide proteasome localization data into a single predictive model for clinical outcomes such as patient survival and treatment response.

Funding: A.C. is supported by grants from the Israel Science Foundation (ISF), the Israel Personal Medicine Partnership (IPMP) administered by the ISF, the Rappaport Foundation, by a gift donated by Craig Darian and the late Albert Sweet and administered by the American Technion Society (ATS), and by a collaborative grant from the Adelson Medical Research Foundation (AMRF). A.C. is an Israel Cancer Research Fund (ICRF) USA Professor. A.C. and M.S. are supported by a collaborative grant from IBM

E-PS-08-038

AI-assisted analysis of HER2-low and ultra-low breast cancer in correlation with low ER and PR expression

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Background & Objectives: HER2-low and HER2-ultralow breast cancer classifications have emerged as distinct subgroups with potential therapeutic implications. Understanding their correlation with oestrogen receptor (ER) expression, particularly ER-low cases, is crucial for refining treatment strategies. This study utilizes AI-driven analysis to assess the relationship between HER2-low, HER2-ultralow, and PR and ER-low breast cancer cases.
Methods: A dataset of 105 comprising breast cancer biopsies analysed prospective via AI-assisted immunohistochemistry (IHC) was evaluated. HER2 expression was categorized as low (IHC 1+ or IHC 2+/non-amplified) and ultralow (IHC 0 with faint staining). ER expression levels were stratified, focusing on ER-low cases (defined as 1–10% ER positivity), and the same definition for PR. AI-assisted quantification Mindpeak provided an objective assessment of biomarker expression.
Results: Findings indicate a higher prevalence of HER2-low status in ER-low tumours compared to HER2-ultralow. The correlation suggests a potential biological link between ER-low expression and HER2-low tumours, which may influence responsiveness to targeted therapies. Additionally, HER2-ultralow cases exhibited a broader range of ER expression, with a subset showing ER-low characteristics.
Conclusion: AI analysis confirms a significant correlation between HER2-low and ER-low breast cancer cases, supporting the hypothesis that these tumours may represent a unique biological entity. Further research is warranted to explore the therapeutic implications, particularly in the context of novel antibody-drug conjugates targeting HER2-low disease.

Conclusion on HER2, ER, PR, and KI-67 Differences

1. **HER2:**
   HER2-Low (score 1+ or 2+ without amplification) represents **53%** of cases.
   HER2-Ultra-Low (score 0 but with detectable expression) accounts for **27%** of cases.
2. **Hormone Receptor Expression:**
   High Estrogen Receptor (ER) Expression is dominant, with no recorded cases of low ER expression in this dataset.
   High Progesterone Receptor (PR) Expression is also prevalent, with no cases of low PR expression reported.
3. **(KI-67):**
   High Proliferation (>20%) is observed in **30%** of cases.
   Low Proliferation (≤20%) is seen in **68%** of cases.

E-PS-08-039

Using 3D histology to create training data for deep learning

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Background & Objectives: Deep learning has numerous applications in histopathology, including cell segmentation, cancer diagnosis, cancer grading, metastasis detection and prognosis prediction. While model architectures are well researched by computer scientists, insufficient data is often the bottleneck of deep learning in histopathology. Since traditional 2D histology requires labour-intensive sectioning and staining steps, we aim to use 3D histology to produce data for training a tissue classification model.
Methods: We obtained 6 tissue blocks of different tissue types (ileum, lung, pancreas, spleen, tongue epithelium, tongue muscle). Each tissue block underwent the 3D histology protocol. We performed oblique 3D slicing to increase the amount and variety of training images, as this was the key advantage of 3D histology over 2D histology. After that, we used this dataset to train a model to classify the 6 tissue types. We used the EfficientNetB0 model architecture pretrained on ImageNet.

We evaluated the model using a testing dataset of real-world H&E images unseen by the model.
Results: The model achieved 99.4% accuracy on the training dataset and 91.0% accuracy on the testing dataset. On the testing dataset, the model performed well on ileum, lung, spleen and tongue epithelium. Notably, the model could classify ileum images correctly despite variations in longitudinal, transverse and tangential images. However, the model performed less well on pancreas and tongue muscle. We found that discrepancies between training and testing images led to poorer classification performance of pancreas and tongue muscle.
Conclusion: Although we have only used 1 tissue block for each tissue type, we could already train a model which achieves 91.0% classification accuracy on real-world images. This shows the remarkable ability of 3D histology to use limited tissue blocks to generate training data for deep learning.

E-PS-08-041
Does size and colour matter in computational pathology? First results
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Background & Objectives: Computational pathology is gaining increasing popularity, expanding both its clinical applications and computational demands. Unlike radiology, digital pathology relies on extremely high-resolution, colour-rich images, resulting in substantial storage and processing requirements. This raises a critical question: are high magnifications and colour information truly essential for computational pathology models?
Methods: We analysed three open-access datasets: RINGS (prostate cancer, tile-based, binary segmentation), CoCaHis (colon cancer, tile-based, binary segmentation), and PANDA (prostate cancer, whole-slide images, multi-class segmentation). Each dataset was used to train a U-Net model implemented in PyTorch Lightning with MONAI, utilizing both colour and grayscale inputs. For PANDA, models were trained at 5x (colour + grayscale) and 10x (only colour) magnifications. An approximate 80/20 train-test split was applied. To ensure consistency in colour models, H&E staining was normalized using the modified Reinhard method.
Results: On validation data, the PANDA model trained at 5x outperformed the 10x model (Dice: 68.74% vs. 64.49%), but this trend reversed on the test set (47.10% vs. 63.94%). For CoCaHis, colour-based models consistently outperformed grayscale models (validation Dice: 80.07% vs. 50.87%; test Dice: 51.38% vs. 39.80%). The same pattern was observed for the RINGS dataset (validation Dice: 59.13% vs. 52.36%, test Dice: 61.42% vs 50.96%). For PANDA at 5x magnification, the colour model performed better during validation (68.74% vs. 63.81%) but worse during testing (47.10% vs. 61.95%).
Conclusion: Color input generally improved performance, though not universally. Similarly, higher resolution enhanced test performance in the PANDA dataset. These findings align with current best practices but suggest that the benefits from high resolution and colour may not always be consistent. As these are preliminary results, further investigation is needed to determine when such enhancements are truly justified. Limitations such as inprecise labels, the use of only three datasets (with only one whole-slide image dataset) should be addressed in following work.

E-PS-08-042
Virtual H&E staining and computer assisted assessment of lymph node metastases in colorectal carcinoma and neck dissections
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Background & Objectives: A chemical produced H&E- stain (Haematoxylin and Eosin) is high in resources and needed chemicals. To find a more sustainable and faster alternative an algorithm to virtually stain tissue was developed and applied to tissue specimens processed in daily routine. A computer assisted detection method for automated detection of metastasis in lymph nodes was also applied. Comparison of the results with standard processing and histological evaluation enabled a proof of concept of this attempt.
Methods: Slides of unstained tissue were scanned using a commercially available scanner and virtually stained using a research software optimized to the features of the scanner. Evaluation of virtual stainings was done by a team of pathologists. Then standard H&E stainings were done and microscopic evaluation followed. Results of virtually stained and H&E stained slides were compared added by the results of the computer assisted assessment of lymph node metastases.
Results: Lymph nodes in 43 cases of colorectal carcinoma and 20 cases of neck dissections were analysed. In both groups of tissue no significant difference was found between virtual and H&E-stained slides (Fig. 1). Moreover, the computer assistance was able to detect metastasis in lymph nodes of colorectal carcinoma with computer assistance with a sensitivity of 100% and a specificity of 93%.
Conclusion: These data demonstrate, that it is possible to apply virtual staining in a sufficient and reliable way. This possibly will help to improve diagnostic processes by avoiding time consuming staining processes. Moreover, it is possible to save tissue sections useable for other additional stainings and/or molecular analysis. Overall, these algorithms could change the way of staining and evaluating tissue in the long. At the time there has to be spent further efforts to integrate these algorithms in daily routine work. Nevertheless, we assume these efforts as worth it.

E-PS-08-043
Stepping into digital transformation of a pathologist's work in Greece
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Background & Objectives: Digital Pathology (DP) transforms the everyday workflow of Pathologists. Although Greek hospitals have not integrated DP yet, there is growing interest towards upgrading the healthcare system. A group of Pathologists decided to capture the willingness for that advancement by making a thorough questionnaire.
Methods: After a thorough literature review, seven pathologists created a questionnaire consisting of 46 questions—categorized into different sections—on the current use of and views on digital pathology. This questionnaire was distributed electronically among members of the Hellenic Society of Pathology. The response format included

yes/no questions, multiple-choice dropdowns, and one open-ended question.
Results: A total of 118 responses were obtained, from pathologists of various age groups and professional experience levels. Despite 78% having read relevant literature, only 33% reported DP usage, mainly for education and research. Most respondents (82.5%) considered DP necessary, >70% would use DP for primary diagnosis and IHC evaluation, and 47.9% support full implementation within the next five years. DP was considered useful mainly for remote diagnosis (90.7%) and access to expert opinions (85.6%), while technical problems (57.8%) and cyber security (49.5%) were major risks. The lack of a national strategic plan (95,1%), relevant infrastructure (93,5%), and DP value recognition by Hospital Administrations (80,7%) and high costs (84,5%) were identified as major barriers in DP integration.
Conclusion: Overall, the findings highlight a strong interest in Digital Pathology (DP). However, concerns about technical infrastructure, training requirements, and regulatory frameworks remain significant. Addressing these challenges requires a coordinated effort from healthcare institutions, professional societies, and policy makers. As awareness builds around the experience of pathology laboratories around the world that have already moved towards the digital way, more and more surveys conclude into the advantages of the new work environment of Pathologists.
Acknowledgements: We would like to thank the Hellenic Society of Pathology for its support.

E-PS-08-044
Application of digital pathology foundation models for disease scoring in MASH
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Background & Objectives: Liver biopsy remains the gold standard for assessing metabolic dysfunction-associated steatohepatitis (MASH) due to its direct examination of hepatic histological abnormalities. However, the complex pathological features in MASH and inconsistent disease definition may lead to inter-/intra-pathologist score variability. Artificial Intelligence (AI) may offer a solution by providing more consistent and granular continuous scoring, which enhances the evaluation of disease progression or treatment response. Foundation models maximize AI's potential through self-supervised learning, allowing an increasingly larger model to be trained on a wealth of unannotated datasets. Here, we evaluated the application of several recently developed foundation models in computational pathology for MASH scoring.
Methods: We utilized 120 H&E-stained & Masson's Trichrome (MT)-stained whole slide images (WSIs), with the associated NASH-CRN scores evaluated by four expert hepatopathologists. We employed three foundation models (UNI, Prov-Gigapath, H-optimus-0) on the H&E WSIs, divided into 256x256 non-overlapping patches at 20x, to extract feature representations of each patch and fit a linear regression model on the max-pooled features. Model performance was evaluated using Pearson's correlation between the predicted score and the median pathologists' grading on a 5-fold cross validation run.
Results: The foundation models overall achieved high correlation on most NASH-CRN categories, with H-optimus-0 outperforming all other foundation models in the benchmark (fibrosis: 0.83, steatosis: 0.8, ballooning: 0.67, lobular inflammation: 0.38). Most interestingly, all foundation models achieved a correlation greater than 0.7 on H&E WSIs against pathologists' fibrosis stage graded on MT slides, indicating that the models can capture subtle fibrotic features on H&E-stained slides that may not be as apparent to pathologists.
Conclusion: Our results highlight the potential of foundation model for future deployment in MASH scoring. Future work needs to include a more rigorous testing and benchmarking across a wider patient cohort as well as model explainability to foster greater trust between AI and pathologists.

E-PS-08-045
Unhuddle: a heuristic method for deconvolution of shared border signal in image-based spatial proteomics
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Background & Objectives: Histopathology and immunohistochemistry (IHC) are foundational for cancer diagnosis and classification. Recently, understanding the local immune environment has gained prominence due to advances in immunotherapy. Highly multiplexed IHC methods (>20 markers) enable simultaneous analysis of numerous immune markers within tissue sections but pose substantial interpretative challenges, requiring robust computational pipelines. A common step in spatial analysis is cell segmentation, which attributes signal intensities to individual cells. However, most existing approaches rely on absolute segmentation, which fails to account for shared signal at the cell-cell borders, originating from insufficient resolution, lateral bleed of signal, and z-level overlap. Without correction, this "neighbor noise" leads to systematic misclassification of cell types. This issue is particularly pronounced in dense tissues, where typically >50% of informative pixels for a cell's membrane marker are located in the outer border (benchmark: 1um resolution).
Methods: We developed a computational workflow to correct shared intensity at cell-cell borders via deconvolution, following absolute segmentation in image-based spatial proteomics. We validated the method on *in silico* tissues reconstructed from individually curated cells, serving as ground truth. And we benchmarked performance on real-world human lymphoma data, by measuring the fraction of ambiguous phenotype calls using a pre-trained random forest classifier.
Results: Unhuddle reduced error to ground truth in reconstructed tissues and in 68 real-world lymph node and lymphoma samples, Unhuddle assigned definitive phenotypes in 63% of prior ambiguous cells.
Conclusion: The "Unhuddle" algorithm effectively resolves a significant part of segmentation-related noise in multiplexed IHC images, enhancing accuracy in high-density tissues such as lymphoid tissues or infiltrates. We envision that integration of this method into high-plex IHC workflows will improve phenotypic accuracy, allowing identification of subtle variations in the immune microenvironment. Consequently, Unhuddle has the potential to drive novel spatial biomarker discovery and enhance the selection of personalized immunotherapeutic strategies in oncology and diagnostic pathology.

Funding: MSCA-PF 2024

E-PS-08-048
Artificial Intelligence-based detection of Tumour-Infiltrating Lymphocytes (TILs) in breast carcinomas: an approach
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Background & Objectives: Tumour-Infiltrating Lymphocytes (TILs) constitute an important biomarker, with an increasingly developing importance in the prognostic assessment and therapeutic interventions of triple-negative breast carcinomas (TNBCs). High TILs scores have been linked with better overall prognosis of TNBCs, while they indicate them as potential candidates for immunotherapy. Artificial Intelligence (AI) algorithms have been recently developed to assist and facilitate the time-consuming process of biomarkers assessment in H/E slides. The aim of this study is to evaluate a novel system of TILs detection in breast carcinomas, and to discuss its advantages and disadvantages.
Methods: 86 cases of breast carcinomas, either NST or lobular type, have been selected for the study. The H/E slides were scanned, and digital slides were uploaded in V7 annotation platform. The annotation process included, for each slide, 4 tissue segmentation Regions Of Interest (ROIs) and 4 cellular detection ROIs, in order to train the EidosAI™ Technology algorithm to estimate TILs scores. Two pathologists assessed the slides and excluded the TILs scores for each slide. The TILs scores of the pathologists and the pertinent scores of the algorithm were analysed.
Results: The provisional results showed an overall good concordance between the pathologists and the AI algorithm, regarding the compared TILs scores. There was a slightly increased estimation according to AI algorithm (mean TILs percentage 5.6%), while the remaining 64% of cases were underestimated by the algorithm (mean TILs percentage 13%). Interestingly, lobular carcinomas, mimicking lymphoplasmacytic infiltrates, showed a severe discordance. Additional technical interventions, as well as better case selection, are needed to optimize the observed results.
Conclusion: AI technology may be of great assistance in the detection of TILs scores in breast carcinomas, aiding the pathologists in their routine. Thorough training of the AI-based algorithms is of paramount importance, in order to surpass possible discrepancies between pathologists and algorithms.

E-PS-08-049
Determining the significance of tumour-stroma ratio in high-grade serous ovarian carcinomas using multi-prototype few shot learning
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Background & Objectives: Tumour-Stroma ratio (TSR) has been shown to be as a marker of clinical outcome in various solid tumour entities (Wu et al., 2016). However, in the case of ovarian carcinomas, its overall significance is still unclear, due to limited cohort sizes and lack of standardization in determination of TSR (Lou et al., 2024). In this work, we develop a segmentation algorithm allowing us to quantitatively determine TSR in high-grade serous ovarian carcinomas.
Methods: A cohort of 150 cases of high-grade serous ovarian carcinomas was compiled, comprising clinical information on overall survival and progression-free survival. Histologic slides were digitized on a Hamamatsu S210 digital slide scanner at a resolution of 0.22µm/pixel. Using a multi-prototype few-shot learning approach (Benz et al., 2024), an existing segmentation algorithm for colorectal carcinomas was adapted to be applied for segmenting tumour and stroma components, among other histologically relevant compartments (fat, blood vessels, corpus albicans, necrosis) in the Ovarian Carcinoma Cohort. Segmentation quality was supervised by two pathologists. Overall, prototypes were drawn from a sub-cohort of 10 slides.
Results: The network adapted by multi-prototype few-shot learning provided good segmentation quality that captured relevant histologic compartments well across the cohort. Our results show a consistent tendency of low-TSR cases to be associated with reduced overall survival and progression-free survival in our cohort.
Conclusion: Multi-prototype few-shot learning allows developing a consistent and precise segmentation algorithm for high-grade serous ovarian carcinomas. Building on segmentation results, we find that in a cohort of 150 high-grade serous ovarian carcinomas, lower TSR tends to be associated with worse outcome.

E-PS-08-050
Out-of-hospital Digital Pathology environment for increased security, full remote access and important cost reduction
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Background & Objectives: Digital Pathology has demonstrated its importance in the progress of our discipline and the capacity to improve efficiency and to implement continuous advances led by artificial intelligence. The main obstacle to its implementation remains in its high cost.
We have designed a system to achieve significant cost reductions, while improving telecommunications security issues, and facilitating remote out-of-hospital access.
Methods: We operate in three independent private hospitals 80 km apart, with a staff of 10 pathologists, and three scanners of different vendors (Leica GT450, Hamamatsu S210 and 3D-Histech Panoramic-Midi) running on the same Hamamatsu NzConnect server with full compatibility. To meet our objectives, the digital diagnostic server is external and the usual reporting infrastructure has been separated and remains within the hospital intranet with its HIS and LIS. Pathologists use dual monitors to connect to the digital slides server and the LIS. The diagnostic server does not include any patient information or metadata to minimise security risks.
Results: The connection to the hospital LIS is made in the remote accesses through a VPN configured by the hospital IT team and to the diagnostic server with a double access system: web-based and with an independent VPN based on Tailscale. Pathologists have simultaneous access to both servers to perform their work, which can be carried out from any location without the need to be present in the hospital.
Conclusion: The use of the LIS already implemented and separated from the diagnostic server avoids the need for complex integration processes, of a network organisation and the provision of security measures. This reduces the costs of the digital pathology system to hardware (scanners) and minimal server software costs, while maintaining the full efficiency of the digital transition.

E-PS-08-051
IHC staining intensity normalization to account for IHC variability in quantitative computational pathology analysis
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Background & Objectives: Immunohistochemical (IHC) staining is commonly employed to assess target expression, which is essential for patient stratification and drug development. Computational methods like Quantitative Continuous Scoring (QCS) can be utilized for highly accurate and reproducible measurement of staining intensities in IHC. IHC staining can vary based on sample preparation, assays,

and scanners, leading to slight fluctuations in the measured raw staining intensities. To enhance the comparability and consistency of measurements across different batches, we have developed a normalization approach for staining intensities.
Methods: To develop and test our approach we used cell line pellets (N=10) embedded into cell micro arrays (CMAs), providing a highly controlled environment. Replicates (N=12) of consecutive slides were prepared on different days. The cell lines exhibited expression levels from negative to high when stained with an established membrane marker, and staining intensities were quantified using QCS. We calculated the *minimum*, *medium*, and *maximum* staining intensities per slide based on three selected cell lines with established negative, medium, and maximum expression levels. To account for the observed IHC variability we developed a step-wise linear minimum-medium-maximum normalization approach that transforms the raw staining intensity distribution per slide such that its *minimum* is shifted to 0, its *maximum* to a fixed constant SI_{max} and its *medium* to $SI_{max}/2$.
Results: By applying our normalization scheme, we achieved a significant decrease in variability of IHC staining intensity. This reduction was observed in all CMA cores and was quantified using the Normalized Root Mean Square Deviation (NRMSD) per core across all slides (average NRMSD-baseline: 0.046, average NRMSD-normalized: 0.020, Wilcoxon $p<0.001$).
Conclusion: This proof-of-concept study demonstrates that normalization significantly enhances the consistency of IHC staining intensity measurements. By utilizing on-slide or batch controls to determine *minimum*, *medium*, and *maximum* staining intensities of the analysed data, our approach can be readily applied to reduce inter-slide or inter-batch variability.

E-PS-08-052
Pathology image generation with flow matching diffusion models
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Background & Objectives: Generative models offer an alternative data source that overcomes issues such as scarcity, manual labelling, and privacy concerns. Early generative architectures such as Generative Adversarial Models (GANs) have been widely used across medical applications. Despite the high quality image generation, GANs lack diversity, are unstable, and suffer from mode collapse. Denoising Diffusion Probabilistic Models (DDPMs) offer a more stable alternative that can outperform the image quality of GANs. However, these models work by iterative denoising through numerical ordinal differential equation solvers, leading to slow inference. Here, we employ optimal transport flow matching diffusion to accelerate training and inference time.
Methods: We extracted 5000 images patches from 112 WSI of squamous cell carcinoma in situ biopsies. An optimal transport flow matching diffusion model based on a UNet backbone with flash attention was trained for 100 epochs using the images on a single NVIDIA RTX 3060Ti graphics card, using an Adam optimiser, a batch size of 4 and a learning rate of 0.0001. Synthetic images were subsequently generated using the trained model.
Results: Model training concluded after 6 hours. A total of 1000 images were generated in under 3 minutes of inference (0.163 seconds/patch). Pathologists were not able to reliably distinguish between the real and synthetic images. Pathologists (4 specialists, 6 residents) were given a Turing test with 20 images in which they were required to discriminate between real and synthetic images (10 images in each category). Specialists had a higher average accuracy than residents (51.66% vs. 44%).
Conclusion: Our study highlights how optimal transport flow matching diffusion models offer a lightweight, compute-efficient alternative to GANs and classical diffusion models. The model can be trained on several thousands of images in the span of a few hours on an affordable, consumer-grade GPU, while also providing practical inference times, all while generating reliable synthetic images.

E-PS-08-055
Artificial intelligence in the detection of homologous recombination deficiency in ovarian cancer
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Background & Objectives: In ovarian carcinoma, the primary molecular pathogenetic mechanism is homologous recombination deficiency (HRD), a repair dysfunction that leads to genomic instability (GI). Patients with HRD are eligible for therapy with PARP inhibitors. Currently, advanced molecular diagnostics are the only means of accurately assessing HRD deficiencies and GI.
Methods: Our study investigated the impact of GI on the microscopic morphology of ovarian cancer and explored the potential for its detection using artificial intelligence. Cancer slides were digitized using the Pannoramic P1000 digital slide scanner (3DHistech). Our dataset included 293 haematoxylin and eosin (H&E) stained whole-slide images (WSIs) scanned at high magnification with a resolution of 0.1219 µm/pixel and 388 WSIs scanned at standard magnification with a resolution of 0.2438 µm/pixel. Each WSI represents a representative slide from a different case.
All WSIs underwent automated quality control, feature extraction, and analysis using multi-instance learning (MIL) detection algorithms. The methodologies included fine-tuned ResNet-18 CNN models, which were analysed using either MIL VarAttention or a combination of CLAM/VarAttention with different feature sets. As the next step, we will use CNNs provided by Aiforia Create, part of the Aiforia Platform, to validate these results and to find complementary outcome of the study.
Results: For the high-resolution WSI dataset, the classifier achieved a mean area under the curve (AUC) of 0.8 and a mean F1 score of 0.71. For the lower-resolution dataset, both the mean AUC and F1 score were 0.71 and 0.64, respectively.
Conclusion: This suggests that microscopic morphology possesses distinct characteristics that could serve as criteria for genomic instability score (GIS) and HRD detection. Notably, in some cases, GIS/HRD positivity could be identified solely using H&E-stained WSIs. Our findings indicate that scanning at higher resolutions enhances detection accuracy, as most probably cell nuclear morphological features might play a significant role in the analysis.

E-PS-08-056
AI-assisted TPS and CPS scoring of PD-L1 expression in kidney cancer
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Background & Objectives: As part of the European Care1 project on metastatic kidney cancer, Programmed death-ligand 1 (PD-L1) expression is studied as a predictive biomarker for immune checkpoint

inhibitors (ICI) treatment. Quantified with eyeballing methods on immuno-histochemistry stains, their evaluation is laborious and suffers from moderate inter-observer variability. Pathologists could therefore benefit from Artificial Intelligence (AI) assistance in clinical diagnosis scenarios.
Methods: Using annotated whole slide images (WSIs) from CARE1 european project, we developed computer vision algorithms to select and segment tumour regions as well as the surrounding inflammatory regions. In those identified regions, Deep learning-based cell detection and classification are applied, including cell type and PD-L1 expression. Based on this data, tumour proliferative score (TPS) and combined positive score (CPS) are computed and compared to a threshold for positive or negative PD-L1 expression assessment.
Results: The proposed method enables consistent and precise localization of the diagnostic area in WSIs. We also demonstrate promising robust Deep learning algorithms in PD-L1 expression evaluation with accuracy metrics at slide-level on a multi-centric dataset.
Conclusion: In this study, we propose an end-to-end automatic pipeline able to both identify tissue regions on IHC WSIs and achieve accurate and efficient PD-L1 scoring.

E-PS-08-058
Enhancing security and traceability in clinical and forensic histopathology: a pilot study on digital pathology and secure data transmission
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Background & Objectives: The application of whole slide imaging (WSI) in forensic and clinical histopathology requires improvements to ensure the security and traceability of histopathological documentation in legal and medico-legal procedures. This study aims to enhance and ensure the security and privacy of the transmission of these image-based documents for judicial purposes.
Methods: A network and cloud infrastructure were set up for sharing these WSI with secure access controlled by user credentials. Following the updated recommendations from the College of American Pathologists Pathology and Laboratory Quality Centre, this pilot study assessed the reliability of a digital approach for forensic and clinical histopathological secure data transmission. The slides were digitized using the Aperio GT 450 DX Digital Slide Scanner (Leica Biosystems, Nussloch, Germany).
Results: A total of 160 representative slides of organic lesions related to deceased individuals, included in judicial records—both forensic and clinical autopsies—were digitized and transmitted via the local network to a cloud-based repository securely. In detail, the secure access to the repository was ensured through a four-step process: 1) multi-factor authentication, 2) role-based access control, 3) audit logging, and 4) secure network protocols. Only the coexistence of all four factors met the required security criteria.
Conclusion: This pilot study highlights the potential of digital pathology to improve the security, traceability, and efficiency of forensic histopathological documentation, while ensuring data integrity and confidentiality in legal contexts.

E-PS-08-059
Comparison of plasma cell quantification using digital pathology software in bone marrow trephines associated with multiple myeloma
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Background & Objectives: Diagnosis and prediction of treatment response in multiple myeloma is achieved by accessing plasma cell infiltrates in bone marrow trephines. Current methods involve manual interpretation of histologically stained bone marrow trephines by pathologists. However, current limitations include inter and intra observer variability, lack of reproducibility and is very time consuming. Advancements in digital pathology has allowed for faster and potentially more accurate method of plasma cell counts. Thus, we aimed to compare two digital pathology software's, Visiopharm® and Qupath, and analyse their accuracy against the current gold standard scoring method undertaken by pathologists.
Methods: Ten sections stained for plasma cell marker CD138 were analysed using both digital pathology software's and positive cell classification counts were compared to pathologist scoring. Analysis was undertaken using SPSS to calculate Pearson correlation for manual scoring vs Visiopharm® (Ma-Vi) and manual scoring vs Qupath (Ma-QU).
Results: Overall correlation for Ma-Vi and Ma-Qu were $r=0.96$ $p<0.001$ and $r=0.69$ $p<0.05$ respectively. For cases with diffuse plasma cell infiltrates, there was significant correlation associated with Ma-Vi ($r=0.99$ $p<0.001$) however Ma-Qu showed no significant correlation ($r=0.43$ $p>0.05$). Similarly, for cases with patchy infiltrates and aggregates, significant correlation was associated with Ma-Vi $r=0.95$ $P<0.05$ however Ma-Qu showed no significant correlation $r=0.41$ $p>0.05$.
Conclusion: These results suggest that digital pathology does offer a potentially viable alternative to accurately quantify plasma cell infiltrate. Visiopharm® demonstrated greater significant correlation with the pathologist compared to Qupath overall and in specific sub cases. Qupath struggled to identify both positive and negative cells in background/artefact regions. As Visiopharm® contains far more adjustable parameters and functions, it allowed for better characterisation of positive cell counts.

E-PS-08-060
The utility of AI-associated algorithm in determining the PD-L1 status in non-small cell lung cancer
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Background & Objectives: AI algorithms are increasingly being integrated into immune marker assessment, enhancing routine pathology workflows and reducing workload. However, their comparability with human pathologists remains uncertain, as potential inaccuracies could impact future treatment decisions. This study examined the compatibility of PD-L1 expression assessment in non-small cell lung cancer (NSCLC) between an expert pathologist and an AI algorithm.
Methods: The study cohort included 333 NSCLC cases evaluated by an expert pathologist and uPath, a VENTANA PD-L1 (SP263) Assay Algorithm. All slides were digitally scanned for whole-slide analysis. Samples were stained with the SP263 clone antibody, and PD-L1 expression was assessed using the TPS formula. Expression was

categorized as negative (TPS <1%), low (TPS 1–49%), or high (TPS ≥50%). Samples were considered PD-L1-positive if TPS was ≥1%.
Results: We observed a high level of concordance between uPath and pathologist assessments. In 317 cases (95.2%), the samples received the same PD-L1 status (κ = 0.945 [0.932–0.956]), and in 313 cases (94%), they were assigned the same PD-L1 category (κw = 0.92 [0.89–0.96]). There were no significant differences between the results provided by uPath and those given by the pathologist (p = 0.33). On average, PD-L1 expression assessed by uPath was 3 percentage points (pp) higher than that determined by the pathologist, with a 0.5 pp difference in the <1% TPS group, 6.7 pp in the 1–49% TPS group, and 4.3 pp in the ≥50% TPS group. Compared to the pathologist, uPath downstaged 13 cancers and upstaged 7. In our cohort, if clinical decisions had been based solely on uPath assessment, up to 6% of patients might have been affected.
Conclusion: AI-based algorithms show high concordance with expert pathologists in assessing PD-L1 status; however, relying solely on them may impact clinical decision-making. Until more high-quality data become available, verification by a pathologist is recommended.

E-PS-08-061
Digitisation of the London Neurodegenerative Diseases Brain Bank histology archive
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Background & Objectives: The London Neurodegenerative Diseases Brain Bank (LNDBB) is one of the largest brain banks in the United Kingdom with access to central nervous system (CNS) tissue from over 3,000 donors. Formalin-fixed, paraffin-embedded (FFPE) sections from multiple CNS regions stained with H&E, immunohistochemical markers and tinctorial stains are available. We set about digitising slides from over 640 patients, mainly with Alzheimer's disease (AD), with a view to creating a rich digital atlas of the histomorphological features of the CNS and its perturbation in AD.
Methods: Archived slides were retrieved, catalogued, and scanned using Hamamatsu NanoZoomer scanners (S360 and S60), with a custom mount for irregular format slides (2.0-RS). Scanning involved semi-automated focus point setting and quality checks, with rescanning as needed. Whole-slide images (WSI) were de-identified using a Python script/NZMask and uploaded to an OMERO server for management and visualisation.
Results: To date, 11,129 WSI from 271 cases (~40%) have been generated: 10,336 standard/mega and 793 irregular slides. Each case includes an average of 41 slides (range: 12–113), covering 47 CNS regions, seven of which are comprehensively covered (with data from at least 75% of the cases). H&E comprise 29% of the WSI; other common stains include Tau (20%), α-synuclein (15%), amyloid-β (12%), Bielschowsky (8%), TDP-43 (7%), and p62 (6%). The total data size is 30TB.
Conclusion: Despite format variability and data volume challenges, digitising the LNDBB archive is producing a high-value resource for neuropathology research. The WSI dataset will enable computational quantification of histological features and support the development of machine learning models for disease classification and staging. Integration with structured clinical data, whole genome sequencing, and spatial transcriptomics (being generated in parallel) will offer new opportunities for multi-modal analysis and deeper insight into disease mechanisms. The WSI database will be made available to the research community in due course.

Funding: The Jean Shanks Foundation/The Pathological Society of Great Britain & Ireland

E-PS-08-062
Computational pathology improves concordance of Her2-Low diagnosis in breast cancer between experts and routine pathologists from 64 countries using a dataset from CADQAS Her2 IHC digital interpretive proficiency testing (DIPT)
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Background & Objectives: CADQAS digital interpretive proficiency testing (DIPT) demonstrated high concordance in Her2 IHC diagnosis amongst participants using the two-tier system (Her2-Positive/Her2-Negative). With the three-tier system (Her2-Positive/Her2-Low/Her2-Negative), there were more clinical errors (20.58% for 3-tier versus 1.89% for 2-tier). We analysed the DIPT responses to identify cases that contributed to the most clinical errors and re-evaluated them using computational pathology to determine if it would improve concordance.
Methods: A total of 724 participants from 64 countries scored 61 cases (7783 scores) in CADQAS Her2 IHC PT from 2021 to date. We identified eight cases (12.5%) that had high discordance amongst DIPT participants. These cases were digitised using a Roche DP600 and assessed with the Roche Her2 algorithm. In parallel, a consensus diagnosis was provided by four experts. The eight cases were assessed independently and any discordance resolved through conference microscopy. Computer-aided diagnoses were compared with expert consensus to assess degree of concordance. We simulated the impact on diagnostic errors if computer-aided diagnoses were used by participants in these challenging cases.
Results: In the simulation, changing participants' diagnoses for computer-aided diagnoses for the eight challenging cases increased concordance with the expert consensus across the whole spectrum of 61 cases and reduced clinical errors. We describe these 8 challenging cases to define parameters identifying cases that should be referred prospectively for computational pathology.
Conclusion: The use of computational pathology for challenging cases improves concordance amongst pathologists. Greater improvement could be obtained by referring challenging cases for expert second opinion but this would impact turnaround times and is limited by capacity of expert pathologists. Implementing computer-aided assistance could be an effective tool to support pathologists in routine practice.

E-PS-08-063
Prediction of pulmonary adenocarcinoma driver mutations using whole slide images through a home made deep learning model
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Background & Objectives: Although driver mutations do not affect the test algorithm for lung adenocarcinomas (LACs), it is known that there are some relationships between morphology and driver mutations. Using artificial intelligence (AI), it may be possible to predict driver mutations based on morphological features. In this study, we aimed to

investigate the extent to which some common driver mutations in LAC can be predicted using AI on H&E (Haematoxylin and Eosin) sections.
Methods: We built a deep learning model (Lung Adenocarcinoma Mutation Prediction Software-LAMPS) to classify LAC mutation based on morphology utilizing 212,592 patches (1024x1024 resolution) from 162 NGS-confirmed cases across five mutation groups (1.KRAS-n:46, 2.EGFR-n:36, 3.BRAF-n:5, 4.Other-n:23, 5.Negative-N:47). We implemented a ResNet50 architecture using TensorFlow, fine-tuning the last 50 layers while preserving nuclear details at 512x512 resolution compatible with WSIs at x20 magnification. Training occurred on Google Colab's A100 GPU using case-based data splitting (70/15/15%) without augmentation to maintain morphological integrity. We employed adaptive learning rates (initial: 4e-5) with automatic reduction upon validation plateau. Classification decisions integrate patch-level predictions to determine case-level results.
Results: Preliminary results at epoch 2 demonstrate 36% case-level accuracy across five mutation groups, significantly exceeding random classification (20%). The model currently shows equivalent patch-level (36.26%) and case-level (36%) accuracy, suggesting consistent feature identification across magnification levels. The classifier performs better on groups with larger sample sizes (G1, G2, G5). We anticipate substantial improvement as training progresses through the remaining epochs with adaptive learning rate adjustments. Based on learning curve trajectories, we project final case-level accuracy above 70%.
Conclusion: LAMPS demonstrates promising potential for predicting LAC mutations from histomorphology providing cost-effective and rapid diagnostic approaches, and act as a screening tool particularly in regions with limited access to genetic testing. Future work will focus on continued training, incorporating additional patient data, and exploring specific histomorphological features associated with each mutation.

E-PS-08-064
Modeling the impact of recall bias on digital pathology and AI performance evaluation and validation
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Background & Objectives: Intra-pathologist concordance is a fundamental measure to examine the impact of an intervention on the diagnostic outcome. For example, when AI is clinically validated, a pathologist may be asked to review the same case with and without AI and the results may suggest improvement in accuracy, speed, or reproducibility. However, the influence of study design must also be considered, as viewing the same slide twice can introduce recall bias. Common approaches to reduce recall bias include:

- **Introducing a washout period.** However, as previously shown, even after doubling washout from 2 to 4 weeks ~30% of slides may still be recalled.
- **Randomizing presentation order.** Interleaving AI trials with the control can destroy the correlation between presentation order and the intervention, but for concordance studies the influence of recall persists.
- **Introducing a third trial.** Presenting the slide a third time can enable direct measure of the impact of recall by repeating a previous presentation.
- **Relying on inter-pathologist review.** Each pathologist's performance can be measured against their population results to estimate the effect of the intervention.

Methods: We developed a computational model to simulate the influence of recall bias in a validation study. We then simulated each of the above designs to model the impact of each approach on recall bias.

Results: We found that as recall magnitude and likelihood grows, concordance becomes overestimated. Introducing washout was insufficient to eliminate the impact of recall bias and was only effective when recall approached zero. We found that factors such as strategic and cognitive biases, expectation bias, and difficulty of the task differentially amplified these effects. Inter-pathologist review was the most effective method, but only when inter-pathologist variability was known or measured.
Conclusion: These results emphasize the importance of study design in any validation and provide a reference frame from which to better interpret studies in AI.

E-PS-09 E-Posters Electron Microscopy

E-PS-09-001
Collagen deposition of small bowel neuroendocrine tumour and associated mesenteric deposits under digital investigation
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Background & Objectives: Small bowel neuroendocrine tumours (sb-NETs) and related mesenteric tumour deposits (MTDs) can frequently present dense collagen and fibrosis. Remarkably, the relationship between collagen deposition in SB-NETs and MTDs has been poorly evaluated so far, despite their crucial clinical consequences for affected patients in terms of bowel obstruction and ischemia. In this setting, this study explored the relationship between sb-NETs and MTDs fibrosis via tissue-tethered collagen quantitation (CQ).
Methods: Sirius-Red-stained histology sections of sb-NETs and MTDs were retrospectively collected for whole slide image (WSI) development with Leica Aperio AT2 scanner. WSIs were analysed for CQ (i.e., percentage of tissue area occupied by collagen over the whole tissue area of interest) via an automated image analysis algorithm (ImageScope, software version 12.4). CQ was performed on sb-NETS and MTDs as a whole and in sb-NETS mucosa/submucosa and serosa/subserosa compartments.
Results: Seventy sb-NET patients (median age: 70.5 years; 48/70 males) and related MTDs (n=52) were analysed for CQ. Focusing on sb-NETs, we observed significantly higher ($p<0.001$) collagen deposition in the serosa/subserosa (mean CQ: 20.0%) compared to the mucosa/submucosa (mean CQ: 11.4%). The CQ of the sb-NETs as a whole (mean CQ: 14.6%) and of MTDs (mean CQ: 14.5%) did not differ significantly ($p=0.9$). Still, we observed a mild yet significant ($p=0.008$) positive correlation ($r=0.3$) between sb-NETs serosa/subserosa and MTDs CQ.
Conclusion: Our pilot study documented that the overall collagen deposition in sb-NETs and related MTDs did not differ significantly. However, MTD CQ was directly related to the CQ of the sb-NET serosa/subserosa compartment. These preliminary findings indicate that compartment collagen deposition rather than absolute quantitation may be relevant for sb-NET MTD patients. Therefore, we endeavor to further

enrich our tissue-tethered CQ analysis with spatial metabolomic and molecular granularity to evaluate and identify clinically meaningful predictive biomarkers.

E-PS-09-002

Ultrastructure of transformed smooth muscle cells in the myometrium of patients with placenta accreta spectrum

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Background & Objectives: The myometrium of patients with placenta accreta spectum disorder (PAS) in late gestation undergoes significant changes, especially in the area adjacent to the scar.
The aim of the study: To investigate the ultrastructure of smooth muscle cells (SMCs) in the periscar area.
Methods: The myometrium of 19 patients (28-42 years old) with a gestation of 32-38 weeks diagnosed with placenta increta, excised from the area adjacent to the scar, was examined. Tissue fragments were fixed with glutaraldehyde, embedded in araldite, samples were studied using a transmission electron microscope. Semi-thin sections were stained with PAS reaction.
Results: In the myometrium adjacent to the scar, a peculiar transformation of some SMCs was found (tSMCs), determined only at the ultrastructural level. tSMCs, with an average diameter of 5,2±1,1 μm, were located among SMCs of normal structure and size (average diameter 6,9±2,1 μm). The cytoplasm of tSMCs was almost completely devoid of myofibrils, contained ribosomes, small clusters of cisterns of granular endoplasmic reticulum, rare mitochondria, nuclei contained dispersed chromatin, fragments of dense bodies were visualized under the plasma membrane. An unusual feature of tSMCs were numerous protrusions of the plasmalemma, with the formation of bubbles, with a diameter of 1,55±0,64 μm, in which microvesicles were preserved. On semi-thin sections clusters of such bubbles were visible in the intercellular space near the SMCs. This resembles a peculiar variant of programmed cell death, but without the change in chromatin condensation characteristic of apoptosis. Such changes were recorded in 31,5% of cases.
Conclusion: In the myometrium of patients with PAS at 32-38 weeks of gestation, tSMCs with unusual ultrastructural signs of cytoplasm budding with the formation of "bubbles" were detected in the area adjacent to the scar. Perhaps, these signs may indicate the initiation of a previously unknown mechanism of peculiar cell death, which requires further study.

Funding: 123030700104-3

E-PS-10 E-Posters Endocrine Pathology

E-PS-10-001

Analysis of the effects of aggressive subtypes of papillary thyroid carcinoma. Histological subtype as a good predictor of clinical outcome

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Background & Objectives: Papillary thyroid carcinoma (PTC) is the most common malignant endocrine neoplasm. Currently, there are no reliable indicators to predict which cases will recur. For this reason, identifying aggressive histological subtypes (AS) is crucial, as it may indicate cases with a higher risk of recurrence. In this study, we aim to reclassify PTC according to the current criteria (WHO, 5th edition) to assess the impact of identifying AS on defining patients at higher risk of recurrence.
Methods: Retrospective cohort study. All PTC cases of AS diagnosed at our centre between 2000 and 2017 were selected as cases, and all non-aggressive subtype PTCs were selected as controls. Each case was histologically reviewed, excluding non-invasive follicular thyroid neoplasms with papillary carcinoma-like nuclear features (NIFTP) and incidental diagnoses. The PTC subtype was re-diagnosed and correlated with 5-year follow-up.
Results: A total of 313 cases were selected. 107 cases were excluded (15 NIFTP, 81 incidental diagnoses, and 11 incidental NIFTPs). Of the 206 included cases, 10 were AS (mean age 55 years, 60% women, 60% with affected lymph nodes at diagnosis; 8 tall cell subtype, 2 hobnail subtype) and 196 were non-aggressive subtypes (mean age 44 years, 75% women, 50% with affected lymph nodes at diagnosis; 72% classic subtype). AS, compared to non-aggressive subtypes, showed a higher frequency of recurrence (50% vs 6.6%, $p<0.05$), angiolymphatic and/or perineural invasion (70% vs 26%, $p<0.05$), and the only case of disease-related death within the 5-year follow-up.
Conclusion: Identifying AS in PTC is essential for identifying cases with a higher likelihood of recurrence. In our cases, aggressive subtypes represent 4.9% of cases but account for 27.8% of recurrent cases. Therefore, it is of utmost importance to identify them, as it seems useful to define a subgroup of patients at higher risk of recurrence.

E-PS-10-002

Unraveling neoplastic progression in NETs: comprehensive genomic profiling of two composite G1-G3 cases

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Background & Objectives: The molecular landscape of NETs is heterogeneous, varying by grade and anatomical site. Due to their rarity and diversity, comprehensive molecular profiling has been limited. G3 NETs have been shown to share a molecular profile with G1-G2 NETs, but little is known about neoplastic progression from G1 to G3. Here, we present two cases of composite NETs, one pancreatic and one rectal, with G1 and G3 components. Separate histopathological and deep genomic profiling on both components were performed, with the aim to investigate neoplastic progression.
Methods: Histological examination, immunohistochemical studies and molecular genetics testing were performed on FFPE material. Genomic profiling was performed with the Ion Torrent Oncomine™ Comprehensive Assay Plus (OCA-Plus), a NGS approach analysing more than 500 genes simultaneously in terms of single-gene variants, copy number variations (CNV) as well as other genetic parameters (e.g., MSI, LOH, GIM).
Results: **Pancreatic NET:** G1 component revealed a KMT2A missense mutation (VAF 64.2%) with no LOH, CNVs, or chromosomal structural aberrations. In contrast, G3 component harboured a VHL frameshift mutation (VAF 34.4%), multiple CNV losses (e.g. PTEN, ARID5B, PBRM1, RASA1), and chromosome arm loss (3q, 10q), with LOH increasing to 12.5%.
Rectal NET: G1 component exhibited a ST6GAL2 missense mutation and CNV losses of X-linked genes, while G3 showed an RBM10 indel (VAF 69.7%), widespread CNV losses (including but not limited to SETD2, ARID5B, PTEN, KMT2A, SMAD4), and a TSC2 gene gain.

The higher CNVs and LOH in rectal G3 NETs support a progressive accumulation of genomic alterations during tumour evolution.
Conclusion: This is the first report of two composite G1-G3 GEP NETs with deep molecular characterization, providing novel insights into neoplastic progression, particularly in rectal NETs, with potential implications for precision oncology.

E-PS-10-003
An almost impossible case - testicular adrenal rest tumour in a patient without congenital adrenal hyperplasia
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Background & Objectives: Testicular adrenal rest tumours (TARTs) are adrenal tumours that develop within the testicle. They are most commonly associated with congenital adrenal hyperplasia (CAH), where their prevalence ranges from 6% to 54%, depending on the subtype. However, in non-CAH populations, TARTs are exceedingly rare, with no documented cases in otherwise healthy individuals.
Methods: We present the case of a 43-year-old male who presented to the emergency room with left testicular pain. A local examination revealed a testicular mass of unclear origin, confirmed by ultrasound. The patient had undergone a left inferior polar nephrectomy two months earlier for clear cell renal cell carcinoma (CC-RCC). Given the potential for metastasis, an orchidectomy was performed. Blood tests ruled out CAH.
Results: Macroscopic examination revealed a 6mm, yellow, nodular mass within the testicular parenchyma, finely encapsulated. Microscopic analysis showed a nodular mass composed of medium- and large-sized cells with abundant multivacuolated cytoplasm, mitotically inactive. The cells were organized in nests separated by fine fibrous septa, with no areas of necrosis and a peripheral pseudocapsule. Immunohistochemistry showed positivity for SF1, MART-1, and AR, while S100, CAIX, PAX8, SALL4, and CD68 were negative. These findings support a diagnosis of TART with a cortical component and exclude the possibility of a metastatic nodule.

Conclusion: Although the clinical context and macroscopic appearance initially suggested a secondary tumour from CC-RCC, this case represents an extremely rare occurrence, likely the only documented instance in the literature. Immunohistochemistry was the sole reliable diagnostic tool in this case.

E-PS-10-004
Thyroid incidentalomas. The experience of a regional university hospital
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Background & Objectives: Papillary carcinoma (PTC) is the most common primary thyroid malignancy. It is clinically suspected after cervical examination and ultrasound examination of the lesion. Incidental pathological diagnosis in some autopsy series rises to 30%.
Methods: A retrospective review of thyroidectomy specimens received at our centre over the past 5 years was conducted, and the clinical characteristics of the patients and the pathological characteristics of the tumours were compiled for those specimens in which a malignant tumour was incidentally diagnosed. Thus, those procedures in which there was prior clinical, radiological, or cytological suspicion of a malignant thyroid tumour were excluded.
Results: Between 2020 and 2024, a total of 377 thyroidectomies were performed at our centre without prior suspicion of malignancy. Of these, 23 PTC(6%) were incidentally diagnosed. In these cases, the tumours had a median size of 5 mm (range, 1–50 mm); the most frequent histological subtype was the classic pattern (16, 69%). The remaining subtypes consisted of 3 cases of encapsulated PTC, 2 cases of encapsulated and invasive follicular papillary carcinoma, 1 case of tall cell variant, and 1 case with a solid-trabecular pattern. The tumour was multifocal in 3 cases; no bilateral tumours were detected. Lymphovascular invasion was identified in 2 cases. Six cases presented involvement of the thyroid capsule.
Conclusion: The incidental finding of papillary thyroid carcinoma in thyroidectomy specimens indicated for benign pathology is not uncommon and should be taken into account when performing the pathological study of these specimens. Although in most cases these are small, early-stage tumours, in which surgical resection is considered curative, their diagnosis is always important for subsequent patient follow-up. Therefore, it is always advisable to perform a comprehensive sampling of the specimen and actively search for them so that they do not go unnoticed.

E-PS-10-005
Atypical parathyroid adenomas - case report series
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Background & Objectives: Atypical parathyroid adenoma (APA) is a rare entity within the spectrum of parathyroid neoplasms, exhibiting histological features suggestive of malignancy but lacking the definitive criteria for parathyroid carcinoma. APA is defined as an intermediate lesion, requiring careful evaluation due to its uncertain malignant potential. Given its atypical histopathological features and potential for recurrence, an accurate diagnosis is critical for optimizing clinical management. This case series presents three patients diagnosed with APA, highlighting the diagnostic challenges and surgical outcomes.
Methods: The study included three patients: two males (66 and 76 years old) and one 46-year-old female, all presenting with elevated serum calcium (Ca) and parathyroid hormone (PTH) levels, consistent with primary hyperparathyroidism. Radiographic evaluation using neck ultrasound and scintigraphy localized enlarged and hyperfunctioning parathyroid lesions. Each patient underwent parathyroidectomy, and the resected specimens were subjected to intraoperative frozen section analysis, which was inconclusive, necessitating further histopathological examination.
Results: Macroscopic examination revealed well-circumscribed tumours without definitive invasion into surrounding tissues. Histopathological analysis demonstrated trabecular and solid growth patterns, increased cellularity, fibrous bands with hemosiderin deposition, and focal nuclear atypia with prominent nucleoli. Immunohistochemical analysis confirmed GATA3, synaptophysin, and chromogranin expression, with low Ki-67 proliferation indices.
Conclusion: APA presents a diagnostic and management challenge due to its histological overlap with parathyroid carcinoma. Unlike benign adenomas, APAs exhibit atypical cytological features and require long-term follow-up due to their potential for recurrence. Surgical resection remains the primary treatment, and accurate classification using WHO diagnostic criteria is essential for appropriate patient management. This case series underscores the importance of comprehensive histopathological evaluation in differentiating APA from other parathyroid neoplasms.

E-PS-10-006

SDHB expression in pheochromocytomas: immunohistochemical correlation and genetic findings

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Background & Objectives: Pheochromocytoma is a rare neuroendocrine tumour originating from the sympathetic or parasympathetic ganglia, primarily in adrenal medulla chromaffin cells. It generally presents with a low incidence and favourable prognosis following surgical resection. Approximately 40% of cases have genetic origins, notably associated with mutations in the SDH, VHL, RET, and NF1 genes.

Methods: A cohort of 30 patients diagnosed with pheochromocytoma at our centre between 2001 and 2024 was analysed. Immunohistochemical (IHC) staining for SDHB expression was performed and evaluated by three pathologists.

Results: The cohort comprised 16 women (53.3%) and 14 men (46.7%), with a mean age of 52.1 years at diagnosis. The right adrenal gland was the most common site of involvement (17 cases, 56.6%). Bilateral involvement was observed in 2 cases (6.6%), both linked to MEN2a syndrome. Only one patient presented with metastatic disease, showing vertebral involvement at D5.

IHC for SDHB was negative in 6 of the 30 cases (20%), indicating a clear loss of expression with proper internal positive controls. Germline genetic testing was conducted in 14 patients, two of whom exhibited SDHB loss without corresponding germline mutations.

Other germline alterations identified in these 14 patients included:

- 4 cases linked to MEN2a, all with medullary thyroid carcinoma.
- 1 case associated with VHL, resulting in clear cell renal carcinoma.
- 1 case with NF1.

Conclusion: Various genetic mutations causing pheochromocytoma have been reported, with SDH complex mutations being the most common, present in over 10% of cases. In our cohort, 20% exhibited SDHB loss, the predominant alteration. Notably, two of the 6 patients with SDHB loss (33.3%) did not have germline SDH mutations, suggesting additional molecular alterations contribute to SDHB loss, underscoring the importance of further molecular analysis in clinically suspicious cases.

E-PS-10-007

Oncocytic adrenal cortical carcinoma in a one-year-old male infant, a rare finding

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Background & Objectives:

- A one-year-old male infant who presented to the Endocrinology out-patient clinic after his mother had noticed increasing hair growth on lower limbs, upper lip and genital area for the past two months. The patient's voice getting deeper, acne starting to form on his forehead, with increasing irritability and aggression. P/E revealed enlarged testicles and a large penile shaft.
- The 24-hour suppression test yielded a cortisol level of 324.24 mcg/dl, i.e. not suppressed. CT-adrenal protocol showed a large left suprarenal mass with foci of calcification and heterogeneous enhancement measuring 6.3 x 4.2 cm.
- DHEAS level was very high of 1000 mcg/dl. 24-hour urine collection for VMA and HVA was within normal range.

Methods:

- The specimen was fixed in 10% buffered neutral formalin. PEFF sections were stained with routine (H&E).

Results:

- M/E shows an encapsulated tumour composed of sheets of oncocytic polygonal cells with granular eosinophilic cytoplasm amongst scattered foci of necrosis associated with dystrophic calcifications. The cells exhibit marked pleomorphism with variably bizarre nuclear forms, including binucleated and multinucleated giant cells, and enlarged "cherry-red" nucleoli.
- Grading done according *to the Weiss criteria:* nuclear Fuhrman grade III or IV, diffuse architecture (more than 33% of tumour volume), patchy necrotic areas with associated dystrophic calcifications, subcapsular sinusoidal invasion, and focal capsular infiltration. Mitotic rate is > 5 /50 HPF, no atypical mitotic figures. Clear cells are < 25% of tumour volume. Tumour achieved a score of 7, rendering the diagnosis, adrenal cortical carcinoma.
- *Pertaining to the Lin-Weiss-Bisceglia (LWB) system:* Tumour exhibits a major criterion: >5 mf/50 high power fields, rendering the diagnosis malignant adrenal cortical tumour.

Conclusion: The annual incidence of adrenal cortical carcinoma (ACC) is extremely low, with only 0.2 to 0.3 cases per million children. Oncocytic ACC in children is an even rarer diagnosis, with around only 20 cases reported in the literature.

E-PS-10-008

Tall cell papillary thyroid carcinoma with desmoid fibromatosis-type stroma: a case report and molecular study

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Background & Objectives: Papillary thyroid carcinoma (PTC) is a common cancer with several histological subtypes. Less than 60 cases of PTC with fibromatosis/fasciitis-like/desmoid-type stroma have been reported, with only a few published molecular data. This subtype has two distinct components: a classic PTC and a stromal component resembling fibromatosis, nodular fasciitis, or desmoid tumours. The latter component complicates both the diagnosis and the treatment.

Methods: We report a case of a 47-year-old woman who came to our hospital for a total thyroidectomy following the incidental discovery of a 26 mm, EU-TIRADS 4 and Bethesda V (suspicious for papillary carcinoma) thyroid nodule. Upon histological examination we discovered a biphasic tumour. The epithelial component was a tall cell papillary thyroid carcinoma, BRAF-V600E positive by immunohistochemistry. The mesenchymal component had a desmoid fibromatosis morphology with long, sweeping fascicles of bland fibroblasts and myofibroblasts. These cells were negative for cytokeratins, BRAF-V600E, TTF1 and PAX8 and positive for SOX11 and SMA, with focal nuclear expression of β-catenin. The tumour invaded focally the strap muscles. No vascular invasion and lymph node metastasis were found. The surgical margins were negative. A large NGS panel was performed by dissecting each component: BRAF-V600E and CTNNB1 mutations were found in the epithelial and the mesenchymal component, respectively. The patient received radioactive iodine therapy and is free of recurrence 12 months after surgery.

Results: This case adds to the current knowledge of the very rare PTC with fibromatosis/fasciitis-like/desmoid-type stroma and highlights the importance of its accurate diagnosis, since it may be easily misdiagnosed, especially as anaplastic carcinoma. The prognosis will be influenced by both components. While distant metastases have not yet been documented in the literature, extrathyroidal extension and lymph node metastases are frequent. Recurrence rates vary between studies.
Conclusion: Greater understanding of this tumour will help pathologists avoid diagnostic errors and clinicians formulate better treatment strategies.

E-PS-10-009
Diagnostic utility of Cadherin 17 in well differentiated neuroendocrine tumours and paragangliomas
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Background & Objectives: Cadherin-17 (CDH17) is a membranous protein expressed primarily in intestinal epithelial cells and tumours of gastrointestinal origin. However, the data on CDH17 in neuroendocrine neoplasms are limited. This study aimed to evaluate CDH17 expression across various subsets of neuroendocrine tumours and to correlate differences with tumour type and primary site of origin.
Methods: Tissue microarrays (TMAs) were created using representative samples from 96 neuroendocrine tumours, including paragangliomas (n = 32), well-differentiated neuroendocrine tumours (WDNETs, n = 59) of different sites, and medullary thyroid carcinomas (MTC, n=5). TMAs were analysed with CDH17 antibody, and the staining intensity was assessed using the immunoreactive score (IRS). The associations between CDH17, tumour subtype and its origin were assessed.
Results: WDNETs exhibited significantly higher expression of CDH17 ($P < 0.00001$) compared to paragangliomas. CDH17 immunoreactivity was observed in 57.6% (34/59) WDNETs, while all the paragangliomas were negative. In the WDNET group, CDH17 expression varied by primary site and it could be detected in 95% (19/20) of gastrointestinal tumours, 57.1% (8/14) pancreatic tumours, 23.5% (4/17) lung tumours. All parathyroid adenomas (n=4) and MTCs (n=5) were negative. The IRS in gastrointestinal tumours was significantly higher (median 8), compared to pancreatic (median 1), lung (median 0), and parathyroid tumours ($p<0.00001$). CDH17 immunoreactivity showed 100% specificity but only 57.63% sensitivity for distinguishing between WDNETs and paragangliomas. Any CDH17 positivity was 95% sensitive and 65.71% specific for WDNETs of gastrointestinal origin.

Conclusion: CDH17 seems to be a highly specific marker of WDNETs and a sensitive marker of a subset of gastrointestinal WDNETs.

Funding: Supported by the project BBMRI-CZ LM2023033, by the European Regional Development Fund-Project BBMRI-CZ.: Biobank network – a versatile platform for the research of the etiopathogenesis of diseases (No: EF16_013/0001674), by the Cooperatio Program, research area DIAG, and Project of Czech Ministry of Defense MO 1012

E-PS-10-010
Improving sensitivity in the study of TERT C228T mutation in thyroid adenoma and carcinoma: use of digital PCR and the challenge of low allele frequencies
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Background & Objectives: The differential diagnosis between follicular or oncocytic thyroid adenoma and carcinoma requires the assessment of invasion, which is only possible in surgical specimens. In this context, the study of the C228T TERT mutation becomes relevant due to its association with carcinoma. At our centre, we replaced pyrosequencing (PS) with digital PCR (dPCR), a more sensitive and precise technique. Using dPCR, we studied thyroid lesions that were considered indeterminate for the TERT mutation by PS.
Methods: All thyroid lesions from our centre with indeterminate results for the TERT mutation over the past 10 years were selected. Additionally, 4 follicular carcinomas and 1 oncocytic adenoma with C228T TERT mutation and 4 without it by PS were included. dPCR for TERT C228T was performed on all samples, with a positive result considered when the allele frequency of the mutation was >1%.
Results: 12 cases indeterminate for the C228T TERT mutation were included (6 follicular carcinomas, 5 oncocytic adenomas, 1 follicular adenoma). dPCR showed concordant results with PS in the 5 positive cases (including the oncocytic adenoma) and the 4 negative ones. Of the indeterminate cases, 4 follicular carcinomas, one oncocytic adenoma, and one follicular adenoma were positive for the TERT mutation. 2 follicular carcinoma and 4 oncocytic adenomas were negative. Adenomas with the TERT mutation showed allele frequencies lower than 8%, but 3 follicular carcinomas that were indeterminate by PS and positive by dPCR showed similar allele frequencies.
Conclusion: dPCR allows determinations of the presence or absence of the C228T TERT mutation in PS-indeterminate cases, with concordance in both positive and negative results. However, C228T TERT mutation should be interpreted with caution as a malignancy criterion, as it may occur in adenomas, especially at low allele frequencies.

E-PS-10-011
Altered expression of autophagy-related molecules and β-catenin in different subtypes of thyroid cancer: colocalization with intranuclear cytoplasmic inclusion
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Background & Objectives: Different histological subtypes of thyroid carcinomas (TCs) are strongly associated with tumour aggressiveness. Autophagy is a crucial cellular process that plays an important role in

maintaining cellular homeostasis. Intranuclear cytoplasmic inclusions (INIs), which represent an important diagnostic pathological feature of papillary (TC), may be involved in autophagy and proteolysis, owing to the presence of the autophagy-associated proteins p62 and LC3 within them. This study aimed to clarify the expression levels of autophagy-related molecules, such as, LC3B, p62, and β-catenin, in cases of TC of different histological subtypes and clinicopathological characteristics.
Methods: A total of 70 surgically resected thyroid nodules, including five follicular adenoma (FA), five hyalinizing trabecular tumour (HTT), five follicular TC (FTC), 43 PTC, six poorly differentiated TC (PDTC), and six anaplastic TC (ATC), were analysed by dual-colour immunofluorescence for β-catenin, LC3B, and p62. Statistical analyses were used to determine the associations of autophagy-related molecules with *BRAF*^{V600E}*/TERT* promoter mutations, Ki-67 labelling index, and clinicopathological characteristics.
Results: p62 immunoreactivity was most frequently seen in PTC, particularly in the papillary and tall cell types. This protein appeared to colocalize with LC3B and β-catenin in PTC INIs. Conversely, p62 expression was only rarely seen in both FTC and PDTC. The expression levels of p62 and its colocalizations with β-catenin and LC3B correlated significantly with the presence of the *BRAF*^{V600E} mutation. Frequent colocalization of dot-shape perinuclear β-catenin signals with a component of the trans-Golgi apparatus in tall cell PTC was also observed.
Conclusion: This study revealed differences in the expression patterns of LC3B, p62, and β-catenin among different TC subtypes. Abnormal β-catenin expression may be linked to autophagy dysfunction that triggers genomic instability and promotes tumour aggressiveness. These autophagy-related molecules may be cooperatively associated with formation of INIs during PTC carcinogenesis.

Funding: This work was funded by the Atomic Bomb Disease Institute, Nagasaki University and the Program of the Network-Type Joint Usage/ Research Centre for Radiation Disaster Medical Science

E-PS-10-012

NGS analysis for non-invasive thyroid nodules showing nodule-in-nodule appearance with poorly differentiated component with homemade thyroid cancer gene panel

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Background & Objectives: Poorly differentiated thyroid carcinoma (PDTC) is aggressive and is reportedly evoked by well-differentiated thyroid follicular-patterned tumours (TFTs). TFTs showing nodule-in-nodule (NN) appearance with PD component (PDc) but neither invasion nor metastasis are regarded as benign nodules despite their high-grade histological features. Our recent study demonstrated the prevalence of *NRAS* and *TERT* promoter (*TERT*-p) mutations in PDc was comparable to that of carcinomas, presuming that PDc in NN is potentially a precursor lesion associated with PDTC (*Cancers 2022:14,3577*). Therefore, this study analysed NN with PDc by NGS on our homemade thyroid cancer panel (HTCP) to furtherly characterized its genetic profiles.
Methods: Total 87 cases of TFTs, such as NN with PDc (n=13), adenomatous goiters (AGs, n=27), Follicular adenoma (FAs, n=24), and follicular TCs (FTCs, n=23), were available in this study. All subjects were FFPE samples and analysed using a HTCP containing 29 oncogenes by HiSeqX Ten (Microgen, Tokyo, Japan).
Results: Frequencies of *RAS* mutations were significantly higher in NN with PDc [76.9% in both PDc and Outer nodule (OutN)] than AG (7.4%) or FA (25.0%) but not significantly different from FTC (39.1%). *TERT*-p mutations were more frequent in PDc (23.1%) than OutN (7.7%), AG (3.7%), and FA (4.2%) but comparable to FTC (21.7%). Double mutation in *RAS* and *TERT*-p were found in 15.4% of PDc and 21.7% of FTC, but not in OutN. Furthermore, our analysis with our HTCP could detect any mutations (MAF>10%) in 92.3% of NN with PDc, 48.1% of AG, 45.8% of FA, and 65.2% of FTC.
Conclusion: This study demonstrated a higher incidence of detectable mutations in NN with PDc than FTC. *TERT*-p mutations in PDc were comparable to FTC. *TERT*-p mutations are most common in PDTC but rare in TFTs, supporting our hypothesis that PDc in NN is potentially a precursor lesion associated with PDTC.

Funding: This work was funded by the Atomic Bomb Disease Institute, Nagasaki University; the Grant-in-Aid for Scientific Research from the Japanese Ministry of Education, Science, Sports and Culture grant numbers [20K07424, 21K15402, and 22K06982]; and the Program of the Network-Type Joint Usage/Research Centre for Radiation Disaster Medical Science

E-PS-10-013

Prognostic markers in paragangliomas: the role of histopathology, SDHB, MAML3 and MCM6 expression

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Background & Objectives: There are currently no definitive prognostic markers that accurately predict malignant behaviour in paragangliomas. While metastasis develops in only 10-15% of adrenal-origin tumours, this rate can rise up to 50% in those with extra-adrenal localization. This study aims to investigate the potential predictive effect of known histopathological features in paragangliomas, alongside SDHB, S100, Ki-67 proliferation index, and the expression of MAML3 and MCM6 in predicting metastatic disease.
Methods: The specimens of 71 patients who were diagnosed with pheochromocytoma and paraganglioma and underwent total excision between 2010 and 2021 were re-examined. Demographic, clinical, and histopathological data, as well as immunohistochemical results for Ki-67, S100, SDHB, MCM6, and MAML3, were recorded.
Results: While distant organ metastasis was observed in 3.4% (n=1/29) of pheochromocytomas and 21.2% (n=7/33) of head and neck paragangliomas, this rate was found to be significantly higher at 66.7% (n=6/9) in abdominal paragangliomas ($p<0.001$). No MAML3 overexpression was observed in any of the cases. Distant organ metastasis was more frequently detected in cases with MCM6 overexpression.
Conclusion: Although there is still no definitive feature that predicts metastasis, in line with the literature, extra-adrenal localization, vascular invasion, capsular invasion, nuclear pleomorphism, hyperchromasia, and confluent necrosis were found to be associated with distant organ metastasis in our study. Additionally, in the multivariate analysis, larger tumour size (>5.1 cm), the presence of >3/10 HPF mitosis, and SDHB loss were associated with lower metastasis-free survival. While no conclusions could be drawn regarding MAML3, the prognostic value of MCM6 appears promising.

E-PS-10-014

Metastatic mesenchymal chondrosarcoma with unusual thyroid involvement

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Background & Objectives: Mesenchymal chondrosarcoma is a rare, high-grade malignant chondrogenic tumour, characterized by a biphasic pattern consisting of a primitive mesenchymal component and a well-differentiated cartilaginous matrix. It typically arises in soft tissue or bone. Distant metastasis can be observed even many years later. Visceral involvement/presentation is rare, only a few cases of metastasis to the thyroid have been reported.
Methods: A 32-year-old male patient presented with a thyroid mass. A 4 cm nodule was detected in the right thyroid lobe. Due to an inadequate fine-needle aspiration, total thyroidectomy was performed for definitive diagnosis.
Results: Gross examination revealed two separate firm, cream-white nodular lesions (4.5×3.4×2.5 cm and 1×0.8×0.8 cm) in the right lobe. Histologically, tumour showed small to medium-sized, poorly differentiated high cellular round cells, along with well-differentiated hyaline cartilage tissue. The round cell component was accompanied by staghorn vascular structures and had high mitotic activity (24/10 HPF, 12/mm²). Immunohistochemically, the tumour was diffusely SOX-10 positive. CD99 was positive in the round cell component, and S100 in the chondroid component. TLE-1 was patchy, while TTF-1, PAX-8, SS18-SSX were negative.
Further investigation revealed a prior diagnosis (2 years earlier) of a 'mitotically active spindle cell tumour' in the lung. NGS analysis of this tumour identified a HEY1-NCOA2 fusion.
Based on these findings, we established the diagnosis of metastatic mesenchymal chondrosarcoma.
Conclusion: Mesenchymal chondrosarcoma is a rare tumour, primarily affecting young adults. Pulmonary and thyroid involvement are uncommon, making diagnosis challenging, especially in small biopsies without a cartilaginous component, in such situation tumour can be misdiagnosed as other small round cell neoplasms, such as Ewing sarcoma, lymphoma, synovial sarcoma, rhabdomyosarcoma without immunohistochemical evaluation. The HEY1-NCOA2 gene rearrangement is a key molecular marker. Given its aggressive nature, complete surgical resection followed by adjuvant chemotherapy remains the preferred treatment.

E-PS-10-015

Shared and pattern-specific molecular signatures in anaplastic thyroid carcinoma identified by spatial transcriptomics and immunohistochemical profiling

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Background & Objectives: Anaplastic thyroid carcinoma (ATC) is a rare and highly aggressive malignancy characterized by marked histological heterogeneity. However, the extent to which this morphological variation reflects underlying molecular programs remains poorly understood. This study aimed to identify both shared and histologic pattern-specific molecular features by integrating spatial transcriptomics with immunohistochemical analysis.
Methods: Spatial transcriptomic analysis was performed on a tumour specimen containing ATC coexisting with papillary thyroid carcinoma. Five histologic patterns—epithelioid, squamoid, spindle, inflammatory, and mixed—were analysed. Differential gene expression and pathway enrichment analyses were conducted to identify common and pattern-specific molecular alterations. Selected transcriptomic findings were validated by immunohistochemistry using tissue microarrays comprising various types of thyroid tumours.
Results: A consistent set of differentially expressed genes was identified across all histologic patterns, independent of morphological subtype or *BRAF* mutation status. These genes were associated with extracellular matrix remodelling, tumour invasion, and the downregulation of tumour-suppressive functions. Immunohistochemical analysis confirmed differential protein expression between ATC and other thyroid tumour types, consistent with transcriptomic findings. Pathway enrichment analysis revealed distinct histology-specific profiles: the spindle pattern demonstrated upregulation of oxidative phosphorylation, tricarboxylic acid cycle, and glutathione metabolism pathways; the mixed subtype was enriched for ECM-receptor interaction and focal adhesion; and the squamoid pattern showed selective enrichment in PI3K-Akt signalling. The inflammatory pattern exhibited marked activation of innate immune and immunoregulatory pathways, including neutrophil extracellular trap formation, NF-κB signalling, IL-17 signalling, and leukocyte transendothelial migration.
Conclusion: ATC demonstrates both shared and histologic pattern-associated molecular alterations. Uniformly dysregulated markers may serve as robust diagnostic indicators, while pattern-specific pathways provide insight into the biological mechanisms underlying morphological heterogeneity. These findings underscore the utility of spatial transcriptomics in the molecular characterization of aggressive thyroid tumours.

Funding: This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: RS-2021-KH113146)

E-PS-10-016

Primary Pulmonary Paraganglioma Presenting as a Solitary Lung Nodule: Case Report

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Background & Objectives: Primary pulmonary paraganglioma (PPP) is an extremely rare neuroendocrine tumour arising from extra-adrenal paraganglia in the lung. It is typically asymptomatic and incidentally detected, though symptoms such as cough, haemoptysis, or chest pain may occur. Due to its rarity and morphological overlap with carcinoid tumours, distinguishing PPP requires detailed histopathological and immunohistochemical evaluation.
Methods: A 24-year-old male with no known medical conditions or smoking history presented with haemoptysis. A similar episode 25 days earlier was attributed to mucosal irritation. Chest CT revealed a 2.5 cm nodular mass in the right upper lobe, without lymphadenopathy or pleural effusion. A right upper lobectomy was performed.
Results: Macroscopically, the tumour was well-circumscribed, bronchi-associated, and solid without necrosis or haemorrhage. Microscopically, it exhibited Zellballen architecture, cytoplasmic eosinophilia, intracytoplasmic vacuoles, and well-formed nests of neoplastic cells. Immunohistochemically, the tumour was diffusely positive for synaptophysin, chromogranin, CD56, GATA-3, and tyrosine hydroxylase, while pan-cytokeratin and p40 were negative. Sustentacular cells were highlighted by S-100. SDHB loss raised suspicion of an SDH-related

syndrome. The Ki-67 index was 3-5%. No lymph node metastasis was detected.
Based on histomorphological features and immunoprofile, a diagnosis of PPP was made. Genetic counselling and further systemic evaluation were recommended.
DOTA-PET imaging demonstrated no additional lesions, confirming primary pulmonary origin rather than metastatic disease.
Conclusion: PPP should be considered in the differential diagnosis of lung masses, particularly in young patients. Given histological similarities, PPP must be distinguished from carcinoid tumours through comprehensive immunohistochemical evaluation. SDHB loss raises suspicion for an SDH-related syndrome; however, genetic analysis is necessary for definitive diagnosis. The presence of sustentacular cells is crucial for confirming the primary pulmonary origin. Additionally, thorough clinical and radiological evaluation should be performed. Early recognition, complete surgical resection, and genetic assessment are essential for optimal management and surveillance.

E-PS-10-017
A novel approach to the follicular neoplasm category in thyroid fine-needle aspiration: assessing the applicability of Nikiforov's nuclear scoring scheme
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Background & Objectives: Although the follicular neoplasm (FN) category is well-defined within the Bethesda System for Reporting Thyroid Cytopathology, FN cases range from benign to malignant lesions. This study evaluates the utility of Nikiforov's nuclear scoring system in subclassifying FN nodules and its correlation with histopathological outcomes to improve risk stratification and clinical decision-making.
Methods: This retrospective study included 38 patients diagnosed with FN at Ankara City Hospital between 2019 and 2024. Patients who underwent thyroidectomy and had slides for reassessment were selected. Cases were confirmed and subclassified based on nuclear atypia presence. Histopathological diagnoses followed the WHO classification of endocrine tumours. Statistical analyses included chi-square testing, sensitivity, specificity, and likelihood ratio calculations.
Results: Among 38 thyroidectomy cases, final histopathological diagnoses included 9 benign cases (follicular nodular disease: 3, follicular adenoma: 6), 10 low-risk neoplasms (Non-invasive follicular thyroid neoplasm with papillary-like nuclear features: 7, well-differentiated tumour of uncertain malignant potential: 2, follicular tumour of uncertain malignant potential: 1), and 19 malignant tumours (classic papillary thyroid carcinoma PTC: 7, follicular variant PTC: 8, oncocytic carcinoma: 2, follicular carcinoma: 1, poorly differentiated thyroid carcinoma: 1). Nuclear scoring distribution showed 7 cases with low scores (0-1) and 24 with high scores (2-3). The presence of nuclear atypia in FNAs was significantly associated with malignancy risk ($p = 0.047$). The nuclear scoring system demonstrated high sensitivity (81.48%) despite relatively low specificity (54.55%), indicating its potential role in risk assessment.
Conclusion: Nikiforov's nuclear scoring system effectively predicts malignancy in follicular neoplasm thyroid nodules but remains an imperfect tool in cytological evaluation. Further refinement is needed to enhance its clinical applicability. Our findings emphasize subclassification's role in refining risk assessment, potentially improving surgical decision-making by reducing unnecessary procedures while ensuring appropriate management of high-risk cases.

E-PS-10-018
Immunophenotypical expression variability in aggressive poorly differentiated and anaplastic thyroid carcinoma – case series
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Background & Objectives: Poorly differentiated thyroid carcinoma (PDTC) and anaplastic thyroid carcinoma (ATC) represent rare but aggressive thyroid malignancies, accounting for 2 – 5% of all thyroid cancers for PDTC and less than 2% for ATC. They have a worse prognosis and a low capability of up-taking I^{131}.
Methods: We analysed a series of 12 cases with aggressive thyroid tumours (9 with PDTC and 3 with ATC) subjected to total thyroidectomy and immunotherapy / chemotherapy combination treatment. The surgical specimens were investigated by means of histopathology and immunohistochemistry. The immunophenotype expression was investigated using B-RAF, K-RAS, TERT and PAX-8 on FFPE tissues. Univariate biostatistical method was performed.
Results: Histopathology investigation showed a diffuse proliferation of small to medium size tumour cells arranged in cords and nests in PDTC (G2) and a diffuse proliferation of a mixture of spindle-shape cells, pleomorphic and multinucleated giant cells in ATC (G3), accompanied by various degrees of necrosis. The mitotic rate was high (> 5 mitoses / HPF). The pattern of IHC expression was heterogenic with variable intensity in the tumour cells. B-RAF was positive in half of cases with a high cytoplasmic variability. K-RAS had a high diffuse cytoplasmic expression level in 8 cases. TERT expression was between 15 – 50% in all cases, with strong perinuclear reaction. Significant statistical correlations were found between B-RAF and K-RAS ($r = 0.56$, $p = 0.04$) and B-RAF and TERT ($r = 0.49$, $p = 0.0003$) respectively. A slightly positive correlation was also found between TERT and PAX-8 ($r = 0.35$, $p = 008$).
Conclusion: Besides the histological criteria, the immunophenotype expression of the aforementioned markers have their own significance. Despite their variability, B-RAF and K-RAS remain mutually exclusive main drivers in aggressive thyroid carcinoma, while TERT mutation represent the most common alteration in PDTC and ATC in conjuncture with PAX-8 and B-RAF abnormal status.

Funding: This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CCCDI-UEFISCDI, project number PN-IV-P7-7.1-PED-2024-0307 within PNCDI IV

E-PS-10-019
Papillary thyroid cancer: the role of oxidative stress and positive mast cells
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Background & Objectives: Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer. The rate of development and growth of tumours is regulated by a delicate balance between pro-and anti-tumorigenic effects, stimulated by the tumour cells themselves, as well as the surrounding microenvironment. On the other hand the oxidative stress (OS) plays a major role in thyroid carcinogenesis. Patients

PTC have a worse oxidative profile and increased lipid peroxidation compared to healthy individuals and patients with autoimmune thyroid disease.
Methods: We investigated immunohistochemically tryptase- and chymase-positive mast cells (MCT and MCC). The study group consists of 69 patients, males (n=9) and females (n=60), (median 54.17±14.48years). MC counts have been reported to correlate with tumour stage, prognosis, and invasiveness. For OS we use EPR spectroscopy in group from 51 patients and 23 controls.
Results: In our study we demonstrated that mast cell, MCT and MCC numbers were significantly more in PTC as compared to the surrounding normal thyroid structure ($p<0.001$).) Patients with lower numbers of MCT in tumour stroma ($p=0.043$) tended to have worse survival. With EPR spectroscopy we observed inverse correlation between nitroxide radical TEMPOL (in PTC 5.856 ±0.598 v.s TEMPOL/ controls 11.27) compare with confirmatory method ROS (in PTC 5.411±0.789 v.s ROS/controls 0.467±0.390).
Conclusion: MCs in the process of angiogenesis release proangiogenic factors, such as VEGF, thymidine phosphorylase, tryptase and chymase, stored in their secretory granules. It is well demonstrated that MCT is one of the most powerful angiogenic mediators released by human MCs, is involved in tissue remodelling, and it may also act indirectly on tissue neovascularization by releasing latent angiogenic factors bind to the extracellular matrix. ROS accumulation confirmed the presence of oxidative stress in patients with PTC.

Funding: This research was funded by the Bulgarian Ministry of Education and Science (MES) in the frames of the Bulgarian National Recovery and Resilience Plan, Component "Innovative Bulgaria", Project No. BG-RRP-2.004-0006-C02, "Development of research and innovation at Trakia University in service of health and sustainable well-being" and NIP 9/2022

E-PS-10-020
Parathyroid carcinoma in haemorrhagic thyroid cyst – case report
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Background & Objectives: Parathyroid carcinoma is rarest endocrine malignancy, with prevalence of 0.005% of all cancers and incidence of 11 in 10 million adults. It occurs in less than 1% of all cases of hyperparathyroidism.
Methods: We present a 46-year-old male with an unusual clinical-radiological and pathomorphological presentation of parathyroid cancer.
Results: Clinically, on front right side of neck, there was palpable, painless, mobile tumour mass without local reactions on the skin. Radiological methods, US and CT, it was described that right lobe of thyroid gland was occupied by heterodense, expansive, clearly limited, probably haemorrhagic cyst, measuring 49 x 39 x 68 mm. Reactive submandibular and parajugular lymph nodes were evident. Operative treatment is indicated. Intraoperatively, right lobe of thyroid gland was enlarged due to cyst filled with haemorrhagic contents. Pathohistological analysis of frozen sections revealed a cystic formation filled with coagulated blood and necrotic debris. A thyroidectomy is performed. On definitive pathohistological sections, invasive tumour tissue with infiltration of the thyroid gland parenchyma was found only in 10% of the tissue sections from the cystic lesion. The tumour was composed of small bands and rare medium-large folliculoid formations, which are made up of mild atypical tumour cells with pale eosinophilic cytoplasm and eccentrically placed hyperchromatic nuclei. Definitive diagnosis was confirmed by immunocytochemical profile: Thyreoglobulin-, TTF 1-, Calcitonin-, GATA3+, Chromogranin +, Ki 67 shows proliferative activity in 10% of tumour cells. Multiple endocrine neoplasia is ruled out. Three years after the operation, the patient has no recurrence of the disease.
Conclusion: Our case shows an extremely unusual presentation of parathyroid carcinoma, and also indicates the importance of proper and complete lesion sampling for pathohistological analysis, as viable tumour cells were present in only 10% of cyst wall sections. Once again, the importance of immunohistochemical analysis in the diagnosis of malignant tumours was confirmed.

E-PS-10-021
Breast carcinoma metastasis discovered during thyroidectomy for worsening thyroiditis more than a decade after the primary diagnosis: a case report
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Background & Objectives: Metastasis to thyroid gland is highly unusual and represents only about 1.4% to 3% of all thyroid cancer despite high vascularization and rapid blood flow. Thyroid metastases are difficult to diagnose as it typically presents as nodules with minimal symptoms. While primary breast cancer usually spreads to bones and visceral organs, metastasis to the thyroid is rare and is associated with poor prognosis.
Methods: A 70-year-old female patient with non-toxic multinodular goiter, medically managed hypothyroidism caused by autoimmune thyroiditis presented with symptoms of dysphagia and worsening lethargy. X-ray showed compression of the trachea and narrowing of the oesophagus. Notably, the patient underwent partial mastectomy for invasive ductal carcinoma 13 years ago. Due to worsening symptoms, thyroidectomy was decided to be performed.
Results: Histopathological examination, in addition to findings of advanced thyroiditis, revealed diffuse multiple microfocal neoplastic infiltration in both lobes. Infiltration was composed of medium-sized cells with mild-moderate polymorphism features and pronounced spreading to the vessels. Tumour cells reacted positively with the GATA3, oestrogen and progesterone receptor immunomarkers (significantly less pronounced than primary tumour), and the same as primary- were negative for HER2 immunomarker.
Conclusion: A metastasis from a primary cancer diagnosed 13 years ago, now affecting the thyroid gland was identified. This finding highlights that primary thyroid pathology can sometimes mask the presence of metastatic disease in the thyroid gland. A thorough review of a patient's medical history is essential to ensure that potential metastases are not overlooked and managed properly. Although primary thyroid conditions, such as thyroiditis, are far more common than metastases to the thyroid gland, it is crucial to maintain suspicion for metastasis, even many years after the successful treatment of the primary cancer, and even in the absence of obvious metastatic signs.

E-PS-10-022

Immunophenotype of parathyroid adenoma, multiglandular parathyroid disease and parathyroid carcinoma: diagnostic implications

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Background & Objectives: Reflecting the dominant role of surgery for treatment of primary hyperparathyroidism, significant changes were implemented in WHO classification of parathyroid lesions (2022). In particular, the entity of multiglandular parathyroid disease (MPD) was defined, a term that is more in line with surgeon's needs than the former primary parathyroid hyperplasia. Diagnostics of hyperparathyroidism is based on laboratory and radiological investigations. However, pathological assessment of surgically removed glands can help to verify the diagnosis or to reach it in difficult and/or recurrent cases. The **aim** of our study was to evaluate immunophenotype of parathyroid adenoma, MPD and parathyroid carcinoma.
Methods: Expression of Ki-67, parafibromin, p53, p21, p27, cyclin D1, intermediate filaments (IFs), CD56, CD44, E-cadherin and Bcl-2 was detected and quantified by immunohistochemistry/ digital morphometry in adenomas (102), MPD (27) and parathyroid carcinomas (5); normal glands (45) formed the control group. Descriptive statistics, Kruskal-Wallis and Mann-Whitney tests were performed.
Results: The expression of parafibromin, Ki-67, p21 (all: $p<0.001$), p27 ($p=0.01$) and cyclin D1 ($p=0.002$) showed statistically significant differences. The mean fraction of Ki-67 [95% confidence interval] was 1.6%[1.3-1.8] in adenoma, 1.0%[0.7-1.3] in MPD and 5.8%[0.2-11.4] in carcinoma; of p21: 12.8%[11.4-14.2] in adenoma, 15.7%[13.4-18.0] in MPD and 7.6%[0.0-18.8] in carcinoma; of cyclin D1: 12.0%[10.5-13.6] in adenoma, 24.8%[14.6-35.0] in MPD and 31.5%[0.0-80.1] in carcinoma. Only carcinomas showed loss of p27(59.0%[13.3-100.0]), contrasting with adenomas (92.8%[89.7-96.0]) and MPD 94.3%[90.9-97.8]. Similarly, loss of BCL2 was notable in carcinoma (28.2%[0.0-76.4]), compared to adenoma (66.7%[59.7-73.7]) and MPD (61.3%[44.3-78.2]). Loss of parafibromin was invariable in all carcinomas, contrasting with adenomas (0%). CD56, CD44, E-cadherin, IFs and p53 have no role in differential diagnostics of parathyroid lesions.
Conclusion: Loss of parafibromin is the hallmark of parathyroid carcinoma. However, carcinomas feature also loss of p27 and Bcl-2, contrasting with benign lesions. Adenoma show higher proliferation, but lower p21 and cyclin D1 expression than MPD.

E-PS-10-023

Clear cell parathyroid adenoma: a rare diagnostic challenge in endocrine head and neck pathology

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Background & Objectives: Uniglandular parathyroid adenoma is a benign neoplasm responsible for over 85% of primary hyperparathyroidism (PHPT), with a female-to-male ratio of 2-3:1. These adenomas comprise oncocytic, clear, or transitional cells, lipoadenomas and clear cell adenomas. Clear cell subtype constitutes 1.5 per 1000 cases. Up to 10% have a hereditary component, and neck radiation exposure is a risk factor. Clinically, they present with hypercalcemia, weakness or anxiety. Genetic alterations include 11q13 loss of heterozygosity and MEN1 inactivation. Preoperative localization employs ultrasound, scintigraphy, or PET/CT, though clear cell adenomas are frequently asymptomatic and undetectable by scintigraphy. Differentials include renal cell carcinoma. Most cases are effectively treated surgically. This case report provides a comprehensive description of the diagnosis, treatment, and clinical outcomes, contributing to the limited literature on clear cell parathyroid adenomas and offering valuable insights for pathologists and clinicians.
Methods: We present the case of a 56-year-old female with a history of chemical PHPT. A thyroid scan using 5mCi Technetium revealed a nodule in the posterior aspect of the right thyroid lobe's lower pole, with no thyroid uptake. She underwent right parathyroidectomy. Postoperatively, her PTH levels normalized (15.9 pmol/L preop to 1.6 pmol/L post-op). Macroscopically, a dark brown nodular fragment (1.7 x 1.0 x 0.9 cm, 0.7 g) with a thin pseudocapsule was observed.
Results: Histopathology revealed a hypercellular parathyroid gland predominantly composed of clear cells with vacuolated cytoplasm and mild nuclear atypia, surrounded by a fibrous capsule with atrophic peripheral parathyroid tissue. Immunohistochemistry showed strong GATA-3 and weak PAX-8 reactivity, with negative TTF1 and thyroglobulin. These findings, along with intraoperative PTH reduction, confirmed a uniglandular clear cell parathyroid adenoma.
Conclusion: This case underscores the importance of accurate diagnosis and effective treatment, highlighting parathyroidectomy as the definitive intervention for PHPT. Further molecular studies may elucidate genetic factors associated with this rare and morphologically distinct subtype.

E-PS-10-024

A rare tumour: signet-ring cell adenoma of the thyroid

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Background & Objectives: Folicular adenoma is a benign, encapsulated tumour that exhibits thyroid follicular cell differentiation. Signet-ring cell adenoma of the thyroid is a rare variant of it. The important thing in this entity is the correct differential diagnosis of it from metastasis of malignant tumours showing signet-ring cell differentiation.
Methods: A soliter and solid nodule was found by ultrasonography incidentally in the thyroid left lobe of a 74-year-old man during the hospital check-up because of palpitation. In the fine needle aspiration cytology smears thyrocytes with microfolicular organisation and some cells with clear cytoplasms were seen. However immunohistochemical or histochemical staining was not posssible in order to understand the nature of these clear cells as only two slides were sent after fine needle aspiration process. He was hematologically euthyroid. Then bilateral total thyroidectomy process was applied by the General surgeons.
Results: In the macroscopic sections of the material, a solid encapsulated nodule with a diameter of 2,2cm was found. Total of the nodule was evaluated microscopically and an encapsulated tumour composed of clear cells with a folicular organisation was seen. In the immunohistochemical evaluation; clear cells expressed TTF-1, Thyroglobulin, Pankeratin, CD56; however they were not stained with RCC, s100, GATA3, HBME-1, Galectin3, Calcitonin, Synaptophysin. The cytoplasmic vacuoles contained Pas with and without diastase positive mucin. The whole capsule of the nodule was examined and capsular or vascular invasion were not present. The lesion was diagnosed as Signet-ring cell adenoma of the thyroid.
Conclusion: Signet-ring-cell adenoma of the thyroid is a rare variant of Folicular adenoma. It is a benign tumour; however pathologists should keep this rare primary tumour of the thyroid in mind when examining thyroid lesions and not confuse it with metastatic signet-ring cell carcinomas of other organs or the thyroid.

E-PS-10-025

Identification of predictive variables of clinical outcomes in benign parathyroid tumours and parathyroid carcinomas: a multicentre study

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Background & Objectives: Primary hyperparathyroidism is mainly caused by benign parathyroid adenomas, but atypical adenomas and carcinomas show greater aggressiveness. Identifying clinical, biochemical, and histopathological factors, along with immunohistochemical markers like parafibromin, is crucial for improving prognostic stratification and optimizing postoperative management.

Methods: A multicentre, retrospective cohort study in three Spanish hospitals, including referred cases. Patients with non-metastatic parathyroid carcinoma or atypical adenoma (WHO 2022) were compared to typical adenomas. Clinical, biochemical, histopathological, and immunohistochemical variables were analysed, including the expression of parafibromin, Galectin 3, PGP9.5 and ki67.

Results: A total of 139 patients were included (90 typical adenomas, 21 atypical adenomas, and 28 carcinomas). Preoperative hypercalcemia was higher in atypical adenomas (12.92±2.11mg/dL) and carcinomas (13.14±2.37mg/dL) compared to typical adenomas (11.54±1.44mg/dL,$p<0.001$). Postoperative hypocalcemia was more frequent in atypical adenomas (27.8%) and carcinomas (24%) than in typical adenomas (3.3%,$p<0.001$). Capsular invasion was observed in 76.2% of atypical adenomas and 100% of carcinomas ($p<0.001$). Loss of parafibromin expression was more frequently identified in carcinomas and atypical adenomas ($p<0.001$) linked to aggressive histological features, such as higher cellular proliferation and an infiltrative growth pattern. Additionally, its absence correlated with a higher recurrence risk and a shorter disease-free survival in survival analysis ($p<0.05$).

Conclusion: Preoperative hypercalcemia, postoperative hypocalcemia, and capsular invasion are associated with the aggressiveness of parathyroid tumours. Loss of parafibromin expression is linked to a more aggressive phenotype, a higher recurrence risk, and worse prognosis, highlighting its relevance as a key biomarker for risk stratification and postoperative management.

E-PS-10-026

Exploring histologic patterns in anaplastic thyroid carcinoma: a case series with molecular correlation

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Background & Objectives: Anaplastic thyroid carcinoma (ATC) is a highly aggressive thyroid malignancy composed of undifferentiated cells that may exhibit areas of follicular differentiation or remnants of well-differentiated thyroid carcinoma. Despite advances in treatment modalities, overall survival remains below two years in most cases. Therefore, the integration of histopathological features with prognostically and therapeutically relevant molecular findings is essential for clinical decision-making.

Methods: We present a case series of four patients diagnosed with ATC between 2015 and 2025 at Hacettepe University Faculty of Medicine, all of whom underwent molecular analysis. Histological evaluation included haematoxylin and eosin staining and immunohistochemistry. Next-generation sequencing (NGS) was performed in two cases, while the remaining two were tested for the BRAF V600E mutation.

Results: **Case 1:** A 63-year-old female patient presented with foci of papillary thyroid carcinoma exhibiting tall cell features and anaplastic carcinoma with squamoid differentiation. NGS identified *TP53* p.V272M and *HRAS* p.Q61K missense variants.

Case 2: A 50-year-old male patient showed sarcomatoid-type ATC arising in the background of follicular carcinoma. NGS revealed two *TERT* promoter mutations (c.-124C>T and c.-245T>C), with c.-124C>T representing a well-characterized gain-of-function variant associated with increased *TERT* expression. Additionally, an *FGFR1–FGFR3* fusion was detected.

Case 3: A 60-year-old male patient demonstrated anaplastic carcinoma with squamoid morphology adjacent to papillary thyroid carcinoma. A *BRAF* V600E (c.1799T>A) mutation was detected.

Case 4: A 70-year-old female patient exhibited classical and follicular variant papillary thyroid carcinoma with transition into squamoid areas of anaplastic carcinoma. A *BRAF* V600E (c.1799T>A) mutation was confirmed.

Conclusion: ATC displays a wide morphological spectrum. Adequate and extensive sampling is key to identifying transition zones between differentiated and anaplastic areas. Molecular profiling supports diagnosis and therapeutic planning and should be interpreted alongside histopathologic findings.

E-PS-10-027

Metastatic medullary thyroid carcinoma to the gallbladder and prostate gland in a patient with MEN2B syndrome (*RET* p.M918T mutation)

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Background & Objectives: Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumour, accounting for only 5% of thyroid cancers, with up to 25% of cases being hereditary. It has a high metastatic potential, most commonly to the lymph nodes, lung, liver and bones with distant metastases frequently present at time of initial diagnosis. This study presents the case of a male patient with MEN2B syndrome (*RET* p.M918T mutation), who underwent a total thyroidectomy at age seven, leading to an MTC diagnosis. Twenty-two years later, he developed MTC in the gallbladder and prostate gland with increasing calcitonin levels starting at 560 pg/ml.

Methods: Imaging revealed a gallbladder mass, and despite surgical removal of the organ, calcitonin levels continued rising. Four months later, a prostate lesion was identified and the gland was excised. Gross sectioning of both specimens showed a yellow-toned, solid and elastic tumour. Histopathology and immunohistochemistry were performed.

Results: Microscopic examination demonstrated neoplastic infiltration in both organs of similar morphology by a well-differentiated neuroendocrine neoplasm exhibiting a nested pattern within an amyloid-like stroma and no necrosis. Immunohistochemistry confirmed neuroendocrine differentiation with chromogranin A and synaptophysin positivity. Cytokeratins and calcitonin were expressed. The proliferation rate was up to 1.4 mitoses in 2mm2 and Ki67 up to 8% in both. Immunohistochemical and morphological similarities between the thyroid, gallbladder and prostate suggested the metastatic nature of the later lesions.

Conclusion: MEN2B syndrome with *RET* p.M918T mutation has an aggressive biological behaviour, characterised by the early onset of MTC and necessitating prophylactic thyroidectomy within the first year of life. Without timely intervention, these patients face an increased risk of developing metastatic MTC, with an average life expectancy of under 30 years. We note the low incidence in the literature of metastatic

MTC in the gallbladder and prostate, as well as the diagnosis of secondary tumours in these organs.

E-PS-10-028

MGMT protein expression by immunohistochemistry and promoter methylation status in metastatic endocrine tumours

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Background & Objectives: O6-methylguanine-DNA methyltransferase (MGMT) is a DNA repair enzyme characterized by its dealkylating effect. Low MGMT levels may sensitize tumours to alkylating agent. Thus, MGMT is emerging as a biomarker in metastatic endocrine neoplasm (m-EN), assessed by immunohistochemistry (IHC). However, there are no recommendations on the contribution of molecular biology in this context. This study aims to explore the relationship between MGMT protein expression and methylation status.

Methods: Over a one-year period, we prospectively analysed MGMT expression by IHC and promoter methylation using ddPCR in 42 FFPE tumour samples from consecutive m-EN. MGMT expression was assessed by two pathologists using the IHC H-score [0–300], with a threshold ≤ 100 to consider expression loss and ddPCR value >6% to consider methylated status.

Results: MGMT loss of expression by IHC (median H-score 7.5[0–100]) and promoter methylation were, respectively, found in: 8/23 & 2/23 digestive neuroendocrine neoplasms, 1/5 & 0/5 adrenocortical carcinomas, 3/6 & 0/6 atypical carcinoids, 0/5 & 1/5 medullary thyroid carcinomas, and 2/3 & 0/3 pheochromocytomas. IHC and ddPCR concordance was 29/42, mainly for IHC expression retention and unmethylated promoter (27/28). 12/34 don't expression MGMT and had no methylation, and 1/3 had a methylation with high expression. Discordant samples had higher tumour cellularity and were frequently surgery specimens. Follow-up under treatment is yet to be assessed to confirm the predictivity of the two markers.

Conclusion: IHC can predict absence of expression of MGMT and potentially the absence of full promoter methylation status in m-EN. But may be more sensitive to detect MGMT loss in the tumour. Indeed, H-scores >100 may indicate a non-methylated profile. It may also be more sensitive to detect MGMT loss in the tumour. These findings could support the use of IHC as a cost-effective screening tool in m-EN and the need to better understand the methylation profile in this tumour.

E-PS-10-029

Study of immunohistochemical profile in pituitary neuroendocrine tumours: correlation trends of Ki67, p53, and CK18 immunomarkers

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Background & Objectives: Currently, Ki-67, p53, and CK18 immunohistochemical markers are being studied across various tumour types. However, their role and co-interactions in pituitary neuroendocrine tumours (PitNETs) are still not fully characterized. The aim of this study is to investigate the possible relationship between these markers in PitNETs.

Methods: Immunohistochemical assessment of Ki-67, p53, and CK18 protein expression was conducted using monoclonal antibodies SP6 (Vitro S.A., Spain), DO-7 (Roche Diagnostics, Switzerland) and DC-10 (Vitro S.A., Spain), respectively. CK18 immunohistochemical reactions were classified as "Positive" or "Negative". Ki-67 and p53 were evaluated in hotspot areas by manually assessing 300 tumour cell nuclei, and positivity was expressed as a percentage (%). Ki-67 immunohistochemical reaction results were categorized into "<3%" and "3%+" groups. P53 intensity expression (p53H) was assessed by calculating the Histoscore (H-score): 1 × percentage of weakly + 2 × percentage of moderately + 3 × percentage of strongly staining nuclei. The inter-observer and intra-observer variability was evaluated by Kappa statistics (Cohen's kappa coefficient>0.9). Spearman's correlation, Chi-Square test, and Mann-Whitney U test were applied ($p<0.05$).

Results: A total of 99 PitNET samples were evaluated for CK18, Ki-67 and p53 protein expression in neoplastic cells. A weak positive correlation ($\rho=0.261$, $p=0.011$) was detected between Ki-67% and p53%, and likewise between Ki-67% and p53H ($\rho=0.223$, $p=0.031$). No statistically significant differences were found between Ki-67 groups and CK18 results ($p=0.774$), nor between p53H and CK18 results ($p=0.140$).

Conclusion: Immunohistochemical profile of pituitary neuroendocrine tumours with correlative trends of Ki67, p53, and CK18 protein expression within neoplastic cells are characterized. Proliferation-demonstrating markers (Ki67, p53) demonstrated significant correlative trends, whereas there were no significant correlative trends between Ki-67 groups and CK18, as well as p53H and CK18, suggesting differences in diagnostic potential of these markers while implementing them in pituitary neuroendocrine tumour diagnostics in clinical pathology setting.

E-PS-10-030

Complex case of synchronous medullary and papillary thyroid carcinoma with oncocytic adenoma and central compartment lymph node metastasis

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Background & Objectives: We describe the clinical and pathological features of a patient diagnosed with unilateral medullary thyroid carcinoma (MTC), stage pT1aN1a, associated with multifocal bilateral papillary thyroid carcinoma (PTC), stage pT1a (m), and oncocytic adenoma.

Methods: A 66-year-old patient was followed up clinically with variable, albeit progressively increasing, calcitonin levels. She had a benign/Bethesda 2 fine needle aspiration (FNA) cytology report in 2019. Due to progressive serum calcitonin elevation and the presence of a hypoechoic nodule in the left thyroid lobe, FNA was repeated in 2024, with a suspicious for MTC/Bethesda 5 diagnosis. A total thyroidectomy with central compartment dissection was performed.

Results: Histopathology revealed two ill-defined foci in the right thyroid lobe, one with papillary architecture and the other with follicular architecture. Tumour cells showed enlarged, irregular, and clear nuclei, while adjacent thyroid parenchyma appeared normal. In the left lobe, an ill-defined tumour with medium-sized cell nests in a collagenous stroma was found. The left-sided lesion was positive for calcitonin and CEA and negative for thyroglobulin. A well-defined oncocytic adenoma was also found adjacent to this tumour. PTC foci were present

in the middle and lower thirds of the left lobe as well. Two of the six central compartment lymph nodes harboured MTC metastases.
Conclusion: This study exemplifies the scenario when histological divergent tumours (MTC, PTC, and oncocytic adenoma) are present within the same thyroid. The immunohistochemical profile supports the diagnosis of MTC. Lymph node metastasis underscores the progression of the disease. These findings emphasize the need for thorough diagnostic evaluation and suggest that early detection and appropriate treatment strategies are critical for managing patients with mixed thyroid malignancies.

E-PS-10-031
A large parathyroid gland adenoma clinically misinterpreted as an atypical thyroid nodule in a patient with tertiary hyperparathyroidism and persistent parathyroid hyperplasia
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Background & Objectives: Secondary hyperparathyroidism (SHPT) causes parathyroid hyperplasia, which is a non-neoplastic process of multiple parathyroid glands. After long-standing SHPT, one of the glands, through a "hyperplasia-to-neoplasia progression sequence", may autonomously gain function, developing tertiary hyperparathyroidism (THPT). We report a case demonstrating both an adenoma and parathyroid hyperplasia simultaneously.
Methods: The patient was a 58-year-old male with chronic kidney disease (CKD) of unknown aetiology, who had received a kidney transplant 30 years ago and progressively developed loss of function. Cervical imaging exams were obtained during follow-up, partly due to complaints of cervical pain. Ultrasound revealed a large nodule in the right thyroid lobe ("TI-RADS" 3), while scintigraphy favoured a large hyperfunctioning right-sided parathyroid gland. A fine needle aspiration cytology of the nodule was performed.
Results: Cytology revealed rare three-dimensional groups composed of small epithelial cells. The report conclusion was atypia of undetermined significance - other. The patient underwent total thyroidectomy and subtotal parathyroidectomy. Macroscopically, the nodule measured 85 mm in its longest axis and was connected by a thick stalk to the right lobe. The remaining specimen was unremarkable. Microscopically, the nodule corresponded to a parathyroid gland with an organoid chief cell proliferation without malignant features. Additionally, both thyroid lobes had multiple foci of papillary thyroid carcinoma measuring between 1 and 4 mm. Contrary to expectations, only one other parathyroid gland was isolated, which also displayed chief cell proliferation. Thus, the final diagnosis was of an adenoma superimposed on parathyroid hyperplasia, consistent with THPT.
Conclusion: Postoperatively, due to the persistence of CKD, PTH levels and other analytical parameters remained abnormal, indicating persistent parathyroid hyperplasia. The patient died 4 months after surgery due to myocardial infarction. This case highlights the challenge of making certain diagnoses (especially when organs are closely related) and underscores the importance of correlating clinical, analytical, imaging and pathological findings.

E-PS-10-032
Prognostic profiling of papillary thyroid carcinoma: unraveling the impact of PD-L1 expression and genetic alterations on tumour behaviour and clinical outcomes
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Background & Objectives: While papillary thyroid carcinoma (PTC) generally has an excellent prognosis, a subset of cases exhibits aggressive behaviour, leading to recurrence and metastasis. Identifying robust prognostic biomarkers is crucial for refining risk stratification. This study explores the prognostic relevance of PD-L1 expression, assessed using the Tumour Proportion Score (TPS), in relation to key molecular alterations (BRAF, TERT, RAS) and clinicopathological features in PTC.
Methods: A retrospective cohort of 84 PTC patients diagnosed between 2016 and 2024 at King George's Medical University, India, was analysed. PD-L1 expression was evaluated by immunohistochemistry on formalin-fixed paraffin-embedded tissues, with TPS categorized as high or low based on the median value. Genetic testing identified BRAF, TERT, and RAS mutations. Clinicopathological data, including tumour stage, lymph node involvement, extrathyroidal extension, and recurrence, were examined. The relationship between PD-L1 expression, molecular alterations, and clinical outcomes was assessed statistically.
Results: PD-L1 expression was observed in 60.7% of cases, with 38.1% classified as TPS high. High PD-L1 expression correlated significantly with older age, advanced stage, lymph node metastasis, and aggressive histological subtypes ($p < 0.05$). BRAF and TERT mutations were more frequently detected in PD-L1 high tumours ($p = 0.032$ and $p = 0.038$, respectively). High PD-L1 expression was associated with an increased risk of recurrence ($p = 0.043$) and distant metastasis ($p = 0.002$). Multivariate analysis identified multiple mutations as independent predictors of poor survival (AOR = 15.8, $p = 0.021$) and recurrence (AOR = 11.22, $p < 0.001$).
Conclusion: High PD-L1 expression, particularly in tumours harbouring BRAF and TERT mutations, is indicative of aggressive disease in PTC. These findings support the potential role of PD-L1 as a prognostic biomarker and highlight its relevance for risk stratification and personalized therapeutic approaches. Further prospective studies are required to validate these results and investigate the clinical utility of immune checkpoint inhibitors in PTC

Funding: Indian council of medical research

E-PS-10-033
Mixed corticomedullary tumour of the adrenal gland: a rare entity
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Background & Objectives: This work aimst o present a rare case of a Mixed corticomedullary tumour of the adrenal gland, along with a brief overview of its histopathological and clinical features.
Methods: A 62-year-old woman with a history of hypertension, type 2 diabetes, breast cancer, and total thyroidectomy for multinodular goiter was referred to the Endocrine Surgery clinic due to an incidental finding of a 25 mm right adrenal mass. Functionally, there was an elevation of both plasma and urinary metanephrines. Due to suspicion of pheochromocytoma, she started medical treatment and was scheduled for laparoscopic right adrenalectomy. Surgical specimen was submited for histopathological analysis.
Results: Gross description: Adrenal gland weighing 10.5 grams and measuring 40 x 25 x 14 mm. At the transition between the cortical and medullary regions, a brownish nodule measuring 27 x 23 x 14 mm was identified.
Microscopy: mixed tumour with elements of pheochromocytoma and adrenal cortical adenoma was observed. Architecture in Zellballen pattern, trabeculae, and large nests and pseudorosettes (<1%) were seen. No marked nuclear pleomorphism, capsular, lymphovascular, or perineural invasion. No necrosis was observed. <1 mitosis/mm2 with a Ki-67 of <2%. Immunohistochemical study revealed positivity for synaptophysin and chromogranin in the pheochromocytoma component and positivity for alpha-inhibin, melan A, and calretinin in the adrenal

cortical component. The tumour was limited to the adrenal gland without extending beyond the capsule.
Conclusion: Mixed corticomedullary tumour of the adrenal gland is an extremely rare condition, characterized by the coexistence of cells of both cortical and medullary origin within a single tumour mass. These tumours have the potential to simultaneously secrete catecholamines and adrenocortical steroid hormones, leading to a complex clinical presentation. To date, fewer than 40 cases have been described.

E-PS-10-034
Anaplastic thyroid carcinoma: clinicopathological, immunohistochemical and molecular study of 10 cases
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Background & Objectives: Anaplastic thyroid carcinoma (ATC) is one of the most aggressive solid tumours, often presenting as a rapidly enlarging cervical mass with invasion of adjacent structures, causing dyspnea, dysphagia, and hoarseness. Although it accounts for only 1–2% of thyroid carcinomas, it causes over 50% of thyroid cancer-related deaths. We aimed to describe the clinical, histopathological, immunohistochemical, and molecular features of a series of ATC cases diagnosed at our institution.
Methods: All ATC cases diagnosed between January 2010 and January 2025 were retrospectively reviewed. Clinical data, histological features (H&E and immunohistochemistry), and molecular results from Next Generation Sequencing (Oncomine Comprehensive Assay, Thermo Fisher) were analysed.
Results: Ten patients were included, 80% women (8/10), with a mean age of 73.2 years (range, 55–88). Half presented with stage IVC at diagnosis, with the lungs as the most common metastatic site (4/5). A surgical specimen was available in all but one case. The mean tumour size was 9.5 cm (range, 4–20). Histologically, 8/10 tumours exhibited a sarcomatoid pattern with undifferentiated follicular cell proliferation, showing spindle-shaped atypical cells, frequent mitoses, and fascicular or storiform architecture. Two cases displayed a pleomorphic pattern with giant tumour cells and marked pleomorphism. Necrosis was present in 9/10 cases, lymphovascular invasion in 5/10, and a differentiated component in 7 tumours (4 with Hürthle cell carcinoma and 3 with papillary carcinoma). Immunohistochemically, 80% were negative for TTF-1, PAX8, and thyroglobulin, while the rest showed weak, focal TTF-1 positivity. P53 mutations were identified in 6 cases; BRAF and NRAS mutations in 3 and 1 cases, respectively. Overall survival was 8.2 months (range, 1–22), with 8 patients deceased.
Conclusion: ATC is a highly aggressive neoplasm with predominant sarcomatoid morphology, extensive necrosis, high mitotic activity and loss of thyroid-specific markers. Due to its rarity and poor prognosis, further studies are needed.

E-PS-10-038
Study of clinical and histopathological features of pheochromocytomas diagnosed at 2007-2024: morphological trends of rare clinical entity
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Background & Objectives: Pheochromocytoma is a neuroendocrine neoplasm that originates from chromaffin cells of the adrenal medulla. The incidence of pheochromocytomas ranges from 0.4 to 9.5 cases per 1 million person-years with national and regional differences. The aim is to overview clinical and histopathological features of pheochromocytomas cases in local pathology department.
Methods: Pheochromocytoma cases processed and analysed morphologically in pathology laboratory from 2007 to 2024 were selected for the study. The patient's age, sex and pathology report data were collected, and cases were re-examined based on TNM classification, GAPP grading system (histological patterns, cellularity). Statistical analysis was performed ($p \leq 0,05$).
Results: Among 114 cases, 43% were male (n=49; median age: 53 years, IQR: 23) and 57% female (n=65; median age: 58 years, IQR: 23; U=1476, p=0.51). The number of cases increases linearly, peaking at 45-60 years for males (40.8%, n=20) and 55-75 for females (49.2%, n=32). Number of cases increased from 0.9% (n=1) in 2010 to 13.2% (n=15) in 2023. Right-sided tumours were subtly more common (51.8%), with 1.8% (n=2) bilateral cases. Most tumours (65.5%, n=74) were <5 cm. The zellballen pattern was most frequent (49.1%, n=56) mostly in females (60.7%, n=34), followed by large and irregular cell nests (47.2%, n=51, p=0.374). Moderate cellularity was most common amongst different patterns (43.5%, n=47, χ^2=2.741, p=0.602). Metastasis was found in 7% (n=8) of the cases and in 75% (n=6) females. Metastasis occurred mainly 10-12 years after the primary tumour diagnosis with tumour size <5cm (87.5%, n=7).
Conclusion: The incidence of diagnosed pheochromocytomas has been increasing annually. Pheochromocytomas were more prevalent in older age groups predominantly in females. No significant distribution difference was observed between left- and right-side tumours. Most metastases were detected 10–12 years after the initial tumour diagnosis, mostly in females, suggesting that follow-up should be prioritized beyond a decade after the primary diagnosis.

E-PS-10-039
Expression of neuroendocrine markers in digestive neuroendocrine neoplasms - an immunohistochemical study of 104 cases
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Background & Objectives: Immunohistochemistry is essential for the diagnosis of digestive neuroendocrine neoplasms (NENs), even when the morphology is obvious. The European Neuroendocrine Tumour Society (ENETS) requires that at least two neuroendocrine markers be positive for the diagnosis of digestive NENs. These markers include Chromogranin A (CgA), Synaptophysin (SYN), and Insulinoma-associated protein (INSM1), which was recently introduced into the WHO 2022 classification of NENs.
The aim of this study was to examine the expression of neuroendocrine markers in digestive NENs and to compare INSM1 with traditional neuroendocrine markers (CgA and SYN).
Methods: A retrospective comparative study of the three neuroendocrine markers (CgA, SYN, and INSM1) on a series of 104 cases of digestive neuroendocrine neoplasms diagnosed at the Department of Pathology and Cytology at Blida University Hospital over a period of 5 years (2017 - 2021).
Results: CgA was positive in 98.9% of well-differentiated neuroendocrine tumours (NETs) and 88.2% of neuroendocrine carcinomas (NECs). SYN was positive in 98.9% of NETs and 94.1% of NECs. INSM1 was positive in 95.4% of NETs and 94.1% of NECs.
Conclusion: We conclude that INSM1 is a useful marker of neuroendocrine differentiation in Gastroenteropancreatic neuroendocrine

neoplasms. Compared with traditional neuroendocrine markers, INSM1 is less sensitive but more specific.

E-PS-11 E-Posters Gynaecological Pathology

E-PS-11-001

Evaluation of clinical and pathological prognostic findings in granulosa cell tumour cases: a retrospective study

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Background & Objectives: Adult granulosa cell tumours are the most common type of ovarian sex cord-stromal tumours, yet they remain rare. These tumours typically present in perimenopausal women, often with estrogenic effects. Due to their rarity, studies on these tumours are limited.
Methods: 55 patients diagnosed with granulosa cell tumours at Dokuz Eylül University Hospital between 2004 and 2023 were identified. The clinical and pathological characteristics of these patients were analysed.
Results: The mean age was 53.2 ± 12.98 years,with an average tumour size of 8cm(range: 0.5- 25cm). Vascular invasion was detected in 2 patients(12 patients were not evaluable). Unilateral tumours were observed in 40 patients,and a bilateral tumour in 1 patient. The tumour was located on the right side in 24 patients and on the left side in 21 patients.Tumour rupture was present in 10 patients and absent in 32. 25 tumours were cystic, while 12 were solid.Metastasis was detected in 8 patients, and 10 patients had died. The distribution of tumour stages was as follows:31 patients in stage 1a, 1 patient in stage 1b, 8 patients in stage 1c, and 1 patient in stage 2a. Among 38 patients, 23 had endometrial hyperplasia, 3 had endometrial tumours, and 12 had a normal endometrium.The average time to metastasis was 5.43 ± 5.68 years.No significant association was found between rupture and metastasis($p = 1$).A significant relationship was observed between stage and metastasis($p = 0.003$). No association was found between tumour rupture and mortality($p = 1.0$), while a borderline relationship was observed between stage and mortality($p = 0.057$) and a significant association was found between metastasis and mortality($p < 0.001$).
Conclusion: Granulosa cell tumours are generally low-grade, with a better prognosis compared to other ovarian tumours.These hormone-secreting tumours, as demonstrated in our study(in 69.42% of cases), are often associated with endometrial pathologies. Given the potential for late-onset metastasis, long-term follow-up is essential.

E-PS-11-002

Ovarian fibrothecomas, fibromas, and thecomas: a clinicopathological and imaging analysis of 73 cases

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Background & Objectives: Ovarian fibrothecomas, fibromas, and thecomas are rare sex cord-stromal tumours with overlapping clinical and pathological features. This study aims to analyse their incidence, clinical characteristics, imaging findings, and histopathological features to better characterize their presentation and management.
Methods: This retrospective study analysed 73 cases diagnosed at our institution from January 2011 to December 2024. Clinical parameters, imaging findings, tumour markers, and histopathological features were assessed.
Results: The cohort included 49 fibromas, 14 fibrothecomas, and 10 thecomas. The mean patient age was 59 years (±12). The median tumour size was 85 mm (IQR: 60–120 mm). Three cases (4.1%) were bilateral, and two were extraovarian. Half of the cases were incidental, while symptomatic patients presented with chronic or acute abdominal pain (18 cases, 24.7%), ascites (4 cases, 5.5%), or vaginal bleeding (1 case, 1.4%). Most patients (46/73, 63%) underwent total hysterectomy with bilateral adnexectomy, while most of the remaining patients primarily had unilateral adnexectomy. Imaging findings varied, with lesions appearing solid, cystic, or mixed on ultrasound. CT and MRI typically confirmed an adnexal origin, with most lesions showing mild, heterogeneous post-contrast enhancement. CA-125 was elevated in 10/29 patients and CEA in 3/12. Histopathological analysis revealed tumours with generally low mitotic activity, with only three classified as cellular and mitotically active. Sudan staining, performed in 22 cases, was positive in 2 thecomas and 10 fibrothecomas, supporting lipid-rich stromal differentiation. Reticulin staining, when performed, confirmed a pericellular pattern. No recurrences were observed during follow-up.
Conclusion: Ovarian fibrothecomas, fibromas, and thecomas are uncommon neoplasms predominantly affecting postmenopausal patients. While imaging and tumour markers aid preoperative assessment, diagnosis is histological. Fertility-sparing tumour resection is preferred in younger patients when feasible, while radical surgery is generally indicated for perimenopausal and postmenopausal patients.

E-PS-11-003

Extraovarian fibrothecomas: a report of two rare cases, including one associated with Meigs syndrome

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Background & Objectives: Fibrothecomas are rare ovarian tumours, accounting for approximately 4% of all ovarian neoplasms. Extraovarian fibrothecomas are exceptionally rare, with only 15 cases reported in the literature. These tumours have been identified in the broad ligament, retroperitoneum, and mesocolon. Accurate diagnosis requires thorough histopathological and immunohistochemical evaluation.
Methods: We present two cases of extraovarian fibrothecomas with distinct clinical, radiological, and histological features.
Results: The first case involved a 56-year-old woman with a mass adherent to the omentum and intestines. Ultrasound revealed a solid, well-defined 15 cm lesion with free fluid in the Douglas space. Tumour resection, along with a 22 cm segment of the small intestine, was performed. Histopathological analysis confirmed a fibrothecoma with low mitotic activity, positive for vimentin, SMA, WT1, focal inhibin, and calretinin. There was no recurrence observed. The second case was a 75-year-old patient with a 25 cm abdominal mass, ascites, and pleural effusion, consistent with Meigs syndrome. Imaging suggested a cystic-solid ovarian tumour with significant free peritoneal fluid, and CA-125 was markedly elevated. The patient underwent tumour resection along with a total hysterectomy and bilateral salpingo-oophorectomy. Surgery revealed intact ovaries and an extraovarian tumour, likely originating from the broad ligament. Histopathological examination showed typical features, including a characteristic reticulin framework and Sudan-positive lipid droplets, with low mitotic activity. Immunohistochemistry confirmed positivity for FOXL2, CD56, and focal inhibin and calretinin. Postoperatively, the patient's preexisting pleural effusion worsened, requiring drainage, but she recovered well with supportive treatment. There was no tumour recurrence, and follow-up remained uneventful.
Conclusion: Extraovarian fibrothecomas are rare and can clinically mimic ovarian malignancies. Awareness of their clinicopathological and radiological characteristics is essential for accurate diagnosis and optimal management.

E-PS-11-004

Malıgnant transformatıon in mature cystıc teratoma: a serıes of 6 cases

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Background & Objectives: Mature cystic teratoma is the most common ovarian germ cell neoplasm. Malignant transformation is rarely observed, usually in older patients and typically in patients with unilateral tumours. The most common somatic malignancy in ovarian teratoma is squamous cell carcinoma. Sarcomas occur more often in younger patients than carcinomas. Tumour marker concentration levels (CEA), age, and the tumour maximum diameter are predictive indicators for malignant transformation. The prognosis of patients with malignant transformation is unfavourable, only 15-30% of patients survive 5 years.
Methods: In this study, between 2017 and 2024, at İstanbul Prof. Dr. Cemil Taşcıoğlu City Hospital, malignant transformation was observed in 6 out of 247 patients diagnosed with mature cystic teratoma.
Results: In one of these six cases, neuroendocrine tumours were observed, while three cases had papillary thyroid carcinoma, one case had squamous cell carcinoma and one case presented with thyroid oncocytic adenoma. In half of these six cases, the tumours originated from the left ovary. Median age was found to be 48,3 (31-74 years) and the average tumour size is 8,4 cm (5,5-17). However, elevated CEA levels were not observed in any of our patients. The prognosis of patients with mature cystic teratoma with malign transformation in unfavourable. Better prognosis has been reported when the malignant element is a squamous cell carcinoma confined to the ovary. In such cases, the reported 5- year survival is 63%. All of our patients are still alive today.
Conclusion: In conclusion, although mature cystic teratoma is the most common benign germ cell neoplasm of the ovary, malignant transformation can occur. Malignant transformation should remain in consideration, especially with increased patient age, tumour size, or tumour marker levels. Macroscopically, careful examination should be performed, and multiple samples should be taken from different areas.

E-PS-11-005

Unveiling mesonephric-like adenocarcinoma: a case series highlighting variability in immunohistochemical expression

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Background & Objectives: Mesonephric-like adenocarcinoma is a rare and recently recognized subtype of gynaecologic malignancy. It was first introduced in the 5th edition of the World Health Organization Classification of Female Genital Tumours and is still frequently misdiagnosed. This case series describes the only two cases of mesonephric-like adenocarcinoma in our Pathology Department, emphasizing the diagnostic challenges of this rare tumour.
Methods: We present two cases of mesonephric-like adenocarcinoma involving the uterus and ovaries. The first case is that of a 64-year-old female who underwent a routine CT scan during her neurological check-up, uncovering bilateral adnexal tumours with uterine involvement. She had a total hysterectomy, adnexectomy, peritoneal biopsy, and peritoneal liquid cytology. The second case is a 49-year-old female with recurring pelvic pain, who underwent a CT scan, uncovering a left adnexal cyst. She had a left adnexectomy.
Results: In the first case, histopathology revealed synchronous primary mesonephric-like adenocarcinoma of the uterus and both ovaries, with direct extension to the left fallopian tube and pelvic soft tissues and distant peritoneal metastases. Immunohistochemistry showed PAX8 and TTF1 positive, GATA3 and WT1 negative, thus supporting the diagnosis of mesonephric-like adenocarcinoma. In the second case, histology demonstrated a mesonephric-like adenocarcinoma involving the left ovary, and immunohistochemistry supported the diagnosis with PAX8 and GATA3 positivity, while TTF1 and WT1 were negative.
Conclusion: Mesonephric-like adenocarcinoma is a rare and challenging diagnosis that requires a high level of suspicion and detailed immunohistochemical profiling. The cases described highlight the variability in the immunohistochemical expression of GATA3 and TTF1, which can present in an inverse pattern in different cases. Fewer than 100 cases have been reported in the literature, therefore further research is essential to define diagnostic criteria and guide clinical management of these rare tumours.

E-PS-11-007

Precancerous lesions and squamocellular carcinoma of the vulva

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Background & Objectives: The spectrum of vulvar lesions includes a variety of conditions, from infectious and benign dermatological changes to precancerous lesions and invasive carcinoma. Studies have shown that HPV-associated invasive vulvar carcinomas have better overall survival and lower recurrence rates compared to HPV-negative tumours. The aim of this retrospective study was to analyse the histopathological and immunohistochemical features of squamous precancerous lesions and invasive squamous cell carcinomas of the vulva, as well as the demographic characteristics of affected patients.
Methods: Data were collected from the archives of the Centre for Pathology and Histology at University Clinical Centre of Vojvodina. Tissue samples were obtained through biopsy or excision between January 2021 and December 2024 at the Clinic for Gynaecology and Obstetrics. Analyses included immunohistochemical staining with p16 and p53 antibodies.
Results: The average age of patients was 55 years (range 19–90). Condylomas were the most frequent lesions (35%), while differentiated VIN (dVIN) was least common (3%). Most samples (57%) were obtained via biopsy. Of all lesions, 36.6% underwent immunohistochemical analysis. Among these, HPV-associated carcinomas were the most frequent (32%; average age 57.4), followed by usual VIN (uVIN) uVIN3 (23%; 59.4), HPV-independent carcinomas (18%; 74.5), uVIN1 (14%; 62), dVIN (9%; 56), and uVIN2 (4%; 52). The majority of invasive carcinomas exhibited moderate differentiation (57%), whereas HPV-independent carcinomas showed a higher degree of differentiation (which can complicate diagnosis).
Conclusion: The study concluded that HPV-associated lesions occur in younger patients, while HPV-independent lesions are more common in older individuals and tend to show higher differentiation. This distinction is clinically significant and presents a diagnostic challenge.

E-PS-11-008

Small cell carcinoma of the ovary, hypercalcaemic type

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Background & Objectives: 31-year-old female patient presented with pelvic pain, abdominal swelling and general weakness.

Ultrasound and CT showed bilateral ovarian tumours. Laboratory results showed elevated serum calcium levels and CA-125. Anamnesis showed that the patient's sister died with same diagnosis, aged 32.
Methods: Intraoperative analysis, histology, immunohistochemistry and FoundationOne test were used.
Results: Intraoperative analysis showed bilateral, solid, large ovarian tumours sized 28 and 20 cm, with areas of haemorrhage, necrosis and cystic degeneration.
Histology showed diffuse tumour growth, minimal intervening stroma and follicle-like spaces with eosinophilic secretion. Tumour cells had monomorphic, small, round to ovoid nuclei with small nucleoli, scant cytoplasm and brisk mitotic activity. Immunohistochemically, tumour cells were WT1, EMA, CK8/18, NSE and vimentin positive, synaptophysin focally positive. p53 immunohistochemistry revealed mutated immunophenotype. Inhibin, calretinin, CD10, OCT4, PLAP, C-kit, TTF-1 and melan A stains were negative. Using FoundationOne test, genomic alterations were identified – SMARCA4 E650 loss exons 9-13.
Conclusion: Patient received platinum-based chemotherapy and died ten months after diagnosis.
Small cell carcinoma of the ovary accounts for <1% of ovarian tumours. Somatic or germline mutations on SMARCA4 (gene involved in chromatin remodelling) are detected in almost all tumours. The mutation leads to loss of function and it is highly specific and sensitive for making the final diagnosis.
Differential diagnosis include: juvenile granulosa cell tumour, undifferentiated carcinoma, poorly differentiated Sertoli-Leydig cell tumour, metastatic melanoma and lymphoma.
One third of patients have a germline mutation, even those without a positive family history (35%). Every patient with this diagnosis needs to be referred to a genetic counselling centre.
Stage is the most important prognostic factor, with less than 30% of patients with stage IA being alive without disease after surgery. International prospective multicentre protocols with collection of data are urgently needed to be considered for both first-line and relapsed disease in this particularly rare condition.

E-PS-11-009
Borderline ovarian tumours – frozen section versus final diagnosis
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Background & Objectives: Borderline ovarian tumours are considered low malignant potential tumours, with some characteristics of malignancy but lacking destructive stromal invasion. The most common types are serous and mucinous borderline tumours, while other histological types are rarely encountered. Our study examined the difference between the diagnosis made after the frozen sections and after the surgery.
Methods: A retrospective study conducted at the University Clinical Centre of Vojvodina, Novi Sad, Serbia, evaluated a total of 71 patients diagnosed with borderline ovarian tumours following a frozen section examination during the five years (2019-2023). Archival medical documentation from the Centre of Pathology and histology were analysed.
Results: Borderline ovarian tumours usually occur in the working-age population (median age 49). From a total of 71 patients who were diagnosed with borderline tumours following frozen section examination, after the additional sampling and pathohistological examination of the surgical material, we found that in 51 (71.8%) of cases, the pathologist confirmed the initial diagnosis of borderline tumour. The initial diagnosis was downgraded from borderline tumour to benign tumour in 4 (5.6%) of cases or to benign tumour with focal proliferation of less than 10% in 6 (8.5%) of cases. Upgrade from initial diagnosis of borderline tumour to malignant tumour in surgical material was present in 10 (14.1%) of cases. Almost all tumours were diagnosed in the pT1 stage (94,4%), while the most common histological types encountered were serous borderline tumour (54,9%), mucinous borderline tumour (12,7%), and serous carcinoma (9,9%).
Conclusion: Borderline ovarian tumours are a real diagnostic challenge, with a significant influence on the decision in further treatment of patients. Detailed gross examination and proper sampling during frozen section analysis can significantly reduce errors in making this challenging diagnosis.

E-PS-11-010
The impact of the 2023 FIGO staging system on endometrial carcinoma: a five-year case series analysis
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Background & Objectives: Risk categorization in endometrial cancer (EC) rely on integrating clinical-pathological and molecular features. The 2023 FIGO staging system (FSS) incorporates molecular profiling for prognostic accuracy and personalized therapy. The objective of this study was to compare the 2009/18 and 2023 FSS in a large series of EC.
Methods: A study of EC cases (2020–2024) was performed at a tertiary-level hospital. Clinical and histopathological reports were reviewed for staging using the 2009/2018 and 2023 FSS.
Results: A total of 261 EC cases were diagnosed. Based on the 2009/2018 FSS, 61.7% (n=161) were classified as stage IA, with 44 cases (27.3%) upstaged according to the 2023 FSS: IC (4 cases, 9.1%), IIB (12 cases, 27.3%), IIC (7 cases, 15.9%), and IICm (p53abn) (21 cases, 47.7%). In the 28 cases (14.6%) classified as stage IB, 16 (42.1%) were upstaged: IIB (7 cases, 43.7%), IIC (6 cases, 37.5%), and IICm (p53abn) (3 cases, 18.7%). Conversely, four cases (1.5%) previously classified as stage II were reclassified as stage IIA (three cases, 75%) and IICm (p53abn) (one case, 25%). Stages IIIA, IIIB, IIIC1, IIIC2, and IVA remained unchanged. Of the 18 cases (6.9%) classified as IVB, 6 (33.3%) remained IVB, while 12 (66.7%) were reclassified as IVC.
Conclusion: The 2023 FSS incorporated pathological and molecular features into EC staging. In this study, 25% of stage IA cases were upstaged, and more than 40% of stage IB cases were upgraded to stage II. Stage II remained largely unchanged as no POLEmut cases were downgraded. Stage III cases exhibited no significant changes except for newly added subclassifications. Stage IVA remained unmodified, while stage IVB was subdivided, with one-third of cases being upstaged to IVC. In summary, the 2023 FSS significantly impacts stages I and II, enhancing staging accuracy and optimizing therapeutic management based on clinicopathological prognostic factors.

E-PS-11-011
Uterine carcinosarcoma: a rare biphasic tumour with aggressive features
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Background & Objectives: Uterine carcinosarcomas are rare, aggressive biphasic tumours composed of high-grade carcinomatous and sarcomatous components. They typically occur in postmenopausal women, and are often associated with tamoxifen use or prior pelvic radiotherapy. Thought to arrise from carcinoma through

transdifferentiation, they frequently harbour TP53 mutations, resembling serous endometrial carcinoma.
Methods: This report presents the case of a 69-year-old patient presenting with vaginal bleeding. She had no history of external oestrogen exposure. Pelvic CT showed a thickened endometrium and a distended uterine cavity. The patient underwent curettage biopsy and histopathological examination that was suggestive of carcinosarcoma or undifferentiated adenocarcinoma, requiring further investigation. Surgical treatment involved total hysterectomy, bilateral salpingo-oophorectomy and Wertheim lymphadenectomy.
Results: Gross examination revealed a 6 cm endometrial tumour with necrotic areas, infiltrating the outer layer of the myometrium, with focal serosal involvement. Microscopically, a biphasic malignant proliferation was detected, composed of high-grade endometrioid carcinoma and a poorly differentiated mesenchymal component, confirming the diagnosis of carcinosarcoma. Extensive necrosis (60%) and lymphovascular invasion were present.
Immunohistochemistry showed p53 mutant-type positivity (95% of cells), MMR proficiency, and focal positivity for ER, AE1/AE3 and PAX8 in the epithelial component. The sarcomatous component was negative for desmin, CD34, and strong positive for INI1. HER2neu expression was not detected.
Conclusion: Uterine carcinosarcomas are rare tumours, accounting for about 5% of uterine malignancies. These tumours are usually at an advanced stage at the time of diagnosis. While not required for diagnosis, immunohistochemistry is useful in confirming the biphasic nature.
Co-expression of epithelial and mesenchymal markers by itself is insufficient for diagnosis and heterologous elements in endometrioid carcinoma do not confirm carcinosarcoma. Considering its rarity, recognizing this tumour is important for the accurate management of patients.

E-PS-11-012
Histopathological changes in placentas of substance-using individuals: a retrospective study
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Background & Objectives: In today's society, substance addiction poses significant economic, social, and physiological challenges. Substance abuse can lead to various adverse effects on the human body, including arterial thrombosis in the lungs, acute vasculitis, drug-related liver disease, and arterial thrombosis in the central nervous system. Additionally, substance abuse during pregnancy can result in detrimental effects on the placenta, the enigmatic organ connecting the foetus and the mother, leading to various anomalies and intrauterine growth retardation. In this retrospective study, we examine five placental specimens from pregnancies between 2017 and 2025 at our institution.
Methods: We will examine seven placental specimens collected at our hospital between 2017 and 2025. Six of these specimens are from preterm pregnancies, and one is from a term pregnancy. The specimens, fixed in 10% formalin, embedded in paraffin, and sectioned at 4-5 micrometers thickness, will be stained with haematoxylin-eosin for examination. Macroscopic and microscopic analyses will be conducted using the Placental Work Group Consensus Statement as a guide.
Results: Upon examination of the seven placental specimens, we observed findings consistent with Maternal Vascular Malperfusion (MVM) and Foetal Vascular Malperfusion (FVM). Deciduitis was identified in two of the specimens. Dystrophic calcification was observed in six of the seven specimens, while chorangiosis was observed in three specimens. Sclerosis of some villi was noted, and delayed villous maturation was observed in one placenta. Maternal Inflammatory Response was observed in two placental specimens, while Foetal Inflammatory Response was observed in one.
Conclusion: Our study reveals a significant increase in Maternal Vascular Malperfusion in placentas of individuals with substance addiction compared to those of normal pregnancies. However, we found similar rates of Foetal Vascular Malperfusion, Maternal Inflammatory Response, and Foetal Inflammatory Response compared to normal pregnancies.

E-PS-11-013
Correlation of TP53 mutation types with immunohistochemical p53 staining patterns in high-grade serous ovarian carcinomas
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Background & Objectives: High-grade serous ovarian carcinoma is characterized by a high frequency of mutations in the TP53 tumour suppressor gene. The majority of TP53 mutations are missense mutations, typically clustered around specific hotspot amino acid residues. This retrospective study aimed to analyse the frequency, types, and distribution of TP53 mutations in high-grade serous ovarian carcinoma.
Methods: Data from 75 cases were collected, including p53 immunohistochemical (IHC) staining patterns and TP53 mutations identified through next-generation sequencing (NGS).
Results: According to the next-generation sequencing (NGS) results, the majority of cases exhibited missense mutations (65.3%). Missense mutations were followed by stop-gained variants (13.3%), splice-site mutations (6.7%), and frameshift mutations (5.3%). IHC analysis of p53 staining patterns revealed overexpression in 73.3% of cases and a null staining pattern in 26.7% of cases. When comparing IHC staining patterns with mutation results, it was observed that 93.9% of cases with missense mutations exhibited overexpression staining. Conversely, the majority (81%) of cases with mutations causing significant alterations in protein structure demonstrated a null staining pattern ($p<0.001$). In 5 cases, overexpression staining was observed despite the absence of detectable mutations in the NGS analysis.
Conclusion: In conclusion, the IHC staining patterns of p53 significantly correlated with mutation types. The majority of mutations (88.6%) were located within the DNA-binding domain (DBD) of the TP53 gene (amino acids 102-292).

E-PS-11-014
Hydatidiform moles: the contribution of ancillary techniques in refining the histopathological diagnosis
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Background & Objectives: The hydatidiform mole (HM) is the most common type of gestational trophoblastic disease. Differentiating HM from non-molar pregnancies, and distinguishing complete HM (CHM) from partial HM (PHM), is difficult due to overlapping morphological features. As studies showed a high rate of misclassification, we aimed to assess reliable markers for distinguishing and classifying HM, addressing the limitations of current molecular techniques.
Methods: Our retrospective study included 64 cases of HM and hydropic abortions (HA), diagnosed in women between 17-36 years old, during 2010-2024, within the Pathology Department of "Elena Doamna" Clinical Hospital of Obstetrics and Gynaecology, Iasi, Romania. The surgical specimens were histopathologically assessed by routine histological methods, supplemented with additional immunohistochemical techniques, using a panel of specific markers, together with semiquantitative immunoscores.
Results: The histopathological examination revealed 38 (59.37%) cases of PHM, 16 (23.88%) cases of CHM and 10 (15.62%) cases of HA.

In order to differentiate HM from HA and CHM from PHM, all cases underwent immunohistochemical assessment of p57, Ki-67, β-hCG and E-cadherin. The assessment of p57 showed 18% positivity for CHM and 100% positivity for PHM and HA, the immunoexpression of Ki-67 was weak in 12.5%, moderate in 50% and strong in 37.5% of CHM, while weak in 57.8%, moderate in 23.68% and strong in 10.52% of PHM, and weak in 100% cases of HA. As for β-hCG, the highest immunoscore was assessed in CHM, followed by PHM and HA, while for E-cadherin, the highest immunoscore was expressed in HA, followed by PHM and CHM.
Conclusion: Morphology offers relative information in the diagnosis of molar pregnancies, requiring the corroboration with clinical, paraclinical and imagistic data, as well as a series of ancillary techniques. The histopathological diagnosis of HM continues to be negatively influenced by interobserver variability, an algorithmic histopathology-immunohistochemistry approach, completed by genotyping, refining the accuracy of the histopathological examination.

E-PS-11-015
Exploring TTF-1 expression in endometrial carcinomas: implications for pulmonary metastasis diagnosis and the role of PAX8
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Background & Objectives: The expression of TTF-1 in endometrial carcinomas is rare, found in 8% of cases, and only in 2% of low-grade endometrioid tumours. This necessitates careful management when studying a pulmonary lesion in patients with a history of endometrial carcinoma. PAX8 is a characteristic marker of the gynaecological tract that could assist in differential diagnosis.
Methods: Based on a case of pulmonary metastasis from a TTF-1+ endometrial carcinoma, a search was conducted in the archive of our department over the last 15 years, identifying 26 other cases. The expression of TTF-1 was studied in all of them.
Results: The index case is that of a 79-year-old woman with low-grade endometrioid adenocarcinoma at stage III, treated 5 years ago. Three years later, a pulmonary lesion suggestive of primary neoplasia was identified, and it was diagnosed as primary pulmonary adenocarcinoma with a compatible immunohistochemical profile (TTF1+/NapsinA+/CK7+/CK20-). Following radiological monitoring, two months ago, bone, lymph node, and pulmonary lesions were detected. The pulmonary biopsy showed a morphology compatible with the endometrial lesion, with positivity for TTF1, NapsinA, PAX8, and oestrogen receptors, suggesting metastasis from endometrioid adenocarcinoma. Molecular analysis revealed mutations in KRAS, PI3KCA, and ARID1A. KRAS mutations have been associated with mucinous changes in low-grade endometrioid adenocarcinoma, as well as the rare expression of TTF-1 in these neoplasms. In 19 additional cases, TTF1 expression was negative.
Conclusion: Although advancements in immunohistochemistry and molecular techniques have been crucial in improving diagnosis, the value of morphology should not be overlooked. Immunohistochemical patterns, such as TTF-1+/CK7+/CK20-, are suggestive of primary pulmonary neoplasia, but they should be interpreted alongside clinical history and a detailed morphological evaluation. The expression of TTF1 in other neoplasms, such as endometrial carcinoma, should be considered, and in patients with gynaecological histories, the use of PAX8 for differential diagnosis would be recommended.

E-PS-11-016
Primary ovarian malignant melanoma arising in a mature teratoma with synchronous endometrial carcinoma: a rare case report
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Background & Objectives: Malignant transformation in ovarian mature cystic teratomas is a rare phenomenon, occurring in approximately 1.5–2% of cases. The most common malignant component is squamous cell carcinoma. Malignant melanoma arising within a mature teratoma is exceedingly rare, with only a few cases reported in the literature. Here, we present a unique case of primary ovarian malignant melanoma arising in a mature teratoma, coexisting with synchronous endometrioid endometrial carcinoma—one of the rarest combinations of dual primary gynaecologic malignancies.
Methods: A 59-year-old postmenopausal woman presented with vaginal bleeding. Imaging revealed a complex left adnexal mass and endometrial thickening. She underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, splenectomy, omentectomy, and pelvic-paraaortic lymph node dissection.
Results: Histopathological examination revealed malignant melanoma arising within a mature cystic teratoma of the left ovary, adjacent to teratomatous elements such as squamous epithelium, hair shafts, bone, respiratory epithelium, and sweat glands. The tumour had metastasized to the spleen and 13 pelvic-paraaortic lymph nodes. Immunohistochemical analysis showed positivity for HMB45, Melan-A, SOX10, and PRAME. Additionally, synchronous grade 2 endometrioid carcinoma was identified in the endometrium and tumour cells positive for PAX8, CK7, ER, and PR. p53 exhibited wild-type expression, and MMR protein expression was retained (MS-Stable). A comprehensive systemic evaluation, including dermatological assessment, was performed to exclude primary cutaneous melanoma. No primary cutaneous or ocular lesion was identified, leading to the diagnosis of primary ovarian malignant melanoma. At the 10-month follow-up, the patient remains asymptomatic and is undergoing anti-PD-1 immunotherapy (nivolumab).
Conclusion: Melanoma arising in an ovarian teratoma is extremely rare, and its coexistence with synchronous endometrial carcinoma presents additional diagnostic and therapeutic challenges. Differentiating primary ovarian melanoma from metastatic melanoma is crucial, as management strategies differ significantly. This case underscores the importance of thorough histopathological evaluation and integration of clinical and radiological findings for accurate diagnosis and optimal patient management.

E-PS-11-017
Intravenous leiomyomatosis: a double-sided tumour
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Background & Objectives: Intravenous leiomyomatosis is a rare type of benign smooth muscle tumour that is defined by the presence of vascular extension and invasion of smooth muscle lesions in pelvic or systemic vasculature system. Its incidence low and the pathogenesis is still unclearnowadays. However, most studies prove that the primary tumour is usually located in the uterus then spreads along the intra- and extrauterine veins and can extend to the inferior vena cava, right atrium, right ventricle, and pulmonary artery. Clinical symptoms in aregenerally non-specific and it is easy to be misdiagnosed. It is however an aggressive diseaseand can prevent fatal consequences.
Methods: Our study is descriptive and retrospective about 7 cases. All data were collected from the PCR Laboratory of the ISA between 2010 and 2024. These samples underwent anatomopathological study followed by an immunohistochemical study.
Results: Our patients were aged between 38 and 72 years old. The average age was 46.7. All patients consulted for pelvic pain or metrorrhagia.

CT scan was performed, revealing cavitary fibrous nodules and a similar image in superior veina cava in one case. The patients underwent hysterectomy. Macroscopic examination revealed whitish fasciculated intracavitary nodules. These were associated with intravascular masses in the form of finger-like strips dissociating the muscle with retraction clefts.
On histological examination, the nodules responded to a regular proliferation of smooth muscle cells arranged in long intersecting bundles without cytonuclear atypia, mitotic figures or foci of necrosis. The digitiform masses also had a superposable histological appearance. The tumour cells were Desmine (+), lined with cells CD31 (+) thus confirming diagnosis of intravascular leiomyomatosis.
Conclusion: Despite its rarity, intravascular leiomyomatosis may be associated with high morbidity. Moreover, it presents with non-specific symptoms which could easily be misunderstood. Therefore, early recognition is important and should be considered in patients with a history of uterine fibroids or surgery

E-PS-11-018
Pelvic-genital hydatid cyst: a case report series
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Background & Objectives: Hydatid cyst is a public health problem in endemic areas. It often affects the liver and the lung. Pelvic-genital location in women is rare. We present 4 cases of pelvic-genital hydatid cysts which were diagnosed by anatomopathological diagnosis.
Methods: We collected four cases of pelvic hydatid cysts in our department between January 2016 and January 2023. The epidemiological and clinical data were obtained from patients' medical records, while anatomopathological information was retrieved from anatomopathological reports.
Results: Mean age was 55 years. The hydatid cyst was found in all 4 cases as a pelvic mass during imaging for abdominal pain. In 2 cases, it was located in the pelvic area, in 1 case, it was adjacent to the uterine wall and ovary, and in 1 case, it was located in the left broad ligament. It was multilocular in one case and unilocular in the remaining 3 cases, and there was no extra-pelvic location. Macroscopic examination showed a white cystic wall containing fragments of translucent proligere membrane. Histologically, it was a typical hydatid cyst, with a pericyst, an anhist cuticle, and a germinative proligere membrane.
Conclusion: Echinococcosis can affect individuals of any age, although it is more commonly seen in young adults. Pelvic-genital hydatid cysts are rare, with a frequency ranging from 0.3 to 4.27%. The genital location is the most common site of pelvic hydatidosis. It should be considered in the differential diagnosis of any pelvic-genital cystic lesion, such as ovarian cyst, hydrosalpinx and ovarian tumours especially in endemic areas.

E-PS-11-019
Epithelioid trophoblastic tumour: case report of a rare entity
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Background & Objectives: Epithelioid trophoblastic tumour (ETT) is a rare neoplasm arising from chorionic intermediate trophoblast cells. It typically affects women of reproductive age following a gestational event and presents a diagnostic challenge due to its rarity and histological similarities to other pathologies. We report a case of ETT to highlight its clinical and histopathological features.
Methods: A 45-year-old woman presented with a submucosal lobulated mass in the lower uterine segment, incidentally identified via ultrasonography and later evaluated by magnetic resonance imaging (MRI). The tumour, measuring 3.4 cm on MRI, was initially considered a leiomyoma/adenomyoma with no suspicious features. The patient, who had an intrauterine device (IUD) inserted one year prior, had no symptoms or recent pregnancy history. She underwent a total hysterectomy.
Results: Gross examination revealed a 6.5 cm submucosal mass in the lower uterine segment, with a white-yellowish, fleshy appearance on sectioning. Histological analysis showed a well-circumscribed lesion with nodular perivascular growth forming cords and nests of cells, along with extensive areas of geographic necrosis. The neoplastic cells exhibited vesicular nuclei and abundant eosinophilic cytoplasm. Hyaline eosinophilic material was also observed within the tumour. Immunohistochemical staining revealed positivity for p63, Inhibin, GATA3, CD10 and focal expression of PLAP. The Ki67 proliferation index was 25%. The tumour cells were negative for hCG, oestrogen receptors, and progesterone receptors, supporting the diagnosis of ETT.
Conclusion: Most ETT develop after a gestational event, with a latency period ranging from months to up to 10 years. Accurate diagnosis is crucial for effective management. ETT has a reported mortality rate of 10–24%, with stage IV being an independent prognostic factor. While ETT can sometimes occur as part of a mixed trophoblastic tumour, no other forms of gestational trophoblastic neoplasia were identified in our case. The patient is currently doing well with no signs of metastatic disease.

E-PS-11-020
Adenosarcoma arising in an endometrial polyp - a case report
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Background & Objectives: Uterine adenosarcoma is a rare malignant biphasic tumour composed of a benign epithelial component and a malignant stromal component. It commonly presents with abnormal uterine bleeding. Diagnosis is based on morphological and immunohistochemical features. The occurrence of adenosarcoma within endometrial polyps is rare, with only isolated case reports in the literature. Herein, we report an adenosarcoma arising in a uterine polyp, focusing on its clinical presentation, gross examination, and histopathological findings.
Methods: An 80-year-old woman presented with abnormal uterine bleeding. MRI revealed a 9 cm, heterogeneous lesion with multiple cystic and haemorrhagic nodular areas, filling the uterine cavity and extending to the cervix. CA 125 and CA 19-9 were elevated. Biopsies were performed, with no evidence of malignancy. Due to the suspicious aspects of the intrauterine lesion, total hysterectomy with bilateral salpingo-oophorectomy was performed.
Results: Gross examination revealed a 12 cm polyp filling the uterine cavity. Histologically, it was a conventional endometrial polyp. Focally, in a 2 cm area, a biphasic tumour with stromal growth and a leaf-like pattern, with dilated glandular spaces lined by benign endometrial epithelium was identified. The stroma had areas with moderate cellularity, composed of oval-shaped cells with moderate to severe atypia and a mitotic index of up to 4 mitoses per 10 high-power fields. There was no myometrial infiltration, necrosis, heterologous elements, or vascular invasion. Immunohistochemical analysis showed CD10 positivity, focal expression of oestrogen and progesterone receptors, Ki-67 proliferation index of 15%, and wild-type p53 expression in the mesenchymal component.
Conclusion: The final diagnosis was adenosarcoma in an endometrial polyp (with focal areas of high-grade sarcoma) (pT1a; FIGO: IA). This occurrence is rare and presents diagnostic challenges. It underscores the importance of a thorough gross examination, careful sectioning, the number of sections submitted, meticulous histopathological evaluation, and differential diagnosis with other uterine biphasic and mesenchymal tumours.

E-PS-11-021

Analysis of reticulin, trichrome staining and Ki67 proliferative activity in pregnancy-associated leiomyomas

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Background & Objectives: Pregnancy-associated leiomyomas (PALMs) often pose diagnostic challenges due to histologic similarities to leiomyosarcoma (LMS). A prior study documented differences in reticulin/collagen (trichrome) networks, and differential ki67 labelling at the viable-non-viable interface between leiomyoma (LM) and LMS (PMID 25698060). However, the distribution of reticulin, trichrome and Ki67 staining in PALMs has not been assessed.
Methods: Reticulin, trichrome and ki67 were assessed on whole-tissue sections of 30 PALM with necrosis. Reticulin distribution in nonviable areas was categorized as honeycomb, linear or absent, while trichrome was noted as present or absent. Ki-67 labelling at the viable–nonviable interface was estimated as even, decreased or increased compared to areas away from necrosis.
Results: Complete loss of reticulin, reported in 61% of LMs, was seen in only 11% of PALMs. Trichrome staining was similar to that reported in LMs, being present in non-viable areas of all cases. Ki67 proliferative activity was present evenly in the viable-non-viable interface of 84% PALMs, while 12% showed an increasing gradient; only 4% showed a decreasing gradient toward the interface. This was similar to the reported predominant absent, even or increasing labelling seen in most (77%) LMs, but contrasting with LMS, where 44% show decreased Ki-67 labelling at the viable-non-viable interface.
Conclusion: This study shows differences in reticulin/collagen networks and proliferative patterns in PALM versus LM and LMS.
Similarly to LMS, most PALMs retain honeycomb/linear reticulin patterns in non-viable areas. However, similar to LM and unlike LMS, there was collagen accumulation in the non-viable areas of all PALMs, as well as similar ki67 labelling at the viable-non-viable interface. While ischemia in PALM is a rather recent event given the absence of reticulin remodelling, collagen deposition and shifts in proliferation occur, in keeping with a benign process. A panel of trichrome, reticulin and ki-67 may aid in differentiating PALMs from LMS.

E-PS-11-022

Prognostic significance of tumour budding and stromal tumour-infiltrating lymphocytes in endometrial carcinoma

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Background & Objectives: Endometrial cancer (EC) is a common gynaecological malignancy with increasing global incidence. The tumour microenvironment, particularly stromal tumour-infiltrating lymphocytes (TILs) and tumour budding, has been studied in various malignancies for prognostic significance. The present study aimed to evaluate the association of tumour budding and stromal TILs with clinicopathological parameters in endometrial carcinoma.
Methods: A retrospective study was conducted on 30 cases of histologically confirmed endometrial carcinoma. Tumour budding was assessed in haematoxylin and eosin (H&E)-stained sections and categorized as low, intermediate, or high. Stromal TILs were quantified using the standardized method recommended by the International Immuno-Oncology Biomarkers Working Group and categorized as low (<20%) or high (≥20%). Immunohistochemistry for CD3 and CD20 was performed to assess the immune cell composition. Associations between tumour budding, TILs, and clinicopathological parameters were analysed using Fisher's exact test, chi-square test, and multivariate logistic regression, with a significance threshold of $p < 0.05$.
Results: High stromal TIL levels were significantly associated with lower tumour grade ($p = 0.01$), early stage ($p = 0.04$), lower myometrial invasion ($p = 0.03$), and absence of nodal involvement ($p = 0.01$). Multivariate analysis confirmed an independent association between high TILs and lower grade ($p = 0.04$), early stage ($p = 0.03$), and low tumour budding ($p = 0.02$). Tumour budding was significantly associated with advanced tumour stage ($p = 0.02$), nodal involvement ($p = 0.007$), and higher tumour grade ($p = 0.03$). Immunohistochemistry revealed no significant differences in CD3 and CD20 positivity across cases.

Conclusion: Stromal TILs and tumour budding are significantly associated with key prognostic factors in endometrial carcinoma. High TIL infiltration correlates with favourable tumour characteristics, whereas increased tumour budding is linked to aggressive features. These findings support the potential role of TILs and tumour budding as prognostic markers in EC and highlight their relevance in histopathological assessment.

E-PS-11-023

Expanding the morphological spectrum of Mixed Mullerian Adenosarcoma and adenocarcinoma of the uterus and ovary: report of 3 cases

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Background & Objectives: Mixed Müllerian adenosarcoma and adenocarcinoma (MAA) is a rare gynaecological biphasic malignancy, distinct from carcinosarcoma in morphology and clinical behaviour. Both components are often low grade (LG) and low stage, with prognosis likely driven by the sarcoma. Its pathogenesis remains unclear.
Methods: We report 3 cases of MAA.
Results: Case 1 was a 63-year-old patient with 22cm ovarian mass, featuring predominantly high grade (HG) adenosarcoma with sarcomatous overgrowth and focal heterologous differentiation (chondrosarcomatous, liposarcomatous and rhabomyosarcomatous). There was admixed clear cell carcinoma with focal somatically derived yolk sac tumour (YST) and associated endometriosis. Both components showed wild-type p53 expression. Additionally, a separate mucinous borderline tumour (MBT) with intraepithelial carcinoma was identified in the same tumour. The tumour involved the myometrium (pT2a).
Case 2 was a 67-year-old patient with 5.4cm polypoid endometrial mass, exhibiting predominantly LG adenosarcoma involving adenomyosis without myometrial invasion (pT1a), and focal HG adenocarcinoma with ambiguous morphology confined to the polyp (pT1a). Adenocarcinoma showed normal expression of DNA mismatch repair proteins (MMR) and p53 overexpression, while adenosarcoma showed p53 wild-type expression.
Case 3 was a 64-year-old patient with 4.8cm polypoid endometrial tumour, showing mixed LG endometrioid carcinoma and HG adenosarcoma. The sarcoma exhibited multifocal HG cytological atypia and frequent mitoses, without sarcomatous overgrowth or malignant heterologous differentiation. Adenocarcinoma showed MMR normal expression and subclonal p53 overexpression, while adenosarcoma showed p53 overexpression in HG areas and wild-type expression in LG areas. Both carcinoma and sarcoma involved outer half of the myometrium, with the carcinoma metastatic to both ovaries and pelvic lymph nodes as well (FIGO 2023 Stage IIIC1ii). Adenosarcoma was confined within the uterus (pT1b).
Conclusion: This series broadens the morphological spectrum of MAA, highlighting the occurrence of HG carcinoma, as well as rare somatic YST differentiation and co-existing MBT. Recognizing this entity facilitates proper clinical management.

E-PS-11-024

Pelvic Adenosarcoma arising 10 years after an extrauterine adenomyoma

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Background & Objectives: Pelvic adenomyomas (PA) are rare, benign lesions characterized by the presence of endometrial tissue surrounded by smooth muscle tissue outside the uterus, typically in the pelvic cavity. Adenosarcoma is an aggressive malignant tumour that can arise from such lesions, usually years after initial diagnosis.
Our aim is to shed light on the potential for some benign tumours to undergo malignant transformation through a case of pelvic adenosarcoma arising 10 years after the excision of an extrauterine adenomyoma (EA).
Methods: It is a case of pelvic adenosarcoma arising 10 years after the excision of an adenomyoma (EA), diagnosed at our laboratory.
Results: A 50-year-old woman, who has presented, 10 years ago, with a rapidly growing abdominal mass. Ultrasound and imaging studies had initially revealed a solid-cystic mass independent of the uterus and adnexa, which was diagnosed as an EA. Recently, the patient reported abdominal distention and imaging showed a 16 cm abdominopelvic mass with mild ascites. Surgical resection revealed a myxoid mass with cystic foci and areas of necrosis. Histopathological examination identified two components: a benign epithelial component resembling endometrial glands with areas of squamous metaplasia and a second component of atypical spindle cells within a myxoid matrix. The latter exhibited focal rhabdoid differentiation, expressing desmin and myogenin, indicative of a heterologous rhabdomyosarcomatous component. The diagnosis was pelvic adenosarcoma with rhabdomyosarcoma-like differentiation. The patient underwent successful surgical resection with no immediate complications or recurrence.
Conclusion: Adenosarcomas are rare malignancies that usually arise in the endometrium. Extraendometrial adenosarcomas that originatine from adenomyosis or adenomyomas are rare. The rhabdomyosarcomatous differentiation seen in our case is also rare and can make the diagnosis more challenging. It also highlights the aggressive potential of such tumours
Regular follow-up is crucial in managing patients with these rare lesions to ensure an early detection of potential malignant transformation.

E-PS-11-025

Microinvasive endocervical mucinous adenocarcinoma arising from pseudomyxoma peritonei associated with low grade appendiceal mucinous neoplasm

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Background & Objectives: Pseudomyxoma peritonei (PMP) is a clinical condition characterized by the presence of mucous deposits within the peritoneal cavity, generally arising from the rupture of mucinous tumours of the appendix. Low-grade appendiceal mucinous neoplasms (LAMNs) are commonly associated with deposition of mucin, with or without admixed low-grade epithelium, on peritoneal surfaces, including intraabdominal and pelvic organs. Here, we report a very unusual presentation of PMP presumed to occur in LAMN with an endocervical invasion.
Methods: A 59-year-old female presented with weight loss with no significant past medical history and showed diffuse irregular peritoneal thickening in images. US-guided omental biopsy was diagnosed as PMP and the patient underwent debulking operation with total hysterectomy and bilateral salpingo-oophorectomy.
Results: Intraoperatively, dense adhesion of greater omentum, bowel, bladder, uterus and both adnexa was identified. Appendix was not identified, even though there was no history of appendectomy. On histological examination, grade 1 PMP was diagnosed in omentum, mesentery, and peritoneal surface of both ovaries and fallopian tubes, etc. Separately, a microinvasive low grade mucinous adenocarcinoma was found in the uterine endocervix. A small amount of intraluminal acellular mucin in fallopian tubes and diffuse endometrial reepithelialization by low-grade mucinous neoplasm was also identified. There was no invasion of endometrial stroma. Immunohistochemical stains demonstrated that the neoplastic cells of both peritoneum and endocervix were positive for CK20 and CDX-2 and negative for CK7, indicating intestinal differentiation. According to morphologic and immunohistochemical examination, the endocervial invasive lesion was interpreted as microinvasive low grade mucinous carcinoma originating from ruptured LAMN resulting PMP. The patient continues to do well without evidence of recurrence 3 years after surgery.
Conclusion: Even with low-grade disease, PMP could be make invasive implantations in distant organs, such as ovary and endometrium. In our knowledge, this is the first case which report the endocervical invasion of LAMN with PMP.

E-PS-11-026

Cervical cellular myofibroma/myopericytoma with SRF::RELA fusion, mimicking adenosarcoma, an extremely rare case report and review of literature

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Background & Objectives: We present a 45 year old Phillipino female who presented with a large cervical polyp measuring 35x20x15mm which was excised by hysteroscopy.
Methods: Microscopically sections showed an ulcerated neoplasm with a leaf-like architecture lined by Mullerian-type epithelium composed of uniform ovoid to small spindle cells with subepithelial cellular condensation. Scattered mitoses are noted in the stroma. The epithelial element was cytologically bland. There was no necrosis. Immunohistochemistry showed diffuse and strong stromal staining for SMA, ER and PR. CD10 was positive in the subepithelial areas (cambium layer). On RNA-based Next Generation Sequencing (NGS) testing, an in-frame SRF::RELA fusion was detected.
Results: The lesion was initially thought to be a low grade adenosarcoma but was reviewed later as cellular myofibroma/myopericytoma with SRF::RELA fusion. This is an extremely rare entity which has been described only in three uterine tumours (age range 20-39 years), two intrauterine and one in intracervical canal. Follow up to 15 months was uneventful. Longer follow up is needed to confirm the true biological behaviour (PMID: 35852178). Similar gene fusions have been reported in perivascular myoid tumours. Other locations of these tumours are head and neck, including parotid gland, small bowel wall, extremities and trunk. SRF regulates the activity of immediate-early and muscle-specific genes and participates in cell cycle regulation, apoptosis, cell growth and cell differentiation, especially muscle differentiation.
Conclusion: We presented an extremely rare case of cervical cellular myofibroma/myopericytoma with SRF::RELA fusion in a middle-aged female initially diagnosed as a low grade adenosarcoma. It expresses characteristic histological features of a cellular spindle cell stroma with subepithelial condensation and follows a benign clinical course. It is

important in similar cases to request NGS testing as the diagnosis, based on immunohistochemical stains alone, may be mistaken for a more sinister adenosarcoma, which requires total hysterectomy and neo/adjuvant chemotherapy for treatment.

E-PS-11-027

Evaluation of clinical, pathological, and prognostic data in cervical adenocarcinomas: a retrospective study

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Background & Objectives: Cervical cancer is a significant cause of cancer-related mortality among women. The most common type is squamous cell carcinoma, followed by adenocarcinoma. In recent years, with the increased frequency of screening, the incidence of squamous cell carcinoma has decreased while the rate of adenocarcinoma has risen. The Silva invasion pattern is used in HPV-positive endocervical adenocarcinomas.
Methods: 18 patients diagnosed with cervical adenocarcinoma or adenocarcinoma in situ between 2014 and 2025 at Dokuz Eylül University Hospital were identified. The slides of these patients were retrieved from the archives and evaluated for prognostic parameters.
Results: The mean age was 48 years(range: 25-76).The average tumour size was 2.6 cm(range: 0.7-5.5 cm).Three patients were diagnosed with adenocarcinoma in situ. When classified according to the Silva invasion pattern, 7 cases showed Silva pattern A, 3 cases showed Silva pattern B and 2 cases showed Silva pattern C.Six cases could not be classified: 2 due to biopsy status, 3 due to the presence of only adenocarcinoma in situ, and 1 due to being HPV-negative. Lymphovascular invasion(LVI) was observed in 3 cases. Among patients with Silva pattern C, one had paraservical tissue invasion and LVI, and was alive 4 years post-diagnosis; the other had bladder and rectum serosal invasion and LVI and died within the same year. The last patient with LVI had bilateral pelvic lymph node metastasis and exhibited Silva pattern B. Additionally, 5 patients had HSIL, 4 had LSIL, and 1 had squamous cell carcinoma.
Conclusion: The incidence of cervical adenocarcinomas has increased over the years. Due to their association with HPV, accompanying lesions(such as HSIL) are frequently observed. Patients with Silva pattern B and C may experience variable survival and/or metastasis, with prognoses differing from other patients. Prognostic parameters such as the Silva pattern, presence of LVI, metastasis, and tumour size play critical roles in staging, survival, and disease management.

E-PS-11-029

The role of intraoperative consultation in lymph node dissection for endometrioid carcinoma: a four-year experience

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Background & Objectives: Endometrioid carcinoma is the sixth most common cancer in women, with increasing incidence in some regions. Cases with low-grade histology, less than 50% myometrial invasion, no lymphovascular invasion, and no extrauterine spread typically have a favourable prognosis. Hysterectomy alone is usually sufficient, and frozen section during surgery helps guide decisions on lymph node dissection. This study reviews our institutional experience with intraoperative frozen section evaluation of endometrioid carcinoma cases.
Methods: We retrospectively reviewed 157 endometrioid carcinoma cases subjected to frozen section evaluation between 2019 and 2022. Data on histologic grade, myometrial invasion, cervical/adnexal involvement, tumour size, and lymph node dissection were compared between frozen section and final pathology reports. Statistical analyses were performed to assess correlations between frozen section findings and final diagnoses, particularly regarding lymph node dissection.
Results: The mean age of the cases was 60.8 years, and the mean tumour size was 3.61 cm. Lymph node dissection was performed in 67 cases (42.7%), while it was not performed in 90 cases (57.3%). When comparing the intraoperative consultation reports with the final reports in terms of concordance, the concordance rates were found to be 85.2%, 82.1%, and 92% for histological grade, myometrial invasion, and cervical invasion, respectively. Among the cases where discrepancies were detected, it was found that lymph node dissection was necessary according to the parameters reported in the final report in nine cases, but it could not be performed due to the parameters reported during intraoperative consultation. In two cases, unnecessary dissection was performed.
Conclusion: In endometrioid carcinomas, frozen section examination performed under appropriate conditions and in collaboration with clinical teams plays a crucial role in reducing morbidity and mortality. Evaluating the concordance between frozen section findings and final pathology reports is essential for identifying and addressing potential discrepancies in future cases.

E-PS-11-030

What is the importance of invasion in vulvar Paget's disease?

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Background & Objectives: Vulvar Paget's disease (VPD) is an extremely rare malignancy of the vulva with a high local recurrence rate and low mortality. Due to its non-specific symptoms and lack of clinical knowledge, VPD is often misdiagnosed with eczematous skin lesions and the definitive diagnosis is often delayed. Since there is currently no global consensus on the optimal management of VPD, we aimed to evaluate the clinico-pathological features and survival outcomes among intraepithelial VPD, microinvasive VPD and invasive VPD.
Methods: The cases of VPD operated in the Gynaecological Oncology Department of Dokuz Eylül University Faculty of Medicine Hospital and diagnosed in the Department of Pathology between 2000 and 2021 were retrospectively reviewed. Clinicopathological features of VPD cases were analysed.
Results: A total of 60 patients were identified. 44 patients were diagnosed with intraepithelial VPD, 12 with microinvasive (<=1 mm) VPD and 4 with invasive VPD. Most of the patients 48/60 (80%) were treated with surgery. Local recurrence was observed in 45/60 (75%) patients with no significant difference between the 3 groups ($p = 0.33$). At 120 months, cancer-specific survival was 100% for intraepithelial and microinvasive VPD and 31% for invasive VPD (log-rank $p = <0.0001$).
Conclusion: We found that microinvasive VPD and intraepithelial VPD have the same prognosis. We wanted to emphasise that the biggest risk for VPD patients is tumour invasion.

E-PS-11-031

Fibroblast Activation Protein (FAP) expression in Deep Endometriosis (DE): a feasibility study of using Ga68 Fibroblast Activation Protein Inhibitor (FAPI) PET imaging in DE

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Background & Objectives: Endometriosis affects approximately 10% of reproductive-age women, with deep endometriosis (DE) accounting for up to 20% of cases. DE causes chronic pelvic pain, fibrosis, and adhesions, and increasing the risk of gynaecologic malignancies. Conventional imaging techniques such as ultrasound often fail to detect deep or extra-pelvic lesions. Fibroblast activation protein (FAP), a type II cell surface glycoprotein overexpressed in activated fibroblasts during tissue remodelling and fibrosis, represents a promising molecular imaging target. 68Ga-FAPI-46, a quinoline-based PET tracer that binds to FAP, enables non-invasive visualization of fibrotic activity. In this study, we assessed FAP expression in bowel-involved DE surgical specimens using immunohistochemistry (IHC) to evaluate the potential utility of 68Ga-FAPI PET imaging in this context.
Methods: We retrospectively assessed FAP expression via IHC in 13 rectosigmoid DE surgical specimens resected by segmentectomy or full thickness discoid resection. All lesions had muscularis propria involvement. Five rectosigmoid colorectal adenocarcinomas from male patients served as positive controls, and benign colonic mucosa served as negative controls. FAP expression was evaluated in three compartments: endometrial glands, endometrial-type stroma, and the altered stroma surrounding the lesions. Expression was scored based on extent (focal, patchy, diffuse: 1–3) and intensity (none to strong: 0–3), with H-scores calculated accordingly. H-scores were compared with using unpaired t-test. $P<0.05$ was considered statistically significant.
Results: Endometrial glands in DE showed no FAP expression (H-score = 0). In contrast, the endometrial-type stroma and altered surrounding stroma had mean H-scores of 5.0 (1-9) and 4.4 (2-7.5), respectively ($p < 0.001$ vs. glands). Stromal reaction in colorectal adenocarcinoma exhibited a mean H-score of 7.2 (range: 6-7.5; $p < 0.0001$ vs. endometriosis stroma). No expression was detected in colorectal glands or muscularis propria.
Conclusion: Our findings demonstrate significant FAP expression in the stromal components of DE, supporting the potential use of Ga68-FAPI PET imaging in patients with DE.

E-PS-11-032
A "typic" lesion of the uterine endometrium
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Background & Objectives: Atypical polypoid adenomyoma (APA) is a rare benign uterine lesion composed of endometrial-type glands and a myomatous stroma. It primarily affects premenopausal women and is often associated with abnormal uterine bleeding. APA is commonly located in the lower uterine segment but can also be found in the fundus, corpus, or endocervix.
Methods: A 44-year-old woman presented with abnormal uterine bleeding for one month. An endometrial biopsy revealed endometrial hyperplasia with focal atypia. She underwent a hysterectomy with bilateral salpingo-oophorectomy.
Results: Macroscopic examination showed a $2.7 \times 1.7 \times 1.5$ cm polypoid lesion in the posterior uterine wall without myometrial invasion. Histologically, the lesion had focal complex endometrial glands with mild nuclear atypia and squamous morules within a myomatous stroma. Immunohistochemistry revealed CDX2 and CD10 positivity in squamous morules, while ER and p63 were negative. The myomatous stroma was positive for Desmin, and SATB2, confirming APA.
Conclusion: The differential diagnosis of APA includes several entities that share overlapping histological features. Endometrial carcinoma must be excluded, as it lacks myomatous stroma, exhibits higher nuclear atypia, and has a higher Ki-67 proliferation index. APA can also resemble adenosarcoma, but the latter is distinguished by periglandular stromal cuffs and a higher mitotic index. Malignant mixed Müllerian tumour (MMMT) is another important differential, characterized by highly malignant glandular and stromal components, unlike APA. Additionally, APA can be mistaken for an endometrial polyp, but polyps lack myomatous stroma and nuclear atypia. Given its potential for recurrence and its histological overlap with malignant lesions, APA should always be considered in the differential diagnosis of polypoid uterine lesions. Proper pathological evaluation and adequate sampling are essential to avoid misdiagnosis and unnecessary aggressive treatment.

E-PS-11-034
Mixed trophoblastic tumour of the uterus: a clinicopathological challenge in diagnosis
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Background & Objectives: Gestational trophoblastic tumours are rare neoplasms derived from placental tissue. Among them, epithelioid trophoblastic tumour (ETT) and placental site trophoblastic tumour (PSTT) are even less common than choriocarcinoma. The coexistence of these three components in a single endometrial tumour is extremely rare. We present a challenging case of a mixed trophoblastic tumour involving ETT, PSTT, and choriocarcinoma in the uterus of a middle-aged woman.
Methods: A 47-year-old woman presented with heavy vaginal bleeding. Endometrial sampling revealed decidualized tissue with atypical trophoblastic differentiation. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. Macroscopic and microscopic evaluation, along with a comprehensive immunohistochemical panel, was applied.
Results: A 10 cm tumour was detected in the endometrium, infiltrating more than half of the myometrium. No tumour was observed in the ovaries, tubes, omentum, or sampled lymph nodes. Histopathological examination revealed three distinct trophoblastic components: ETT, PSTT, and choriocarcinoma. The tumour showed lymphovascular invasion and a mitotic count of 18 per 10 high-power fields. Immunohistochemically, tumour cells were diffusely positive for pancytokeratin and showed focal expression of β-HCG, inhibin, p63, p16, EMA, and GATA3. The Ki-67 proliferation index was approximately 50%.
Conclusion: Mixed trophoblastic tumours of the uterus with coexisting ETT, PSTT, and choriocarcinoma are extremely rare and can be diagnostically challenging, especially when presenting with subtle or overlapping histologic features. Accurate diagnosis requires careful morphological assessment supported by immunohistochemistry. Recognizing this entity is essential due to differences in prognosis and therapeutic approaches for each component. This case underscores the importance of considering mixed trophoblastic tumours in the differential diagnosis of endometrial masses, even when β-HCG levels are not markedly elevated.

E-PS-11-035
Molecular characteristics and survival in cervical adenocarcinomas: an in-silico analysis
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Background & Objectives: The objective of this study was to identify the molecular characteristics that influence survival outcomes in cases of cervical adenocarcinoma, utilising data from the TCGA (The Cancer Genome Atlas) database.
Methods: The 'TCGA Firehose Legacy' dataset was accessed through the Cbioportal website (www.cbioportal.org). Cases were divided into two groups according to overall survival status (living or deceased). Subsequent analysis involved the comparison of mutation presence, mRNA expression status, protein expression and DNA methylation data

between these two groups. A pathway analysis for significant genes was performed on the G:Profiler website (https://biit.cs.ut.ee/gprofiler/gost). P and q < 0.05 were considered statistically significant.
Results: The study identified 27 cases of endocervical adenocarcinoma. Of these, 22 (81.5%) were alive, while 5 (18.5%) were ex. A comparison of the two groups in terms of protein expression revealed that PREX1 expression was higher in the living cases (*q=8.700e-3*). While *WDR89* exhibited a higher methylation rate in living cases, *MCEMP1, RNNASE2, RINL, CCL17, THBD, SFXN5, PRR19* genes demonstrated higher methylation frequency in deceased cases (*p and q <0.05*). A subsequent pathway analysis of these genes revealed an association with KLF9, a transcription factor (*p=3.011x10-3*). However, no significant differences were observed in the presence of mutations, mRNA expression and copy number changes (p>0.05).
Conclusion: Cervical adenocarcinoma is a challenging diagnosis in routine practice due to its relatively rare occurrence. The identification of its diagnostic molecular features may facilitate more precise diagnosis and prognosis.

E-PS-11-036
MGMT and p16 immunohistochemistry evaluation in melanomas of the gynaecological system
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Background & Objectives: Primary gynaecological melanomas are rare. Between 3-7% of melanomas in the whole body have been detected in the genital tract. O6-methylguanine-methyltransferase (MGMT), a DNA repair protein that removes methyl groups from the O6-position of guanine. P16 functions as a negative regulator of the pRb/E2F pathway, which is mainly involved in cell cycle control.
Methods: In this study, we re-evaluated a cohort of 13 patients diagnosed with melanoma in our centre between 2010 and 2024. EP337 clone of MGMT immunohistochemistry was applied. MGMT expression was assessed and scored in tumour cells using a 3-tier scale (complete loss=negative or <10% positive tumour staining, partial loss=10% to 50% staining, retained= >50% staining). p16 immunohistochemistry was assessed as lost or retained.
Results: The mean age of the patients was 76.9±10 years. Tumour localisations were recorded in vulva, vagina, cervix and uterine corpus. Diagnoses were usually made from biopsy specimens (n=9 69.2%). The most common tumour localisation was vagina and vulva equally (n=4 30.8%). All cases were positive for at least one melanocytic marker. Loss of p16 immunohistochemistry was present in 7 cases (53.8%). MGMT immunohistochemistry usually showed loss (n=7 53.8%) and these losses were usually accompanied by p16 loss (n=5 38.5%). Complete loss of MGMT was observed in all cases of melanoma of the cervix, whereas complete loss was observed in 25% of cases of melanoma of the vulva. In vulvar melanomas, MGMT was found to be retained in 2 cases (50%). The majority of patients died after a minimum of 3 maximum 69 months (n=11 84.6%).
Conclusion: Most gynaecological melanomas are mucosal melanomas, distant metastasis is common and overall survival is limited. We believe that MGMT and p16 immunohistochemistry together with demographic data in larger case series studies may provide insight in terms of prognosis and recurrence.

E-PS-11-037
Atypical Leiomyomas: the Importance of suspecting Fumarate Hydratase gene mutation
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Background & Objectives: The Fumarate Hydratase (FH) gene mutation is associated with Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC) syndrome, an autosomal dominant disorder. This syndrome presents with multiple and atypical uterine leiomyomas, cutaneous leiomyomas, and renal cell carcinoma (RCC). Early recognition enables targeted oncologic surveillance and genetic counselling.
Methods: We present three cases of FH mutation, focusing on the clinical and histological findings that supported the suspicion.
Results: Case 1: A 32-year-old with a family history of RCC, history of myomectomy, and a polymyomatous uterus with leiomyomas up to 150 mm. Histology showed smooth muscle tumours with eosinophilic inclusions, hemangiopericytoma-like vasculature, alveolar-pattern myxoid degeneration, haemorrhage, and ischemic-type necrosis. FH loss of expression was confirmed by immunochemistry.
Case 2: A 25-year-old with abnormal uterine bleeding and prior multiple myomectomies (52 leiomyomas removed) with rapid recurrence, requiring hysterectomy. Histology demonstrated spindle cells with nuclear atypia and expansive growth.
In the immunohistochemical study performed on the uterine wall neoplasm, the neoplastic cells show expression of actin, desmin, and progesterone-receptors (PR), with an absence of oestrogen-receptors (ER) expression. And "fumarate hydratase" serum demonstrates a loss of expression in the neoplastic cells.
Case 3: A 39-year-old with abnormal uterine bleeding and a 73 mm leiomyoma. Histology revealed spindle cell neoplasms with branched vessels, oedema, and eosinophilic inclusions. The neoplastic cells show expression of actin, desmin, PR, ER; with an absence of STAT-6 and CD10 expression. And "fumarate hydratase" serum demonstrates a loss of expression in the neoplastic cells.
Conclusion: In young women, the presence of rapidly-growing/extensive, or histologically atypical leiomyomas should raise suspicion for an FH mutation. Pathologists and gynecologists are essential in early identification, facilitating genetic referral and renal surveillance. Timely clinical suspicion can significantly impact both individual and familial prognosis by enabling early detection of renal carcinoma and providing guidance on Assisted Reproductive Technologies for preimplantation genetic testing.

E-PS-11-038
Search for morphological criteria of the early and late stages of scleroatrophic lichen of the vulva
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Background & Objectives: Scleroatrophic lichen (LS) is a degenerative skin disease primarily affecting the anogenital region. Vulvar lesions of both benign and precancerous nature pose an interdisciplinary challenge for dermatovenerologists, gynecologists, and oncologists. The aim of the study was to compare early and late stages of LS using histology and immunohistochemistry to identify key disease changes.
Methods: Biopsy specimens from 20 women with LS were analysed. Two groups were defined: 1- patients with clinical manifestations lasting ≤1 year; 2- Patients with clinical manifestations lasting >1 year. Histological staining included haematoxylin-eosin and Van Gieson's picrofuchsin. IHC staining targeted CD31 (angiogenesis marker), CD95 (apoptosis marker), and VEGF (vascular endothelial growth factor).

Results: Histological observation revealed in group 1: parakeratosis in the epidermis, pronounced acanthosis, lymphocytic infiltration in the dermis, swelling of the endothelium in the capillaries. In group 2: atrophy foci in the epidermis, lymphocytic infiltration in the dermis, endotheliocyte apoptosis in the capillaries, thrombotic masses. VEGF expression showed an inverse correlation with disease duration (80% vs 15%). CD31 expression patterns shifted from focal strong to predominantly weak staining. CD95 expression intensity increased dramatically with disease progression (20% to 85%).
Conclusion: Key histological and IHC features diagnostic of early and late LS stages were identified. Microvascular wall damage, confirmed by IHC, suggests that LS-related skin changes result from impaired blood supply due to vascular dysfunction. These findings may inform the use of anti-apoptotic and angiogenic therapies in LS management.

E-PS-11-039
Malign Brenner Tumour with immunohistochemical positivity of MDM2: a case report and literature review
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Background & Objectives: Malignant Brenner tumours (MBTs) are rare ovarian neoplasms, accounting for less than 5% of Brenner tumours. They are characterized by aggressive behaviour and poor prognosis. The molecular and immunohistochemical profiles of MBTs are not well understood, with limited data available in the literature. MDM2, an oncogene known for its role in tumour progression, has been identified in various malignancies but is rarely reported in MBTs. This case report aims to present a rare case of MBT with immunohistochemical positivity for MDM2 and review relevant literature to explore its potential diagnostic and prognostic significance.
Methods: A 52-year-old postmenopausal woman presented with abdominal distension and pelvic discomfort. Imaging studies revealed a cystic right ovarian mass with a fokal solid component and surgical intervention was performed. The histopathological evaluation confirmed the diagnosis of MBT, and immunohistochemical analysis included markers such as MDM2, p53, p63,CK7, WT1, and GATA3. A literature search was conducted using databases to review previously reported cases of MBT and their molecular profiles.
Results: Histological examination revealed cystic areas within the tumour lined by multilayered epithelium, which resembles urothelial epitel and malignant transitional-type epithelial cells with nuclear atypia, prominent nucleoli, and invasion areas in the densely fibromatous background. Immunohistochemistry showed diffuse positivity for GATA3 and CK7 while p53 is wild type and WT1,p63 is negative. Benign Brenner tumour nests support the diagnosis. Strong nuclear immunohistochemical expression of MDM2 is identified in the malignant component. A literature review identified a few cases of MBTs with molecular characterization, with one reporting of MDM2 amplification that evaluated by fluorescence in-situ hybridization (FISH) correlates with immunostaining of MDM2
Conclusion: This case highlights a rare MBT with MDM2 positivity, suggesting a potential role for MDM2 in the tumorigenesis of MBTs. Given its rarity, further studies are needed to establish the clinical and prognostic implications of MDM2 expression in MBTs.

E-PS-11-040
Comparative analysis of the role of endometrial and ovarian factors in the genesis of female reproductive dysfunction
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Background & Objectives: The issue of infertility remains relevant in modern medicine. Endometrial and ovarian factors play a key role in the genesis of reproductive dysfunction. A comparative analysis of the influence of these factors on the receptivity of the endometrium allows a deeper understanding of the mechanisms of infertility and the development of more effective methods of pregravid preparation of patients.
Methods: We have studied pipelle biopsy specimens of endometrium in the secretion phase from 135 patients: 50 patients with endometrial pathology (group 1), 50 with ovarian pathology (group 2), 35 patients - comparison group (healthy women before surrogacy). Chronic endometritis was diagnosed in 50% of group 1 patients, endometrial polyp in 10% of patients, and a combination of the two pathologies in 40% of patients. Group 2 consisted of patients with endometrial ovarian cysts. Sections were stained with haematoxylin and eosin, Mallory staining, IHC analysis was performed with monoclonal antibodies to oestrogen and progesterone receptors.
Results: The study revealed delayed secretory transformation of the endometrium in patients of both groups. Endometrial stromal fibrosis was noted in 45 patients (90%) of group 1 and in 19 (38%) patients of group 2, which was combined with chronic endometrial inflammation. Both groups showed delayed maturation of pinopodes, reduced 2.5 times in group 1, 1.6 times in group 2 in contrast to the comparison group. Disruption of receptivity to oestrogen and progesterone receptors was noted both in the glandular and stromal compartments of the endometrium in patients of group 1, in the glandular compartment - in group 2, in relation to the comparison group ($p<0.05$).
Conclusion: The study demonstrated more significant morphofunctional changes in the endometrium (chronic endometritis, fibrosis of endometrial stroma, delayed maturation of pinopodes, impaired secretory transformation of the endometrium and a more significant decrease in receptivity to hormones) in study group 1 with endometrial pathology.

E-PS-11-041
Primary malignant melanoma of the uterine cervix
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Background & Objectives: Primary malignant melanoma of the cervix (PMMC) is an exceptionally rare and aggressive malignancy, accounting for less than 1% of cervical cancers. Its diagnosis relies on histopathological and immunohistochemical evaluation due to its rarity and similarity to other cervical malignancies. PMMC has a poor prognosis, with no standardized treatment protocol. Management typically follows regimens used for cutaneous melanoma, including radical surgery and emerging immunotherapies. The objective is to describe a case of a women with a primary malignant melanoma of the uterine cervix.
Methods: Clinical data from a patients with primary malignant melanoma of the cervix.
Results: A 60-year-old female, presented with foul vaginal odor and intermittent pelvic pain. Gynaecological examination revealed hyperpigmented macules on the ectocervix. Histopathological analysis confirmed invasive melanoma of the cervix. Histopathological findings included a Breslow thickness of 22 mm, ulceration present, and a mitotic rate of 1/mm². Tumour-infiltrating lymphocytes were present

but not prominent, while lymphovascular invasion, neurotropism, and tumoral regression were not identified. Additionally, with immunohistochemical positivity for SOX10, Melan A, and HMB-45. PET-CT revealed mild hypermetabolism localized to the cervix without evidence of metastasis. The patient remains under surveillance with ongoing molecular analysis and imaging follow-ups.
Conclusion: PMMC remains a diagnostic and therapeutic challenge due to its rarity, nonspecific clinical presentation, and aggressive behaviour. Early detection through biopsy and immunohistochemistry is crucial. Surgical intervention is the mainstay of treatment, with adjuvant radiotherapy and emerging immunotherapies playing an increasing role in management. Further research into targeted therapies and immunomodulatory approaches may improve outcomes for this rare malignancy.

E-PS-11-042
De novo myeloid sarcoma in the uterine cervix: a literature review of its rare topographical manifestation as a myeloid neoplasm
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Background & Objectives: Primarily diagnosed myeloid sarcoma within the gynaecological system is a rare entity. A literature review spanning the past five decades identified 54 reported cases, with the majority 30 (55.6%) localized to the uterine cervix.
Methods: We present the clinical case of a 46-year-old woman who underwent curettage of a hyperplastic endometrial layer and conization of ectocervical tissue, following a clinical and radiological diagnosis of endometrial hyperplasia and cervical squamous carcinoma in situ. Macroscopical examination of the specimen revealed a $4.5 \times 2 \times 0.5$ cm grayish lesion with firm consistency on the cutting surface of the cervix. To determine tumour's nature and origin, beside thorough gross and histological assessment a broad panel of antibodies was analysed using immunohistochemical diagnostic methods.
Results: Macroscopically described tumorous lesion histologically was composed of a diffuse, unconfined proliferation of epithelioid and spindle-shaped atypical cells, with nuclear hypochromasia and multiple mitotic figures. The diffuse positivity of CD45 and CD43 confirmed the hematolymphoid origin of the lesion. Further studies showed extensive expression of CD33, Muramidase, MPO, and scattered positivity of CD68 and CD163, indicating the presence of a dominant myeloid population in the tumour. The immature profile of the tumour was excluded by the negativity of CD34 and CD117.Involvement of cervical tissue by circulating immature myeloid cells in the case of coexisting systemic myeloid leukaemia was ruled out through clinical correlation and the absence of any morphological and phenotypical signs of bone marrow and peripheral blood damage. Based on aforementioned diagnostic procedure and the exclusion of other possible entities, a final diagnosis of myeloid (granulocytic) sarcoma was established.
Conclusion: The rarity of tumour locations, particularly in the absence of preexisting acute or chronic myeloid disorders, can contribute to diagnostic challenges and subsequent delays in initiating appropriate therapy.

E-PS-11-043
Changing glycodelin A level in serum patients with ovarian neoplasms
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Background & Objectives: Ovary cancer is the one of the most common gynaecological neoplasms, which annually takes away more than lives. Mortality from ovarian cancer reaches 152 000 lives per year. Therefore, the search for new markers of early diagnosis of ovarian cancer is relevant. Glycodelin A is a glycoprotein associated with progesterone production, secreted by endometrial glands. According to literature data, the possibility of using the marker in the diagnosis of oncological diseases is being discussed.
The aim was detect the level of Glycodelin A in the serum of women with ovarian tumours.
Methods: We analysed the concentration of Glycodelin A in serum 100 patients 18–78 years old with ovarian neoplasms. The level of Glycodelin A of serum was determined by ELISA. The differences in criteria were considered statistically significant at $p<0.05$.
Results: Benign ovary formations detected in 21 (21%) patients, border tumours in 10 (10%), malignant formations 69 (69%). There were histologically distributed as follows: serous adenocarcinoma amounted to 68% (n=47), mucinous was 11% (n=8), endometrioid was 18.8% (n=13). The level of serum Glycodelin A is associated with the histological type of ovary neoplasms: benign was 2.9 ng/mL (1.95-6.05). In cases of serous adenocarcinoma were in 24.5 ng/ml (7.95-66.90), mucinous was 9.15 ng/ml (3.38-13.53), endometrioid adenocarcinoma was 9.60 ng/ml (5,40-19.10). The level of Glycodelin A correlates with the size of the tumour If the tumour size is more than 5 cm, its average level was 4.10 ng/ml (3.10-6.60); >10 cm (38 patients (55%) were 13.10 ng/ml (5.43-43.48). Depending on the stage Glycodelin A level was increased. Glycodelin A concentration were the highest at III stage in the group with ovarian neoplasms. The average level of Glycodelin A was 22.70 ng/ml(9.50-63.80) which shows its prognostic adverse significance.
Conclusion: Determining the level of Glycodelin A in patients with ovarian neoplasms may be predictive value.

Funding: 123030700104-3

E-PS-11-044
Intravascular endometrial glands and stroma in a patient without endometriosis
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Background & Objectives: Endometrial gland and stroma in the myometrium vessels were initially described as an uncommon finding related to the menstrual period, but later it was reported that it could be related to adenomyosis, not to menstruation. We reported a case of IEM in a hysterectomy and bilateral salpengectomy specimen removed from a 47-year-old premenopausal patient with myoma uteri.
Methods: A 47-year-old female patient with a history of breast carcinoma in her mother and father, and negative for *BRCA1* and *BRCA2* mutations, underwent hysterectomy and bilateral salpingectomy due to myoma uteri.
Results: In the hysterectomy specimen, a total of nine myomas, the largest of which was 7 cm. Strikingly there were endometrial glands and stromal structures in the intravascular spaces of the

myometrium. Endometriosis was not observed in the myometrium or myomas in any of the numerous samples taken. Immunohistochemical stains were performed to identify the intravascular endometrial glands and stroma. Vascular structures were evaluated with CD31, CD34, D2-40, and CD61. Glandular structures in the intravascular space were visualized with Estrogen receptor, and stromal structures with CD10.
Conclusion: Although the identification of this entity is facilitated in the presence of adenomyosis, mimicking vascular invasion poses a diagnostic challenge, particularly in the absence of adenomyosis and even in the presence of malignancy. Therefore, we presented this case to emphasize the importance of awareness of this rare entity.

E-PS-11-045
High–grade endometrial stromal sarcoma with *BCOR-MAML3* fusion presenting as polypoid cervical mass: a case report
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Background & Objectives: High-grade endometrial stromal sarcoma (HGESS) is a rare and aggressive uterine neoplasm originating from the endometrial stroma. Several different molecular alterations have been identified in HGESS, such as *YWHAE: NUTM2A/B* fusions, *BCOR* fusions, and *BCOR* internal tandem duplication (ITD).
Methods: Given the limited number of reported cases, we present a case of a *BCOR-MAML3* fused HGESS, with clinical, pathologic, immunohistochemical, and molecular correlations.
Results: A 40-year-old woman presented with irregular vaginal bleeding for several months. Clinical examination revealed a 45x40 mm, polypoid mass, protruding from the cervical canal. The tumour was surgically removed. Microscopic examination showed a malignant neoplasm with fibromyxoid stroma having spindle and round cells with scant to moderate eosinophilic cytoplasm, with mild to moderate nuclear atypia with mitotic activity of 7-10/10 HPF. Necrosis and lymphovascular invasion were not seen. Immunohistochemically, the tumour cells were positive for CD10, pan-TRK, and cyclin D1, whereas other biomarkers were negative (ER, SMA, desmin, h-caldesmon, CD34, CD117). p53 showed a wild-type expression pattern. Subsequent molecular analysis revealed a *BCOR-MAML3* fusion. *NTRK1-3* fusions were not detected. Consequently, the patient underwent a total hysterectomy with bilateral salpingo-oophorectomy, with no residual disease.
Conclusion: We confirm that HGESS with a *BCOR-MAML3* fusion often shows diffuse immunohistochemical positivity for pan-TRK, not associated with the presence of *NTRK1-3* fusions. Our case study also highlights the importance of molecular profiling in the proper classification of soft tissue neoplasms, such as HGESS.

E-PS-11-046
Serum markers of pathological placental attachment in pregnant women
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Background & Objectives: Currently, there is no clinically reliable biomarker of placenta accreta PAS. Objective: to evaluate changes in serum concentrations of glycodelin A (GdA), placental alpha-microglobulin-1 (PAMG-1) and adiponectin in pregnant women and to determine the possibility of their use in predicting PAS.
Methods: In pregnant women with PAS (n=18) and uncomplicated pregnancy (n=20) at 30-35 weeks of pregnancy, the levels of GdA, PAMG-1, adiponectin in the serum were determined by ELISA and assessed in points: GdA (ng/ml): 0-40 - 3 points, 41-80 - 2 points, 81-130 - 1 point; PAMG (ng/ml): 1-30 - 3 points, 31-60 - 2 points, 61-120 - 1 point; adiponectin (μg/ml): 0-5 - 3 points, 5.1-8 - 2 points, 8.1 to 20 - 1 point; N - the number of caesarean sections in the anamnesis in whole numbers as points, then the points and the "N" are summed up.
Results: Women with PAS had significantly lower serum levels of all studied proteins relative to the comparison group. GdA level was 32.3 (14.1;71.6) vs 65.05 ng/ml (45.95;74.4), PAMG 19.6 (12.1;29.2) vs 33.45 (25.75;58.2) ng/ml, adiponectin 3.96 (3.49;4.69) vs 10.39 (6.52;16.21) μg/ml. The number of CS in the anamnesis was 2 (1;2) vs 0 (0;1). The risk of PAS in points was 10 (8;10) versus 5.5 (5;8). With a total score of 8 or more, PAS is predicted in a given pregnancy with 100% sensitivity and 90% specificity.
Conclusion: A formula for predicting PAS has been established that, with high sensitivity and specificity, a patient's score of 8 or more points indicates the presence of PAS.

Funding: Research within the framework of the State assignment № FGFZ-2025-0005

E-PS-11-047
Invasive stratified mucin-producing carcinoma of uterine cervix: clinicopathological features of 5 cases
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Background & Objectives: Invasive stratified mucin-producing carcinoma (ISMC), defined as a subtype of HPV-associated endocervical adenocarcinoma, is a rare neoplasm characterized by morphologic variability and an aggressive clinical course. We aimed to provide more data on the clinicopathologic features of ISMC.
Methods: Hysterectomy specimens from five patients were analysed. Four cases were consecutively diagnosed as ISMC, while one was identified retrospectively during reclassification of 48 adenosquamous carcinomas. Initial biopsy specimens were obtained at an outside centre after evaluation of the patients' symptoms. Clinicopathologic data and initial diagnoses were reviewed.
Results: The median age at diagnosis was 42.2 (22-50) years. Initial diagnoses included adenosquamous carcinoma (2 cases), squamous cell carcinoma (1 case), poorly differentiated endometrioid adenocarcinoma (1 case), and adenocarcinoma, NOS (1 case). Microscopic examination revealed solid nests of stratified cells resembling squamous cell carcinoma but morphologically similar to adenocarcinoma. Tumour cells showed variable intracellular mucin production as confirmed by mucin staining. Immunohistochemistry showed diffuse block positivity for p16 and peripheral staining for p63. Deep stromal involvement was observed in four cases, with extensive lymphovascular invasion (LVSI) in three cases and focal LVSI in one case. Paraaortic lymph node metastases were found in three cases. According to FIGO staging, two patients were in stage 1 and three in stage 3. The mean postoperative follow-up was 8.4 (3-14) months. Two patients died of the disease in the 3rd and 9th months of follow-up, while three patients are alive.
Conclusion: This study presents five cases of ISMC, highlighting the rarity and aggressiveness of the tumour. ISMC may be misdiagnosed

as adenosquamous carcinoma, conventional squamous cell carcinoma, or cervical involvement of poorly differentiated endometrial adenocarcinoma. Due to its biologically aggressive nature, careful differential diagnosis is essential.

E-PS-11-048

Mesonephric-like carcinosarcoma of the uterus with a BRAF p.G466V mutation: a case report and review of diagnostic and molecular features

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Background & Objectives: Mesonephric-like carcinosarcoma (MLCS) of the uterus is an extremely rare and aggressive neoplasm characterized by the coexistence of a mesonephric-like adenocarcinoma (MLA) and a sarcomatous component. While the mesonephric-like adenocarcinoma component has been increasingly recognized, the biphasic carcinosarcomatous variant remains poorly understood. Molecular alterations involving the MAPK/ERK pathway, mainly KRAS mutations, have been proposed in its pathogenesis. We present a new case harbouring an uncommon BRAF mutation, contributing to the expanding knowledge of this entity.
Methods: A 62-year-old woman presented with postmenopausal bleeding. A diagnostic endometrial biopsy was performed, followed by total hysterectomy with bilateral salpingo-oophorectomy. The surgical specimen was thoroughly examined, including macroscopic assessment, histopathological evaluation, immunohistochemical (IHC) profiling, and targeted next-generation sequencing (NGS) for molecular characterization.
Results: Grossly, a 5.5 cm endometrial mass was identified, infiltrating more than 50% of the myometrial thickness. Microscopically, the tumour showed a biphasic morphology, composed of a predominant epithelial component (70%) with tubular, papillary, and retiform architectural patterns, and a sarcomatous component (30%) of undifferentiated spindle cells, mainly located in the luminal area. The epithelial component expressed PAX8 and GATA3, and was negative for oestrogen and progesterone receptors, with wild-type p53 expression. The sarcomatous component showed positivity for vimentin, caldesmon, and focal CD10 expression, without evidence of aberrant p53 staining. NGS revealed no gene fusions or TP53 mutations but identified a rare BRAF p.G466V mutation, suggesting MAPK/ERK pathway activation. The final diagnosis was mesonephric-like carcinosarcoma, FIGO stage IB.
Conclusion: This case contributes to the limited series of uterine MLCS, underlining the importance of its recognition. The identification of a rare BRAF mutation supports the role of the MAPK/ERK pathway in its pathogenesis and may provide relevant insights for future targeted therapies.

E-PS-11-049

Prevalence of microsatellite instability in cervical adenocarcinoma

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Background & Objectives: Despite widespread use of cytologic screening, the incidence of cervical adenocarcinoma has been increasing in recent years. This histologic subtype is characterized by a poor prognosis and immunotherapy is the promising therapeutic strategy. Microsatellite instability (MSI) is one of the key biomarkers to predict response to immune checkpoint inhibitors, but some data have been accumulated on the frequency of MSI among cervical adenocarcinomas. The aim of this work is to investigate the incidence of MSI in cervical adenocarcinoma as it may reveal new therapeutic strategies to improve patient prognosis.
Methods: Surgical specimens were collected from 38 patients with cervical adenocarcinoma. Immunohistochemistry for MSH2 (FE-11), MSH6 (EP-49), PMS2 (EP-51) and MLH1(ES05) (Dako, Agilent Technologies, USA) was performed on 3-mm thick sections of a representative formalin-fixed, paraffin-embedded (FFPE) tumour tissue using PrimeVision detection system (PrimeBioMed LLC, Russia) in Autostainer 480S immunostainer (ThermoFisherScientific, USA). DNA was isolated from FFPE tumour tissue by phenol-chloroform extraction using a DNA extraction kit (BioLink LLC, Russia). PCR followed by fragment analysis of PCR products by capillary electrophoresis was used as a reference method with application of the reagent kit "COrDIS MSI" (BioLink LLC, Russia) according to the manufacturer's instructions. PCR was performed on the amplifier "BIS" M111-02-96 (NovosibBioPribor LLC, Russia). Fragment analysis was performed according to the GeneMapper manual for Applied Biosystems 3500 genetic analyser (ThermoFisherScientific, USA).
Results: The incidence of MSI in cervical adenocarcinoma was 10,5% (4/38) when analysed by immunohistochemistry and 13,1% (5/38) when analysed by molecular technique (the concordance of the two methods was 98,2%).
Conclusion: MSI in cervical adenocarcinoma is not a common event. The introduction of MSI assay into clinical practice may help to identify a limited group of patients who will benefit from immunotherapy. Both immunohistochemical and molecular technique may be considered depending on the capabilities of the particular laboratory.

E-PS-11-050

Frequency of KRAS gene mutations and their association with histologic variants in cervical adenocarcinoma

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Background & Objectives: Adenocarcinomas account for at least 20% of all cervical cancers. This histological subtype represents a heterogeneous group of tumours that differ in the profile of molecular abnormalities and response to treatment. The targeted drug has been approved in a number of cancers as it has been shown to improve outcomes in patients with activating somatic mutations of KRAS gene. The aim of the present work is to investigate the frequency of these mutations among different histological variants of cervical adenocarcinoma, which may help in the search for personalized treatment strategies.
Methods: Surgical specimens were collected from 24 patients with cervical adenocarcinoma. Distribution by histologic types was as follows: usual 50% (12/24), endometrioid 25% (6/24), mucinous, intestinal subtype 4,1% (1/24), mesonephral 8,3% (2/24), villoglandular 4,1% (1/24), serous-like 8,3% (2/24). DNA was isolated from a representative formalin-fixed, paraffin-embedded (FFPE) tumour tissue block by phenol-chloroform extraction using a DNA isolation kit (BioLink LLC, Russia). DNA samples were tested for mutations in codons G12X, G13X, Q61X and A146X of KRAS gene by real-time PCR using Real-time-PCR-KRAS-4R kit (BioLink LLC, Russia) according to the manufacturer's instructions. Reactions were performed on the CFX96 amplifier (Bio-Rad Laboratories, USA) according to the following protocol: 1 cycle - 95°C 3 min; 48 cycles - 95°C 15 sec, 55°C 40 sec. PCR products of KRAS gene with mutations were detected in 5'-exonuclease reaction using TaqMan probe labeled with fluorophore.
Results: The frequency of KRAS gene mutations in cervical adenocarcinoma was 16,67% (4/24). All specimens with the identified mutation had endometrioid histologic variant and no mutations were found

among other histologic variants. According to the results, KRAS gene mutations were more frequent in endometrioid histologic variant of cervical adenocarcinoma (p=0,0004).
Conclusion: KRAS gene mutation may be considered as a potential therapeutic target in the endometrioid histologic variant of cervical adenocarcinoma.

E-PS-11-051
Keratinising HPV-negative squamous cell carcinoma of the uterine cervix in uterine prolapse
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Background & Objectives: In contrast to the relatively high frequency of uterine prolapse, the coexistence with cervical carcinoma is extremely rare, and the knowledge about its morphologic and molecular characteristics is very scarce. Furthermore, morphologic features of HPV-independent squamous precursor lesions are very limited.
Methods: Detailed histopathological and immunohistochemical analyses of p16, p53 and CK 17 were performed, as was a molecular evaluation for HPV-DNA and p53-mutation of four consecutive cervical squamous cell carcinomas associated with uterine prolapse with the definition of a hitherto not well-described precursor lesion and molecular tumorigenetic pathway.
Results: The cases were diagnosed during a period of seven years with a mean age of 75 (range 69-83) years and a mean tumour size of 7.3 cm (range 5.2-9.4cm). All patients presented with locally advanced disease, and one woman died within four, another within 14 months of follow-up. Histopathologically, all keratinizing squamous cell carcinomas (SCC) with infiltrative growth and were negative for p16, showed an aberrant p53-expression and diffuse and strong staining for CK 17 on immunohistochemistry. On the molecular level, the SCCs were negative for HPV-DNA but harboured a TP53-mutation. An HPV-independent pathogenetic pathway with a p53-alteration was identified for these cases.
Conclusion: The coexistence of cervical SCC with uterine prolapse is extremely rare. These specific SCCs represent highly keratinized, HPV-independent tumours harbouring a TP53-mutation.

E-PS-11-052
***POLE/POLD1* mutations in uterus endometrial carcinoma: study of trends in morphologic / molecular classification and lymphovascular progress of oncogynecologic disease**
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Background & Objectives: Genomic classification of uterus endometrial carcinoma (*POLE/POLD1, TP53* mutations, and microsatellite instability (MSI) markers) was integrated into clinical pathology practice in last decade, carrying a more significant prognostic effect for the progress of this disease. Objective is to detect specific morphologic / molecular features of progressing endometrial carcinoma tested for *POLE/POLD1* mutations.
Methods: 45 cases of endometrial carcinoma verified by morphology analysis of surgical material and tested for *POLE/POLD1* mutations in local clinical pathology laboratory were selected. Morphologic parameters (histologic type, pT, pN stages, differentiation grade (G), lymphovascular invasion (LVI)) were analysed and molecular profile (presence of *POLE/POLD1* mutations, *MSI*, p53, receptors of oestrogens and progesteron (ER, PR)) was determined by immunohistochemic and rtPCR methods. Statistical analysis was performed ($p<0.05$).
Results: Median age of patients was 61 and mostly (n=24, 53.3%) in age group >60 years. Majority of carcinomas were endometrioid type (n=39, 86.7%), pT1b (n=19, 42.2%), pN0 (n=26, 57.8%) and G1-2 (n=34, 75.6%). Lymphovascular invasion (LVI1) was detected in 35.6% (n=16) cases. A small group of carcinomas was *POLE/POLD1*-mutated (n=4, 8.9%). Majority of cases were MSS (n=18, 78.3%), and *TP53* mutations were absent in 71.4% (n=25) cases. Expression of ER and PR was positive in 57.8% (n=26) and 53.3% (n=18) cases, correspondingly. *POLE/POLD1*-mutated cases were more likely to be diagnosed for 40-49 years old patients (p=0.003). LVI1 status was less likely to manifest in endometrioid carcinoma (p=0.01), pT1a / pT1b ($p<0.001$), G1-2 (p=0.003), ER-positive (p=0.037), and non-heterogenic p53 expression (p=0.05) cases. No significant trends were detected between LVI and *POLE/POLD* mutations, *MSI*, and PR expression status ($p>0.05$).
Conclusion: *POLE/POLD1* mutations were more likely to manifest for 40-49 years old patients, and LV progression of uterus endometrial carcinoma was more likely to be detected in ER-negative and heterogenic p53 expression cases, without any significant associations to *POLE/POLD1* mutations, *MSI*, and PR expression status.

E-PS-11-053
A rare clinical presentation – somatically-derived Yolk Sac Tumour of the ovary with chondrosarcomatous differentiation
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Background & Objectives: Yolk sac tumours (YSTs) are malignant tumours derived from germ cells that morphologically mimics the foetal yolk sac.[1] YSTs usually present in children and younger women, they are rare over age 40.[2] Somatically-derived YSTs were first described in 1987, and described as a YST deriving from an epithelial neoplasm through a process of neometaplasia or retrodifferentiation.[3]
Methods: Here, we describe a case of a somatically derived YST with chrondrosarcomatoid differentiation. We present the case of a 59-year-old woman who presented with abdominal pain and nausea in April 2022
Results: A CT scan showed a 15.5cm left ovarian mass as well as extensive metastatic disease involving peritoneal deposits, encasing the bowel. The patient underwent a hysterectomy, bilateral salpingo-oophorectomy and resection of bladder peritoneum. Tumour was present in the left ovary and within the bladder peritoneum, FIGO Stage 3C. Histologically, a tumour with a distinct biphasic appearance was seen. This component was positive with villin, CDX2, Glypican 3, SALL4 & AFP and represented a yolk sac tumour. The second malignant component comprised of solid diffuse arrangements of epithelioid cells, some with rhabdoid morphology within a chondromyxoid stroma. A wide range of immunohistochemistry was performed on this element with no definitive answer, and expert consultation was sought. The final diagnosis was given as a somatically derived sarcomatoid yolk sac tumour with a chondrosarcomatous component.
Conclusion: The patient had a good treatment response to chemotherapy, both 1st and 2nd line, however unfortunately, in September 2024, a large RIF metastatic deposit causing a bowel obstruction was surgically removed. Histologically, this showed a recurrence of the chondrosarcomatous component of the YST. This case is a rare presentation of a somatically derived YST. Less than 50 cases of somatically derived YSTs have been described in the literature and none with a sarcomatoid component.

E-PS-11-054

Advancements in cervical cancer screening in the bulgarian population: improving HPV testing and triage strategies

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Background & Objectives: Cervical cancer is a common gynaecological malignancy, with screening mainly based on Pap smears. Since persistent HPV infection is a key factor, HPV genotyping is considered for primary screening but has low specificity in young women due to transient infections. Patients with low-grade squamous intraepithelial lesion (L-SIL) or atypical squamous cells of undetermined significance (ASC-US) undergo further tests like colposcopy and biopsy to rule out high-grade H-SIL, though 70–90% of L-SIL cases, especially in women under 30, regress spontaneously, leading to unnecessary procedures. To improve risk assessment, immunohistochemical markers like p16/Ki-67 offer reliable alternative, aiding early oncogenesis detection in liquid based cytology (LBC), HPV genotyping, and biopsies.
Methods: Fifty women under 30 undergoing routine screening were enrolled, with liquid-based cytology and HPV testing performed. Based on risk levels, groups were formed, and p16/Ki-67 dual staining was applied to high-risk cases. Results were analysed, identifying high-risk patients needing biopsy in the Bulgarian population.
Results: It was established that LBC is generally preferred due to better sample quality, higher sensitivity, and the ability to perform additional test such as HPV genotyping and dual-stain p16/ki-67. From the investigated cases 12 (24%) were ASC-US, 7 (58%) of them HPV positive and 3 (6%) cases with L-SIL, 2 (67%) of them HPV positive. Dual-stain were performed on 9 cases.

Conclusion: Our study is the first attempt in comparing conventional versus liquid based cytology smears and assess the accuracy of dual-staining p16/Ki-67 combined with HPV genotyping and colposcopy on Bulgarian population. Our results show thatthe p16/Ki-67 test could be useful in the triage of young patients with ASC-US or L-SIL and should be taken into consideration for the diagnostic algorithm and obtain a new management protocol for patients under the age of 30 years positive for HPV and with cytological abnormalities on the LBC.

E-PS-11-055

Solitary pulmonary nodule: an unexpected diagnosis

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Background & Objectives: Low-grade endometrial stromal sarcoma is a malignant stromal tumour composed of cells resembling the endometrial stroma in the proliferative phase and showing infiltrative growth with or without lymphovascular invasion. Patients present with abnormal uterine bleeding, pelvic pain, uterine mass, and / or pulmonary, adnexal or lymph node metastases.
Methods: A 52 year old woman with persistent cough underwent a scanner, which identified a 2 cm solitary pulmonary nodule in the left upper lobe, without others visible lesions. A biopsy of the nodule was perfomed.
Results: The histopathological examination of the pulmonary biopsy showed the presence of small, uniform cells with scant cytoplasm and an oval nucleus, with a delicate arteriolar network surrounding these cells. With the initial suspected diagnosis of lymphoproliferative pulmonary lesion, a complete immunohistochemistry study was performed, which showed negativity for CD45, CD20, CD79a, CD3, CD43, CD23, Cyclin D1, and CD56. The immunohistochemistry study was extended to include oestrogen receptors, progesterone receptors, and CD10, all of which were positive. The patient was evaluated by a multidisciplinary team that decided to perform a lobectomy. A specimen measuring 21 x 10 cm was received, in which a well-defined, reddish lesion of 2.3 cm in size was observed. Microscopic examination confirmed the result of the pulmonary biopsy, reporting it as a metastasis of endometrial stromal sarcoma. A hysterectomy with bilateral salpingo-oophorectomy was performed, the macroscopic appearance showed no abnormalities. However, microscopic examination revealed a focus of low-grade endometrial stromal sarcoma measuring 9 x 13 mm with three lymphovascular invasions.
Conclusion: Pulmonary metastasis from low-grade endometrial stromal sarcoma can be its first clinical manifestation, highlighting the importance of considering this entity in female patients. This case underscores the significance of correlating the clinical context, histopathology and immunohistochemical studies in reaching an unusual diagnosis.

E-PS-11-056

Prognostic significance of Wnt5A expression in cervical carcinoma

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Background & Objectives: Cervical cancer (CC) is the second most common cancer of the female reproductive organs and the fourth leading cause of cancer-related death in women. The Wnt signalling pathway involves numerous proteins essential for initiating cell proliferation and differentiation processes in various organs. There is evidence that the Wnt signalling pathway plays a crucial role in carcinogenesis and tumour progression. Our study aims to determine the expression of the Wnt5A protein in samples of invasive cervical cancer and its impact on survival.
Methods: In the study, a total of 98 patients with cervical cancer were included. Patients were selected randomly, regardless of age and histological tumour type. Patient follow-up: The course and outcome of treatment, survival duration, and cause of death were determined based on medical documentation and data obtained through interviews with the patient or her family. Immunohistochemical detection of antigens was performed using the peroxidase reaction, applying commercial antibodies in appropriate dilutions. Survival probability and the impact of Wnt5A expression on patient survival were calculated using the Kaplan-Meier algorithm. Fisher's exact test and the Log-Rank test were used to determine statistical significance.
Results: Ekspresija Wnt5A (umjerena i visoka) u tumorskim ćelijama CC bila prisutna u 72,4% slučajeva. Ekspresija Wnt5A je odsutna kod 27,6% slučajeva. Utvrđeno je da je procentualno veće preživljavanje pacijentica čiji tumori su bili negativni na Wnt5A (81%), u odnosu na pacijentice čiji su tumori pokazivali ekspresiju Wnt5A (69,2%). Primjenom Fisher-ovog testa nije dobijena statistički značajna razlika ($p = 0.405$) s obzirom na prisustvo i stepen ekspresije Wnt5A u tumorskim ćelijama i preživljavanja.
Conclusion: Wnt5A expression was identified in 72.4% of invasive cervical cancer cases in our study. No statistically significant difference in

survival was confirmed among patients with cervical cancer concerning the presence and degree of Wnt5A expression.

E-PS-11-057

Expression patterns of molecular chaperones Hsp27 and Hsp90 in serous ovarian cancer

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Background & Objectives: Serous ovarian cancer (SOC) is the most aggressive histological subtype of ovarian tumours and a major cause of gynaecological cancer mortality. Heat shock proteins (Hsp27 and Hsp90) are molecular chaperones involved in protein folding, cell survival, and resistance to therapy. This study aimed to evaluate the expression and intracellular localization of Hsp27 and Hsp90 in SOC compared to borderline ovarian tumours (BOT), to assess their potential diagnostic and prognostic significance.
Methods: Tissue samples from 23 patients with newly diagnosed SOC and 6 patients with BOT were analysed using immunohistochemistry (IHC). Paraffin-embedded tumour blocks obtained during diagnostic laparoscopy were stained with antibodies against Hsp27 and Hsp90. The percentage of positive tumour and stromal cells was assessed using optical microscopy and QuPath 0.5.0 software. Statistical analysis was performed using non-parametric tests (Mann–Whitney, Wilcoxon) with significance set at $p<0.05$.
Results: he proportion of Hsp27-positive tumour cells significantly exceeded that of Hsp90 ($p=0.0006$), and both markers showed significantly higher expression in tumour cells than in the stroma. Hsp27 expression in SOC exceeded that in the stroma by 10.8 times (cytoplasmic) and 7.41 times (nuclear); Hsp90 exceeded stromal levels by 40.4 and 86.7 times, respectively. Compared to BOTs, SOC tissues showed a 7.1-fold increase in Hsp27 and a 4.3-fold increase in Hsp90 expression ($p<0.005$). Hsp27 expression was consistently higher than Hsp90 in all intracellular compartments.
Conclusion: Hsp27 and Hsp90 are overexpressed in serous ovarian cancer compared to borderline tumours and stromal tissue, suggesting their potential as differential diagnostic and prognostic IHC markers. Hsp27, due to its ATP-independent function, may serve as a more reliable biomarker and therapeutic target in the hypoxic and metabolically stressed tumour microenvironment of ovarian cancer. Their differential expression patterns also highlight the role of stress-induced chaperone networks in tumour progression, chemoresistance, and metastatic potential, warranting further investigation.

E-PS-11-058

Sclerosing Stromal Tumour. A report of three cases presenting as huge pelvic masses

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Background & Objectives: Sclerosing stromal tumour (SST) is a rare benign ovarian neoplasm classified under sex cord-stromal tumours. It account for 2-6% of ovarian tumours with patients presenting in the second and third decades of life. Patients usually presents with pelvic pain, irregular menses and abdominal mass. We report three cases presenting as huge pelvic masses.
Methods: This is a retrospective study of all cases diagnosed as SST over a ten year period. Electronic records of patients diagnosed as SST was retrieved and data was extracted.
Five immunohistochemical markers were used in this study (vimentin, smooth muscle actin, S-100, cytokeratin and ER).
Results: Three cases were seen during the study period. Their ages are 45, 43, 42 respectively with a mean age of 43.3. All three cases presented with huge pelvic mass measuring up to 60cm, 48cm and 40 cm respectively. Histopathological examination shows spindle areas with pseudo-lobular formation, collagen deposition and cystic changes. Immunohistochemistry shows vimentin, smooth muscle actin and ER positive staining. The rest showed negative staining.
Conclusion: Sclerosing stromal tumour in our setting presents in the fourth and Fifth decade as huge pelvic masses.

E-PS-11-060

A 74-year-old patient with endometrial carcinoma: a case report of a VUS-POLE-mutation with poor prognosis

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Background & Objectives: Recent studies on endometrial carcinoma (EC) emphasize patient survival and prognosis, as mortality rates have increased by 1.5% annually from 2013 to 2022. A diagnostic algorithm based on The Cancer Genome Atlas (TCGA) highlights four prognostic subgroups, with patients exhibiting POLE mutations typically demonstrating more favourable outcomes. However, we present a case of a 74-year-old woman diagnosed with advanced stage EC and demonstrated VUS-POLE mutation for EC, who died 4 months after her diagnosis.
Methods: We searched for the specific POLE mutation in the complete TCGA (Genome Data Commons) catalogs and COSMIC (https://cancer.sanger.ac.uk/cosmic, accessed 16 March 2025).
Results: A 74-year-old woman presented to our clinic with a history of vaginal bleeding lasting one week. Curettage specimen revealed high-grade endometrial carcinoma (MMR intact, p53 wild-type), prompting POLE mutation testing. She underwent debulking surgery and was classified as FIGO Grade IIC, with noted cervical stromal invasion. After three weeks, a lesion at distal vagina was observed and biopsied, revealing infiltration by undifferentiated carcinoma. CT scan indicated multiple lung lesions suspected to be metastatic. The patient passed away after a month of hospitalization, before the genetic analysis was completed, which identified VUS-POLE EDM variant (c.1264C>T p.H422Y, rs745356467) for endometrial carcinoma.
Conclusion: Research in the TCGA and COSMIC databases revealed only three cases of this POLE variant (c.1264C>T p.H422Y, rs745356467), all linked to colorectal cancer, highlighting its rarity in endometrial carcinoma.

E-PS-11-061

Wolffian tumour of the broad ligament: a rare case with diagnostic challenges

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Background & Objectives: Female adnexal tumours of probable Wolffian origin (FATWO) rank among the rarest gynaecologic neoplasms, with fewer than 200 cases documented worldwide. This underrecognized entity frequently mimics malignant adnexal tumours, risking overtreatment. We present an unusual case that presents diagnostic challenges.

Methods: A 57-year-old postmenopausal woman presented with an incidental left adnexal mass. Left salpingectomy and excision of the left broad ligament, along with complete removal of the mass, revealed a well-demarcated nodular lesion measuring 5 cm in diameter adjacent to the fallopian tube.
Results: Histologically, the tumour demonstrated striking morphologic diversity: dominant tubular architecture with focal solid/retiform patterns, moderate cytologic atypia in a sclerohyaline stroma with frequent calcifications.
The mitotic index was 2 mitoses/10 HPF.
The immunohistochemical study revealed diffuse positivity for cytokeratins AE1/AE3, calretinin and WT1, focal expression of alpha-inhibin and CD-10 and negativity for EMA, CK7, CD99, Chromogranine, Synaptophysin, GATA3 and PAX8.
Postoperative surveillance showed no residual disease after total hysterectomy, right salpingectomy and bilateral oophorectomy, confirming the tumour's origin as primary to the broad ligament.
Conclusion: This case provides important insights into the broad ligament as a primary site for Wolffian tumours, a diagnosis that can be challenging in frozen section. It highlights the importance of precise clinical correlation to exclude involvement from an ovarian tumour.

E-PS-11-062
Gynaecologic PEComas: predominantly malignant case series with pathologic and clinical findings
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Background & Objectives: Gynaecologic perivascular epithelioid cell tumours (PEComas) are rare mesenchymal neoplasms with both melanocytic and smooth muscle differentiation. Correct diagnosis is challenging due to morphological and immunohistochemical overlap with more common smooth muscle tumours.
Methods: Institutional archive search identified 13 gynaecologic PEComa cases (2015-2025). Clinical-pathologic data were reviewed.
Results: Patient age ranged 35-83 years (median 50). Specimens included 9 hysterectomies, 3 endometrial curettage and/or myomectomy, and 1 salpingo-oophorectomy. The most common clinical presentation was abdominal pain (5/11;38.5%), followed by postmenopausal/abnormal uterine bleeding (4/11;30.8%). Tumour locations were most frequently uterine (10/13;76.9%), and otherwise 1 case each cervical, ovarian, and pelvic wall (3/13;23.1%). Tumour size ranged 2.3-27.1 cm (median 17.6). Nine tumours (69.2%) were classified as malignant and 4 (30.8%) as uncertain malignant potential by 2020 WHO gynaecologic criteria. Necrosis and lymphovascular space invasion were each present in 4 malignant cases (30.7%). Mitotic count ranged 1-36 per 10 high-power fields (median 15.5). Immunohistochemistry performed on all cases showed widely variable expression of both smooth muscle (SMA, desmin, and/or caldesmon) and melanocytic markers (Melan A, HMB45, and/or MITF). Most tumours showed expression of cathepsin K (10/12;83.3%) and ER (6/7;85.7%). Cases showed variable expression of CD10 (3/6;50%), and none showed expression of SOX10 or S100. All tested cases showed retained fumarate hydratase expression (3/3;100%). Amongst malignant cases, over half demonstrated aberrant p53 expression (4/7;57.1%). Of 10 cases with clinical follow-up, 7 (70%) showed no evidence of disease, 1 (10%) was alive with disease, and 2 (20%) died of disease; all patients with disease on follow-up were originally diagnosed with malignant PEComa.
Conclusion: Pathologic awareness of morphologic features, immunoprofile, and malignancy criteria in gynaecologic PEComas is essential for accurate diagnosis, clinical prognostication, and patient management.

E-PS-11-063
HPV E6/E7 oncogene expression determination in the detection of squamous intraepithelial lesions in women with atypical squamous cell cytology
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Background & Objectives: The overexpression of human papillomavirus (HPV) oncogenes E6/E7 is an indicator of viral integration. Determination of these markers may be important in the diagnosis and clinical monitoring of patients with cervical intraepithelial neoplasia. This study evaluated the determination of E6/E7-mRNA in the detection of cervical intraepithelial neoplasia, in women with abnormal atypical squamous cell (ASC) cytology.
Methods: One hundred twenty-one patients between 18 and 82 years of age with ASC cytology results were included. A cervical swab was taken and embedded in nucleic acid preservation medium, the samples were subjected to RNA extraction. Ninety-eight samples underwent PCR amplification to determine E6/E7-mRNA of HPV 16, 18, and 31. The results of HPV E6/E7-mRNA in the cervical swab samples were compared with the results of the histopathological study as gold standard.
Results: Were positive for E6/E7-mRNA 14.3% (14/98) of the samples. Of these, 71.4% (10/14) were positive for HPV-16 E6/E7, 21.4% (3/14) for HPV-31 E6/E7, and 7.14% (1/14) for HPV-18 E6/E7. The estimated percentages of agreement between these results and colposcopy findings or histopathology ranged from 27.5% to 84.7%. When comparing molecular detection of viral mRNA with the detection of high- and low-grade squamous intraepithelial lesions (HSIL and LSIL), by colposcopy, the following were found: sensitivity of 11.1% (6/54; 95% CI, 5.2% to 22.2%), specificity of 81.8% (36/44; 95% CI, 68.0% to 90.5%), positive predictive value of 42.9% (6/14; 95% CI, 21.4% to 67.4%), and negative predictive value of 42.9% (36/84; 95% CI, 32.8% to 53.5%).
Conclusion: The determination of mRNA of the E6/E7 oncogenes of genotypes 16, 18 and 31 of the human papillomavirus, proved to be a moderately useful test to confirm the presence of HPV E6/E7 mRNA in low and high grade squamous intraepithelial lesions of the cervix, which are the target of early detection programs for cervical cancer.

E-PS-11-064
Endometrial polyps in breast cancer patients: a comparative analysis from King Hussein cancer centre
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Background & Objectives: Endometrial polyps (EPs) are common findings in women, but their association with breast cancer, particularly with hyperplasia or malignancy, remains under-researched in certain regions. This study aims to compare the clinical and pathological features of endometrial polyps in breast cancer patients, managed at King Hussein Cancer Centre, focusing on those with and without hyperplasia or malignancy.
Methods: A total of 196 breast cancer patients were included in the study over 10 years (2014-2023). They were divided into two groups: Group 1 (n=173, 88.3%) consisting of patients with polyps without hyperplasia or malignancy, and Group 2 (n=23, 11.7%) consisting of patients with polyps with hyperplasia or malignancy.
Results: The median age at diagnosis for all patients was 50 years, with no significant difference between the two groups ($p = 0.7479$). The majority had invasive breast cancer (92.3%). Hormonal

treatment, particularly tamoxifen, was administered in 98.8% of the cases, with no significant difference between both groups (p = 1.000).
In Group 1, functional polyps predominates (92.5%), whereas Group 2 shows polyps with hyperplasia 16 (69.6%), and carcinoma (n=7, 30.4%) including serous carcinoma (n=4, 17.4%), endometrioid carcinoma (n=1, 4.3%) and metastatic breast carcinoma (n=2, 8.7%). The overall incidence of malignant changes in endometrial polyps from the overall cohort was 3.6%.
Conclusion: Endometrial polyps in breast cancer patients treated with tamoxifen should be removed and examined to rule out malignancy. The incidence of malignancy in this cohort is 3.6%, which is similar to international figures.

E-PS-11-065
Tumour immune microenvironment of tubo-ovarian high-grade serous carcinoma: unveiling the role of HLA Class I and II
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Background & Objectives: High-grade serous carcinoma (HGSC) is an aggressive ovarian malignancy, responsible for most ovarian cancer-related deaths. Despite advances in surgery and chemotherapy and the introduction of PARP inhibitors (PARPi), long-term outcomes remain poor, with most patients experiencing recurrence after an initial response. Immune evasion, particularly through downregulation of human leukocyte antigen (HLA), limits tumour immunogenicity contributing to treatment resistance.
This study evaluates the expression of Human Leukocyte Antigen (HLA) Class I, HLA Class II, and β2-microglobulin (β2M) in HGSC and their correlation with Homologous Recombination Deficiency (HRD) status, clinico-pathological features and patient outcomes.
Methods: A total of 132 formalin-fixed, paraffin-embedded (FFPE) samples from 66 HGSC patients (FIGO stage II-IV) were analysed. Samples were collected from primary adnexal lesions and metastatic sites. IHC staining assessed HLA I, HLA II, and β2M expression. HRD status was determined by Next-generation sequencing (NGS). Clinico-pathological features, including tumour morphology (SET vs classic), pattern of invasion, mitotic rate, extensive tumour necrosis, tumour-infiltrating lymphocytes (TILs), CA125 levels, and residual tumour, were correlated with HLA-I, HLA-II and β2M expression.
Results: Molecular profiling showed HRD status in 43.9% of cases and *BRCA* mutations in 32.3%. HRD-positive and *BRCA*-mutated tumours correlated with improved DFS (p<0.001). HLA I loss was associated with higher residual disease, baseline CA125 levels, extensive tumour necrosis and reduced CD8+ T-cell infiltration. HLA II and β2M expression showed similar patterns. Spatial Cancer-Immune Phenotype (SCI) compartmentation identified three immune infiltration patterns: desert, excluded, and inflamed. SCIs correlated with higher residual disease, CA125 levels, desmoplastic stroma and SET growth pattern and they were consistent across primary and metastatic sites.
Conclusion: These findings confirm that HLA downregulation plays a pivotal role in HGSC progression. Improving patient stratification through molecular and immune profiling can refine prognostic assessments and guide personalized therapeutic strategies targeting both tumour vulnerabilities and immunity.

E-PS-11-066
Bilateral vulval lactational adenomas, a very rare case report and review of literature
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Background & Objectives: The anogenital mammary-like glands (AGMLG) are sites of origin of vulval mammary-like lesions. We present a very rare case of bilateral vulval lumps (VL) in a lactating female showing histologic lactational breast tissue-like changes in the AGMLG.
Methods: A 34-year-old Asian woman presented complaining of bilateral VL associated with some creamy discharge. She first noticed them six days after her caesarean delivery. She was breast feeding on presentation. She had two previous pregnancies with no such complaint. Both VL were excised.
Results: Macroscopically the VL measured 15X12X11 mm and 15x6x6 mm. They had circumscribed homogeneous soft creamy white cut surface . Microscopically, the left VL showed a well-demarcated area of glandular lobules with back to back acini and central double-lined ducts. The acini showed increased amount of eosinophilic and clear cytoplasm, round nuclei and inconspicuous nucleoli. On the right side, there were more cystically-dilated ducts with eosinophilic secretions. These changes were similar to those seen in lactational mammary tissue. Immunohistochemistry showed GATA 3, ER and PR expression in the acini, while PAX 8 was negative. P63 and CK5/6 stained surrounding myoepithelial cells.
Native AGMLG were first described by Kazakov and colleagues in 2011. Previously, these were considered as ectopic breast tissue representing the caudal remnants of the milk ridges. AGMLG can show mammary-like lactational changes, lactational adenoma, fibrocystic changes, intraductal papilloma, pseudo-angiomatous stromal hyperplasia, fibroadenoma, phyllodes tumour and adenocarcinoma of mammary type.
Conclusion: We have presented a very rare case of bilateral vulval lactational adenomas arising from AGMLG in a young postpartum female. Although a few unilateral cases were reported, bilateral lesions have not been documented. It is imperative for the pathologists to be aware of the presence of native AGMLG. These lesions are no more considered ectopic to this site. Treatment is by surgical excision as these lesions may cause local discomfort.

E-PS-11-067
Clinicopathologic profiling of ovarian clear cell carcinoma: insights from a tertiary cancer centre of North India
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Background & Objectives: Ovarian clear cell carcinoma (OCCC) is a rare epithelial ovarian cancer with overlapping histopathological characteristics with other ovarian tumours. Unfortunately, there seems to be a paucity of clinicopathological data pertaining to OCCC from the Indian subcontinent.
Objective: To comprehensively evaluate the entire spectrum of the clinical, histopathological, immunohistochemical, and survival characteristics of OCCC treated at our centre.
Methods: A retrospective analysis of OCCCs diagnosed over a period of 6 years was conducted.
Results: Median age of the 39 identified patients of OCCC was 50.8 years (range 31-74 years), presenting with chief complaints of abdominal mass and pain. The mean baseline serum CA-125 level was 508.5 U/ml (range 5.9-3907.6 U/ml). Histomorphology revealed papillary, tubulocystic, and solid patterns with variable number of clear cells. NapsinA reactivity on immunohistochemistry was evinced in 91.4%, HNF1β in 100%, and mutant type p53 in 27.3% cases. Majority of the patients presented in FIGO Stage III (43.6%), followed by stage I (35.9%), IV (15.4%), and II (5.1%). 74.4% patients underwent surgical resection, chemotherapy was administered in 84.6% patients while radiation therapy was mandated in a single patient. On a median follow-up of 26 months (range 6–63 months), the mean overall survival time was estimated at 49 months (95% CI: 41.2-57.0 months) and the 3-year overall survival rate 62.8±11.2%. The median progression-free survival (PFS) for stages I & II patients was at 33 months (95% CI: 11.8 to 54.2 months), followed by stages III & IV patients at 20 months (95% CI: 5.7 to 34.3 months).
Conclusion: Majority of the patients presented at a late stage, and the mean serum CA-125 level was higher compared to Western literature. Early-stage patients demonstrated a better PFS than late-stage ones. Such findings highlight the aggressive behaviour of this rare condition, underscoring the vital need for accurate histopathological diagnosis and effective therapeutic management.

E-PS-11-068
Detection of microplastics in human placental tissue using nile red staining and fluorescence microscopy
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Background & Objectives: The presence of microplastics in human tissues has raised concerns regarding their potential health effects. Previous studies have primarily focused on microplastic identification using Raman microscopy, flow cytometry, or homogenized tissue samples, often relying on animal models. However, these approaches do not allow precise histological localization of microplastics within tissue structures. This study aimed to detect microplastics in placental tissue using a fluorescence-based method that preserves tissue architecture.
Methods: Formalin-fixed, paraffin-embedded placental tissue samples were deparaffinized and stained directly on slides. Nile Red staining solution was prepared by dissolving the dye in dimethyl sulfoxide (DMSO), which was diluted with denatured ethanol to achieve an optimal concentration for microplastic labelling. The samples were incubated at 50–60°C to enhance staining efficiency and fluorescence signal. All procedures were conducted under controlled conditions to minimize external plastic contamination. Fluorescence microscopy was used to analyse the stained sections and identify microplastic particles based on their characteristic fluorescence.
Results: Fluorescence microscopy revealed an increased signal corresponding to microplastics in various placental structures. Microplastics were observed in the intervillous space, villous and extravillous trophoblast, and decidua. In the villi, microplastics were frequently associated with vascular walls. The particles were well-defined and ranged in size from 5 to 15 µm.
Conclusion: The identification of microplastics in placental structures highlights the need for further investigation into their potential impact on pregnancy. While this study does not establish a direct link between microplastic presence and placental pathology, future research should explore potential correlations and underlying mechanisms.

Funding: VEGA 1/0646/25 "Alterations in the placental tissue glycocode related to maternal glucose metabolism affecting the course of pregnancy"

E-PS-11-070
Isolated Langerhans cell histiocytosis of the vulva: case report
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Background & Objectives: Langerhans Cell Histiocytosis (LCH) is a rare disorder characterized by the proliferation of Langerhans cells, most commonly affecting the skin, bones, and lymph nodes. Isolated vulvar involvement is extremely rare and often mimics chronic inflammatory or neoplastic conditions, leading to diagnostic challenges.
Methods: We report the case of a 55-year-old female who presented with chronic vulvar ulcerations and pruritus, unresponsive to standard treatments. Clinical examination revealed erythematous, ulcerated plaque on the vulva.
Results: Histopathological examination showed an infiltrate of histiocytes with characteristic nuclear grooves, accompanied by numerous eosinophils. Immunohistochemical staining confirmed the diagnosis of LCH, with positive expression of CD1a, S100, and Langerin. A systemic workup excluded multisystem involvement.
Vulvar LCH is an uncommon presentation that requires a high index of suspicion. The presence of abundant eosinophils is a hallmark histopathologic feature that aids in differentiation from other conditions, such as squamous cell carcinoma, lichen sclerosus, and chronic infectious diseases. Immunohistochemistry plays a crucial role in confirming the diagnosis. Treatment strategies depend on disease extent, with options including local corticosteroids, surgical excision, or systemic therapy in disseminated cases.

Conclusion: This case highlights the importance of considering LCH in the differential diagnosis of chronic vulvar lesions. Early recognition, supported by histopathology and immunohistochemistry, is essential for accurate diagnosis and optimal patient management.
E-PS-11-071
STIC, high-grade serous, and neuroendocrine carcinomas: evidence of a unified pathogenetic origin
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Background & Objectives: High-grade neuroendocrine carcinoma of the uterine tube is a rare neoplasm, with limited cases documented in literature. We present a case of a 77-year-old woman diagnosed with this carcinoma, alongside high-grade serous carcinoma and a precursor lesion of the STIC type, supporting a shared origin.
Methods: The patient underwent excisional biopsy after identifying a hypermetabolic lesion. Histopathological examination revealed a high-grade neuroendocrine carcinoma, with immunohistochemistry showing neuroendocrine markers. Complete tissue embedding confirmed multifocal secondary high-grade serous carcinoma, with a concurrent STIC precursor lesion.

Results: Histology revealed a high-grade small-cell neuroendocrine carcinoma involving the fallopian tube. The tumour exhibited hyperchromatic nuclei, mitotic activity, and lymphovascular invasion. Immunohistochemistry demonstrated positivity for neuroendocrine markers (INSM-1, synaptophysin, chromogranin) and mutations in p53. The fallopian tube also showed multifocal high-grade serous carcinoma, with areas of STIC precursor lesions. The two carcinoma types were adjacent, suggesting a potential biological link. Detailed histopathology indicated a transition zone between neuroendocrine and serous carcinoma components, sharing immunohistochemical characteristics, including mutated p53 and block positivity for p16.
Conclusion: This case highlights the rarity of high-grade neuroendocrine carcinoma of the fallopian tube, particularly in combination with high-grade serous carcinoma and STIC lesions. The presence of these components suggests a common origin and supports the hypothesis that neuroendocrine differentiation may arise from a pre-existing carcinoma. This finding provides insight into the tumour's pathogenesis and emphasizes the importance of thorough histological examination to identify all components of such rare cases. Continued documentation is essential to improve diagnostic and therapeutic strategies.

E-PS-11-072

Second opinion in gynaecologic pathology: evaluating diagnostic concordance and its effect on patient management

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Background & Objectives: In pathology, second opinion allows cases to be reviewed by experienced pathologists, thereby increasing diagnostic accuracy and ensuring appropriate patient management. This study aimed to evaluate the frequency of diagnostic discrepancies in gynaecologic pathology at our institution and their impact on clinical management.
Methods: We analysed all gynaecological pathological second opinion reports conducted at our institution in 2024, and compared them with the original reports. Each patient clinical files were analysed to evaluate the clinical impact of discordances. Cases were categorized into five groups: no diagnostic disagreement, no diagnostic disagreement but pertinent information not included, diagnostic disagreement without clinical consequences (NoCS), diagnostic disagreement with minor clinical significance (MinorCS) and diagnostic disagreement with major clinical significance (MajorCS).
Results: A total of 182 cases was reviewed, including specimens from uterine corpus (n=98), uterine cervix (n=41), ovary/Fallopian tube/peritoneum (n=20), vulva (n=17) and vagina (n=6). The majority were biopsy specimens (n=135, 74.2%).
In 132 (72.5%) cases there was consensus between the original report and the one revised at our institution, but in a subset of these (n=11) second opinion added pertinent information for patient management. Diagnostic disagreement was present in 50 (27.5%) cases, including: 16(8.8%) MajorCS, 7(3.8%) MinorCS and 27 (14.8%) NoCS.
The higher rates of disagreement were similar in uterine corpus (30.6%) and ovary/Fallopian tube/peritoneum (30.0%), and lower in cervix (21.9%) and vulva (17,6%).
Conclusion: We report a higher discordance rate compared to literature, that may be explained by our role as a cancer referral centre for complex cases. Additionally, our access to advanced diagnostic tools, including genetic testing unavailable in local laboratories, enhances second opinion diagnostic precision. Our data reflects a selection bias, as currently only endometrial carcinomas undergo mandatory review, while other topographies are reviewed opportunistically. The discrepancies significantly impact patient care and institutional costs, highlighting the value of expert second opinion in pathology.

E-PS-11-073

FN-EDA fibronectin isoform: harnessing its expression for innovative therapeutic strategies

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Background & Objectives: Over 39,000 ovarian cancer deaths occur annually in Europe and the U.S., highlighting the need for improved diagnostics and treatments. This study evaluates four tumour markers—extra-domains A and B of fibronectin, fibroblast activation protein, and carcinoembryonic antigen—and expands to assess EDA-FN in epithelial ovarian cancer tissue samples.
Methods: An exploratory immunohistochemical analysis was performed on 60 FFPE tissue sections from 47 patients with epithelial ovarian cancer. The samples included 47 specimens collected at first diagnosis, along with 13 relapsed lesions. These tissue sections were stained using validated antibodies to evaluate the stromal immunoreactive score (sIRS) for biomarker expression in 'Exploratory Fase 1' of the study. After completing this phase, the study expanded to investigate EDA-FN. In 'Focus Fase 2', 204 FFPE tissue samples from 102 patients with High Grade Serous Ovarian Cancer (HGSOC) were analysed, including both primary and metastatic sites.
Results: Results of 'Exploratory Phase 1' showed stromal expression of EDA-FN, EDB-FN, and FAP in ovarian cancer, while their levels remained unchanged in matched primary and relapse tumour tissues. CEA was found exclusively in mucinous ovarian cancer. Our analysis revealed that EDA-FN was the most abundant antigen, prompting further analysis in a larger sample size of EOC (Focus Phase 2). When patients were stratified by (i) molecular status (BRCAwt vs BRCAmut), (ii) line of treatment (naive vs relapse), (iii) primary vs metastatic lesions, and (iv) prior bevacizumab treatment, EDA-FN was highly abundant in all cases. Moreover, elevated expression was found in metastases compared to primary tumours.
Conclusion: These findings highlight that EDA-FN is an excellent target for HGSOC, while CEA could serve as a potential target for MOC. Clinical investigations are warranted to validate innovative treatments in ovarian cancer targeting these antigens.

Funding: This work was partially supported by Philogen S.p.a

E-PS-11-074

Impact of molecular profiling in the management of high-grade serous carcinoma: a case of tumour heterogeneity

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Background & Objectives: A 50-year-old woman presented to the emergency department with abdominal pain, and hematemesis for three days. A CT scan showed a 65 mm abdominal mass. She underwent emergency laparotomy, including total hysterectomy, bilateral adnexectomy, omentectomy, and resection of peritoneal nodules and diaphragmatic peritoneum (RT=0). The histology confirmed adnexal high-grade serous carcinoma, FIGO IIIB.

Methods: Two different tumour areas were evaluated, one by the in-house NGS tumour-only multigene panel, the other by FMI-Roche (MITO25.1 trial). In one area (morphological pseudoendometrioid features), NGS programme revealed the following: TP53 (p.R280*, c.838A>/T, VAF% 79.2); MUTYH (p.Y179C, c.536A>G, VAF% 49.8); HRD status by Sophia negative, with GI: -12.4; BRCA1-2 wild type. On the other FFPE block (usual morphological features), the FMI revealed: same TP53 mut; MUTYH (p.Y165C); HRD not detected; BRCA2 R3052Q, with VAF% 41; LOH: 4.7%. Germline testing for BRCA1/2 and MUTYH (p.Y165C) was performed with negative and positive results, respectively.
Results: These two molecular assays highlighted the intratumoral heterogeneity. To clarify this discrepancy, we examined the significance of the BRCA2 R3052Q mutation on ClinVar, where it is classified as VUS/likely benign (if germline) or without clinical impact (if somatic). A review of the literature suggested that this variant may be hypomorphic, with minimal prognostic impact. We reached out to the FMI for clarification with the following response: 'This variant has conflicting evidence listed in ClinVar. Studies by Mesman et al. provided in vitro evidence suggesting that BRCA2 R3052Q may be considered a hypomorphic variant, meaning it leads to partial loss of function in the homologous recombination repair pathway".
Conclusion: The CT scan showed no residual disease. The patient received 5 cycles of chemotherapy (carboplatin AUC5 + paclitaxel 175 mg/m²). Given the molecular heterogeneity observed, the best maintenance therapy remained uncertain. After tumour board review, the patient was considered for MITO 25.1, with liquid biopsy testing ongoing.

E-PS-11-075

Diagnosis of peritoneal tuberculosis from primary peritoneal cancer

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Background & Objectives: Peritoneal tuberculosis (PTB) is a rare extrapulmonary infection that can mimic primary peritoneal cancer (PPC). This study aimed to identify clinical, radiological, and biomarker differences between PTB and PPC to enable earlier and more accurate diagnosis of PTB.
Methods: Medical records of patients diagnosed with PTB from January 2016 to 2024 were reviewed. PTB was confirmed by pathology or Mycobacterium tuberculosis culture/ polymerase chain reaction in ascitic fluid or lymph nodes. A comparison group of PPC patients was included, diagnosed based on histopathology using Gynaecologic Oncology Group criteria.
Results: We analysed data from 7 women with PTB and 15 with PPC. Key differentiators for PTB included a body temperature above 38°C ($p < 0.001$), lower body mass index (BMI) ($p = 0.003$), lower white blood cell (WBC) count ($p < 0.001$), and lower CA-125 levels ($p < 0.001$). Imaging showed more pulmonary infiltration and consolidation ($p < 0.001$) and less omental or mesenteric involvement ($p < 0.001$) in PTB compared to PPC. Patients who underwent surgery received treatment earlier ($p = 0.010$).
Conclusion: The clinical spectrum of PTB includes fever, lower BMI, reduced WBC count, and modestly elevated CA-125 levels. Chest X-rays may show infiltrative lesions, and computed tomography scans are less likely to reveal omental nodules. Early suspicion of PTB in patients with these features should prompt laparoscopy for biopsy, which offers a quicker diagnosis and initiation of antituberculosis therapy. We propose an algorithm to enhance the differentiation between PTB and PPC, emphasizing early laparoscopic biopsy for timely diagnosis and treatment.

E-PS-11-076

Implementation and validation of FOLR1 (clone FOLR1-2.1) immunohistochemistry in high-grade serous ovarian carcinoma: diagnostic experience and quality control considerations

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Background & Objectives: **FOLR1 (folate receptor alpha)** is a potential diagnostic and predictive biomarker in high-grade serous ovarian carcinoma (HGSC). In recent years, its relevance has increased, especially in the context of targeted therapies. The aim of this study is to present our experience with the implementation of FOLR1 immunohistochemical staining (clone FOLR1-2.1) in routine pathological diagnostics.
Methods: Prior to diagnostic implementation, 50 cases of HGSC were analysed using the VENTANA® FOLR1 (clone FOLR1-2.1, Roche) ready-to-use assay on the BenchMark ULTRA platform. The staining protocol included standard CC1 heat-induced epitope retrieval, application of the primary antibody as per manufacturer's instructions, and detection with the OptiView DAB IHC Detection Kit. Positive controls (fallopian tube epithelium) and negative controls (non-serous ovarian tumours and normal tissues) were used. FOLR1 expression was assessed semi-quantitatively, focusing on membranous staining intensity (0, 1+, 2+, 3+) and the percentage of positive tumour cells. High FOLR1 expression (FOLR1-high) was defined as ≥75% of tumour cells with ≥2+ membranous staining.
Results: Optimization of the staining protocol was necessary to reduce background noise and cytoplasmic staining. The selection of appropriate internal and external controls proved essential for reliable interpretation. In several cases, non-specific staining patterns were observed, requiring cautious evaluation, especially in samples with borderline intensity or focal expression. The proportion of FOLR1-high cases was 44%, with variability in staining distribution and intensity.
Conclusion: Implementation of FOLR1 immunohistochemistry using clone FOLR1-2.1 requires careful validation, including the use of standardized protocols and well-defined scoring criteria. The presence of non-specific staining underlines the importance of adequate controls and experience in interpretation. FOLR1 evaluation may support patient stratification for targeted therapies and should be further explored in a clinical context.

E-PS-11-077

A novel *MLLT10::C10orf67* gene fusion detected in a uterine leiomyosarcoma with aggressive behaviour

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Background & Objectives: Leiomyosarcoma is an aggressive malignant mesenchymal uterine tumour. Distinguishing high grade mesenchymal uterine neoplasms can be challenging. Molecular diagnostics therefore can be a valuable tool to establish a definitive diagnosis. We describe for the first time a novel *MLLT10::C10orf67* gene fusion, detected in a uterine leiomyosarcoma, with peculiar histologic features.
Methods: A 64-year-old healthy female with sudden onset right lower quadrant pain was found to have a fibroid uterus with pressure effect on pelvic organs. She underwent a supracervical hysterectomy and bilateral salpingo-oophorectomy at an outside hospital and was diagnosed with 18 cm leiomyosarcoma. One month later, she presented at our institution for consultation and was found to have diffuse pulmonary,

osseous, peritoneal, and pelvic metastases. Microscopic examination, immunohistochemical (IHC) and comprehensive next generation sequencing (NGS) studies were performed on her primary tumour.
Results: Tumour consisted of sheets of polymorphic cells with spindled, epithelioid, focal rhabdoid morphology, ill-defined fascicular pattern, moderate light eosinophilic cytoplasm, scattered lymphocytes, and peculiar numerous scattered small hyaline plaques. Brisk mitotic activity (33/10 hpf) and extensive tumour necrosis were identified. IHC results showed positive caldesmon (diffuse), SMA and CD10, with negative desmin, SMMHC, myogenin, MYO-D1, Melan A, HMB-45, ALK-1, AE1/3, S-100, CD117, and ER. NGS showed a novel fusion of the *MLLT10* (exon 7) gene to the *C10orf67* (exon 3) gene, arising from t(10;10) translocation. Other significant molecular findings included mutations in *TP53*, *CHEK2*, and *PALB2* genes. The patient was started on doxorubicin-trabectedin chemotherapy, however, died of disease 4 months after the initial diagnosis.
Conclusion: Fusions of *MLLT10* with KMT2A or *PICALM* have been described in hematologic malignancies, with reported high-risk features, and with other partners in solid tumours, such as intestinal, lung and skin cancers. To our knowledge, this is the first report of *MLLT10::C10orf67* fusion detected in the literature, including the gynaecologic tract, with aggressive clinical behaviour.

E-PS-11-078
Primary vaginal gastric-type adenocarcinoma arising from sporadic vaginal adenosis: a case report
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Background & Objectives: Vaginal adenosis is a benign metaplastic condition, typically associated with in utero diethylstilbestrol(DES) exposure but also occurring sporadically. While most cases regress through squamous metaplasia, some persist and exhibit gastric differentiation, which may carry malignant potential. Although progression from adenosis to atypical adenosis, clear cell carcinoma, or gastric-type adenocarcinoma is rare, it is clinically significant. Gastric-type adenocarcinoma is an aggressive, HPV-independent subtype that often evades detection by routine screening. This report presents a rare case of primary vaginal gastric-type adenocarcinoma arising in the background of sporadic vaginal adenosis.
Methods: A 44-year-old woman presented with postcoital vaginal bleeding. Gynaecological examination revealed a friable, haemorrhagic mass on the right vaginal wall extending to the posterior cervix. Biopsies were obtained from both sites. Clinical and radiological findings favoured a vaginal rather than a cervical primary tumour. Histopathological and immunohistochemical analyses were performed.
Results: Cervical biopsies revealed glandular atypia and CIN1 without invasion, whereas vaginal biopsies demonstrated adenocarcinoma in situ and invasive adenocarcinoma with gastric morphology. Tumour cells were positive for CK7 and CAIX, with focal MUC6 expression. PAX8 and p16 negativity supported the HPV-independent nature of the tumour. The Ki-67 index was 15–20%. Based on clinical, radiological, and pathological findings, a diagnosis of primary vaginal gastric-type adenocarcinoma was established. Systemic evaluation revealed no distant metastases.
Conclusion: Although vaginal adenosis is generally considered benign, the presence of gastric differentiation may indicate malignant potential. While some adenotic lesions regress, others may progress to malignancy. This case highlights the importance of recognizing and monitoring vaginal adenosis with gastric differentiation as a potential precursor to aggressive malignancies. HPV-independent gastric-type adenocarcinoma can arise in sporadic vaginal adenosis. Given its rarity and aggressive nature, primary vaginal gastric-type adenocarcinoma requires meticulous diagnostic evaluation and clinical management. Heightened clinical awareness and thorough histopathological evaluation are essential for early diagnosis and improved patient outcomes.

E-PS-11-079
Evaluation of Mismatch Repair (MMR) status and breast cancer-1 (BRCA-1) in epithelial cancers of the ovary
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Background & Objectives: India contributes approximately 5.9% of global ovarian cancer cases. The standard treatment for surface epithelial ovarian cancers typically involves a combination of surgery and platinum- or taxane-based adjuvant chemotherapy. However, these therapies are often associated with relapse and early mortality.
BRCA1 (Breast Cancer 1) and Mismatch Repair (MMR) proteins play a critical role in guiding targeted therapy, offering chemo- and immunotherapeutic advantages. This study aims to evaluate BRCA1 and MMR protein expression using immunohistochemistry (IHC) in surface epithelial ovarian cancers. Additionally, it seeks to establish a clinicopathological correlation and assess the concordance between IHC findings and molecular analysis of MMR gene.
Methods: Immunohistochemistry (IHC) was performed on epithelial ovarian cancers for BRCA1, MLH1, MSH2, MSH6, and PMS2, and the results were analysed in relation to clinical and pathological variables. Additionally, 15 samples were processed in duplicate for sequencing studies, using a panel of 13 MMR gene markers, along with appropriate positive and negative controls.
Results: Our study, which included 49 cases of epithelial ovarian cancer, involved documentation of demographic details. According to our findings, 51% of epithelial ovarian cancers were dMMR. However, no significant correlation was observed between dMMR and pMMR tumours in terms of high-grade features. Notably, patients with dMMR exhibited better survival rates, likely due to an improved response to chemotherapy.
Total loss of BRCA1 was observed in 36.7% of cases. While BRCA1 loss was associated with aggressive tumour behaviour, it also correlated with a better response to chemotherapy.
No significant correlation was found between molecular testing and immunohistochemistry (IHC) results for microsatellite instability (MSI) in this study.
Conclusion: Our study demonstrates that a significant proportion of epithelial ovarian cancers exhibit BRCA1 loss and dMMR. Therefore, incorporating IHC-based screening into routine practice could help identify patients who may benefit from targeted therapies.

E-PS-11-080
When metastasis tells the story: a case of lung metastatic extrauterine endometrial stromal sarcoma
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Background & Objectives: Endometrial stromal sarcoma (ESS) represents 1% of all uterine malignancies with known risk factors including prolonged oestrogen use, pelvic radiation and endometriosis. The aim is to report the diagnostic approach, imaging findings, histopathological and molecular features of this entity.
Methods: A 49-year-old woman presented with mild fatigue and pleuritic chest pain. Additional symptoms included dysmenorrhea, deep dyspareunia, irregular menstruation for less than a year, and heavy

menstrual flow. Her family history was notable for gastrointestinal and prostate cancers. Due to the respiratory symptoms, a thoracic CT scan was performed, revealing multiple bilateral pulmonary nodules, which were subsequently biopsied.
Results: Lung biopsy showed a neoplasm composed of oval small cells with scarce cytoplasm and indistinct boundaries, arranged in short, intersecting bundles within a rich capillary network. Some areas displayed perivascular concentric arrangements of neoplastic cells. The nuclei exhibited minimal pleomorphism, with variable chromatin distribution. Mitoses were scarce, and no haemorrhage or necrosis was observed.
Immunohistochemistry revealed neoplastic cells positive for vimentin, CD10, WT1, ER, and PR, focally for CD117 and were negative for inhibin, cytokeratin AE1/AE3, EMA, DOG1, pan-TRK, CD34, CD31, calretinin, actin, and desmin. These findings are consistent with a mesenchymal neoplasm, with features suggestive of Endometrial Stromal Sarcoma with the differential diagnosis with a sarcomatous component of a gynaecological mixed neoplasm.
Pelvic-RM was performed and showed a pelvic mass interposed between the uterus and left ovary.
Pelvic mass biopsy was performed, and both histological and immunohistochemical analysis, were overlapping with the lung lesion.
Next-generation sequencing identified a CTNNB1 translocation p.(Asp32Asn)/DN32N. Pathological study of the surgical specimen confirmed the final diagnosis of Extrauterine Endometrial Stromal Sarcoma.
Conclusion: This rare case highlights the diagnostic challenges of metastatic extrauterine ESS. Several genetic alterations have been reported in ESS, with the CTNNB1 translocation being linked to the presence of whorled and fibromixoid morphology and β-catenin pathway.

E-PS-11-081
Cervical adenocarcinoma with endometrial and fallopian tube metastasis: a case report
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Background & Objectives: Adnexal and endometrial metastasis of cervical adenocarcinoma (ADC) is relatively uncommon. Most of the tubal metastases are associated with ovarian ones. Tubal metastasis that occurs alone is generally asymptomatic and grossly unidentifiable and only a few studies have been published.
Methods: We present a case of a 58-year old woman, diagnosed with HPV-associated AIS cervix in cervical biopsy and treated with total hysterectomy with BSO.
Histopathology showed an HPV-related AIS-like ADC (CK7+/CK20-/p16+/ER-/PR-/vimentin/WT-1-, p53wt), 30 mm in length, extending to the isthmus and endometrium, with areas of non destructive stromal invasion (type A Silva system) up to 1,6mm in depth and a polypoid/exophytic non infiltrating component, 5mm in high, identified in the transition of endocervical-isthmus. Lesions of the same immunohistochemical profil tumour were observed in endometrial fundus, and in mucosa of both fallopian tubes without stromal invasion, supporting the idea of metastasis from the endocervical carcinoma, rather than primary. Both ovaries were free from disease.
No lymph nodes or peritoneal lesions were identified during operation.
Results: According to AJCC 2017, the stage of the carcinoma is pT1A1. According to ISGyP proposal, 2021, and considering the exophytic component as part of the primary tumour and not as endometrial involvement, the stage is pTA2. Currently, the free carcinomatous lesions in endometrium and tubes do not change the stage.
The MDT proposed NAC.
Conclusion: - our case support the transuterine/transtubal spread of exfoliated tumour cells as a mechanism of spread of ADC to the upper genital tract.
- microscopic tubal metastases may happen in non-destructively ADC, warranting an extensive sampling
- tubal metastases from ADC should be distinguished from STIC
- follow up of the case, may contribute to the best treatment and prognosis of these rare cases.

E-PS-11-082
A rare case of carcinosarcoma arising from the Fallopian tube: a unique clinical presentation
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Background & Objectives: Carcinosarcomas of the gynaecological system are most commonly seen in the endometrium, followed by the ovary, while a Fallopian tube origin is exceptionally rare. These aggressive malignancies are often diagnosed at an advanced stage due to nonspecific symptoms. We present a rare case of carcinosarcoma arising from the left Fallopian tube with serous tubal intraepithelial carcinoma (STIC), providing strong evidence of tubal origin. The aim was to contribute further information on the clinicopathologic aspects of this rare disease.
Methods: A 71-year-old female presented with abdominal bloating, distension, and left-sided pain. MRI revealed bilateral adnexal masses with torsion features. She underwent total laparoscopic hysterectomy with bilateral salpingo-oophorectomy. Histopathological and immunohistochemical analyses were performed.
Results: Macroscopic examination showed a multinodular mass (50mm) at the fimbrial end of the left Fallopian tube. The left ovary contained a solid mass (28mm). Microscopically, the tumour comprised predominantly high-grade serous carcinoma and a minor sarcomatous component (<5%) with focal chondromatous differentiation, along with STIC in the left fimbrial end, confirming tubal origin. Immunohistochemistry showed positivity for PAX8, WT1, ER, and PR, with a mutant (null) p53 staining pattern. Tumour involvement was noted in the right ovary, both Fallopian tubes, and uterine serosa. The provisional stage was FIGO IIA. Due to comorbidities, restaging surgery was not performed, and platinum-based chemotherapy was initiated.
Conclusion: Primary Fallopian tube carcinosarcomas are exceptionally rare, with very few reported cases in the literature, and highly aggressive malignancies of the gynaecological system. The presence of STIC in the Fallopian tube reinforces its role as a precursor lesion and provides strong evidence of tubal origin. Early recognition and thorough histopathological assessment, including adequate sampling to detect minor sarcomatous components, are crucial for accurate diagnosis and prognostication

E-PS-11-083
Primary retroperitoneal mucinous borderline tumour: a case report
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Background & Objectives: Primary retroperitoneal mucinous tumours are exceedingly rare, and are classified into mucinous cystadenomas, mucinous borderline tumours (PRMBTs), and mucinous cystadenocarcinomas. To date, only 34 cases of PRMBTs have been documented in the literature. Here, we present the case of a 78-year-old female patient with such a tumour.
Methods: A 78-year-old Caucasian woman was referred for MRI of the lumbar spine due to fatigue, knee pain, and tingling sensations.

Upon detection of a newly developed Grade IV hydronephrosis on the right side and the sonographic confirmation of a mass, a CT scan of the abdomen was performed, raising suspicion of a large renal cell carcinoma. The patient subsequently underwent open nephrectomy on the right side. Intraoperative findings included a large tumour mass in the area of the caudal part of the kidney with pronounced adhesions between the tumour and the omentum, liver, duodenum, and vena cava.
Results: Pathological analysis identified a PRMBT of 10.3 cm in diameter adherent to the kidney and compressing the pyelon resulting in chronic active, localized, abscess-forming, destructive pyelonephritis. Of all reported PRMBTs, 29 involved female and 6 male patients. The median age for female patients was 42.4 years, making PRMTs a potential differential diagnosis for young women with retroperitoneal masses. The exact pathogenesis and genetic factors remain unclear due to the rarity of these cases. After complete surgical resection, five-year disease specific survival reaches 100% in patients with PRMBT.
Conclusion: Publication of individual cases is crucial for improving diagnostic attention to and understanding of this rare tumour over time.

E-PS-11-084

Embryonal rhabdomyosarcoma (*sarcoma botryoides*) mimicking a benign cervical lesion: a case report of a rare gynecopathological entity

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Background & Objectives: Embryonal rhabdomyosarcoma (*sarcoma botryoides*), a rare mesenchymal cervical neoplasm, primarily affects paediatric and adolescent females, commonly arising in the vagina or cervix. The main peak incidence of embryonal rhabdomyosarcoma is <5 years old (y.o.), but it can also be diagnosed in older patients. Characterized by a polypoid, grape-like appearance, it often mimics benign lesions, complicating gynaecological diagnostics of cervical pathology.
Methods: A 16 y.o. female presented with a three-month history of a protruding vaginal mass. Her gynaecological history was unremarkable. Gynaecological examination revealed a 6 cm pinkish tissue mass with haemorrhages and ulcerations, likely extending from posterior cervical lip. Ultrasound demonstrated internal cystic structures, while a 8.5 x 4.8 x 2.7 cm mass prolapsing through vaginal introitus was detected during pelvic MRI. Initially suspected as a fibroepithelial polyp, a biopsy was sent for a morphological examination of gynaecological diagnosis.
Results: Findings in biopsy were initially interpreted as a benign soft tissue tumour, to be differentiated between fibroepithelial polyp and angiofibroma, consisting of hypocellular oedematous areas with accentuated thick-walled blood vessels and covered by non-dysplastic squamous epithelium. Following surgical excision with histological examination of surgical material revealed alternating hypocellular areas with myxoid or oedematous stroma admixed with hyaline-type cartilage foci and hypercellular regions (cambium layer) of primitive, small cells with hyperchromatic nuclei, mitotic activity and significantly increased Ki67 proliferation index (approx. 85%), mostly located in subepithelial zone and around cervical glands. Separate striated rhabdomyoblasts were morphologically identified and confirmed by applying Desmin and MyoD1 immunohistochemical markers. Positive expression of these immunohistochemical markers confirmed the pathology diagnosis of rhabdomyosarcoma.
Conclusion: Embryonal rhabdomyosarcoma (*sarcoma botryoides*) is a rare gynecopathologic mesenchymal malignancy in adolescent females. Complex clinical, morphological, and immunohistochemical evaluation of neoplastic tissue should be performed, including immunohistochemical testing for evidence of skeletal muscle differentiation in neoplastic cells, ensuring timely diagnosis and treatment for the patient.

E-PS-11-085

PTEN in endometrial cancer: evaluation of expression and correlation with histo-prognostic factors: a series of 77 cases

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Background & Objectives: Endometrial cancer (EC) is the third most common female gynaecological cancer in Tunisia, after breast and cervical cancer, with increasing incidence rates in recent decades. Several studies have demonstrated the prognostic importance of various surgical and pathological parameters in this cancer. Therefore, it is essential to identify new additional biomarkers for its prognostic prediction. Among these biomarkers, the PTEN gene has emerged as a prognostic and theragnostic factor for EC. In this work, we were interested in evaluating the immunohistochemical expression of PTEN as well as the correlation of its status with clinicopathological characteristics in EC.
Methods: It was a descriptive, retrospective and semi-quantitative study. All data were collected from the PCR Laboratory of the ISA between 2007 and 2017. These samples underwent anatomopathological study followed by an immunohistochemical study.
Results: Our series included 77 cases of EC. Low-grade endometrioid carcinomas represented the majority of cases (88,3%). On immunohistochemical study, PTEN expression was observed in tumour cells in 12% of cases and in the stroma in 29% of cases. PTEN expression status in tumour cells showed no statistically significant association with histo-prognostic parameters. However, PTEN expression in the stroma was significantly correlated with several important histo-prognostic features, such as tumour appearance (p=0.004), degree of differenciation (p=0.006), surgical margin invasion (p=0.032), and annexal infiltration (p=0.016).
Conclusion: The PTEN gene is emerging as a key biomarker in endometrial cancer, offering promising prospects for the development of targeted treatments and better risk stratification in patients.

E-PS-11-086

A rare case of Intravenous Leiomyomatosis (IVL) with extension into the inferior vena cava and right atrium

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Background & Objectives: Intravenous leiomyomatosis (IVL) is a rare and distinct type of smooth muscle tumour that, despite being histologically benign, exhibits malignant-like behaviour due to its ability to infiltrate the venous system. Smooth muscle cells extend intravascularly, typically originating from uterine leiomyomas. IVL may remain asymptomatic or present with non-specific pelvic symptoms, but can become life-threatening when it extends into large vessels such as the inferior vena cava (IVC) and right atrium.
Methods: A 41-year-old woman presented with a history of an intra-abdominal pelvic mass. The patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy. At the time of surgery, the tumour's aetiology was unclear. The tumour mass extended from the left corner of the cervix towards the iliac region and was localized beneath the left uterine appendages and the broad ligament.
Results: Morphological examination of tumour mass revealed multiple intramural leiomyomas and smooth muscle tumour invasion into the left uterine vein, with extension through the broad ligament and

surrounding pelvic structures. Immunohistochemical study demonstrated diffuse positive staining for desmin, Ki-67 proliferative index ~3%, indicating low proliferative activity. Two years after surgery, this patient underwent a CT scan, which revealed thrombosis in inferior vena cava (IVC) extending into the right atrium and left renal vein, pathological pelvic masses near the left lateral wall of the bladder, within the left retroperitoneal space, and extending along the anterolateral surface of the left psoas muscle, at the level of the renal arteries. No disease progress has been detected during continuous CT scan follow-ups every two years.
Conclusion: This case report emphasizes the malignant potential of histologically benign intravenous leiomyomatosis. While initial surgical treatment focused on uterine mass removal, delayed vascular extension and pelvic recurrence demonstrate the significance of extensive vascular evaluation and long-term follow-up in such patients diagnosed with rare, but potentially life-threatening condition.

E-PS-11-087
Comparative immunohistochemical assessment of SSEA-1, SOX-9, and CD117 in endometriosis and adenomyosis
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Background & Objectives: Adenomyosis and endometriosis are frequent gynaecological entities, yet their underlying mechanisms remain a topic of ongoing discussion. As stem cells are considered to play a crucial role in the initiation and progression of both lesions, different variants of the stem cell hypothesis have been proposed to explain their pathogenesis. This study aims to comparatively assess the immunohistochemical expression of endometrial stem cells markers, SSEA-1, SOX-9, and CD117, in adenomyosis and endometriosis.
Methods: Our retrospective study was conducted at "Elena Doamna" Clinical Hospital of Obstetrics and Gynaecology, Iasi, Romania and included 261 cases of adenomyosis and endometriosis, diagnosed and surgically treated between 2019-2024. The cases were histopathological diagnosed on standard H&E slides, and immunohistochemically assessed for SSEA-1, SOX-9, and CD117.
Results: The histopathological examination of the surgical specimens identified adenomyosis in 70.11% (n=183) of the cases, endometriosis in 24.13% (n=63) of the cases, 5.74% (n=15) presenting both lesions simultaneously, associating adenomyosis with different endometriotic lesions, with the following sites: ovarian (endometriotic cysts (n=47) and implants (n=10)), abdominal wall (n=12), tubal (n=6), and cervical (n=3). The stem cell marker SSEA-1 presented positive immunoexpression in both adenomyosis and endometriotic lesions. A higher diffuse cytoplasmic expression of SSEA-1 of glandular epithelial cells was found in adenomyosis compared to endometriosis. Nuclear immunoexpression of SOX-9 was positive in glandular epithelial cells from endometriotic lesions as well as in adenomyosis, but also with higher levels in adenomyosis. In the endometrial stroma, CD117 was significant elevated in endometriosis compared to adenomyosis, their distribution showing a periglandular pattern.
Conclusion: The study reveals that both entities contain the evaluated stem cells. However, the different immunoexpression profile of endometrial stem cells in endometriosis and adenomyosis may support the etiopathogenic differences between the two. Future studies are needed for a broader etiopathogenic characterization of these lesions, in order to develop new therapeutic strategies.

E-PS-11-088
Mammary-type Myofibroblastoma of the vagina: a case report of a rare polypoid lesion
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Background & Objectives: Mammary-type Myofibroblastoma (MTMF) is a rare benign mesenchymal tumour, primarily described in the breast but also reported in extramammary sites, including the soft tissues, inguinal region, and lower female genital tract. It is part of the spectrum of the so called 13q/*RB1* family of tumours, which includes tumours such as spindle cell / pleomorphic lipoma and cellular angiofibroma. Its pathogenesis remains poorly understood, though hormonal influences are suggested by its frequent positivity for oestrogen and androgen receptors. Clinically, MTMF presents as a well-circumscribed, slow-growing mass, which may be mistaken for other mesenchymal neoplasms. This report aims to describe a rare case of vaginal MTMF, emphasizing its clinico-pathological features and differential diagnosis.
Methods: A 74-year-old woman presented with a 2 cm pedunculated vaginal polypoid lesion with a 0.9 cm base. The lesion was covered by whitish mucosa and had a firm, elastic consistency. Complete excision was performed, and the diagnosis of Mammary-type Myofibroblastoma was made.
Results: Histological examination revealed a subepithelial spindle-cell neoplasia with a "grenz zone," moderate cellularity, spindle and stellate-shaped cells with ocasional multinucleated cells. The stroma was collagenous with keloid-like fibres and hyalinized-walled blood vessels. There was no mitotic activity or necrosis. Immunohistochemistry showed strong desmin positivity, highlighting dendritic morphology of some spindle cells, and positivity for CD34, ER, AR, Bcl-2, CD99, and CD10. The lesion was negative for caldesmon, calponin, SMA, S100, and AE1/AE3.
Conclusion: Vaginal MTMF is an uncommon benign neoplasm that should be considered in the differential diagnosis of vaginal spindle-cell lesions. Given its indolent behaviour, conservative surgical excision is the treatment of choice. Recognition of this entity is crucial to avoiding unnecessary aggressive interventions and distinguishing it from malignant mesenchymal tumours.

E-PS-11-089
CPSF2 expression in endometrial carcinoma: analysis of 100 cases
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Background & Objectives: Cleavage and Polyadenylation Specificity Factor 2 (CPSF2) is a component of the mRNA processing machinery, and its dysregulation has been implicated in various cancer types. However, the clinical significance of CPSF2 expression in endometrial carcinoma remains underexplored. We analysed CPSF2 expression in a cohort of endometrial carcinoma cases and to evaluate its potential correlation with key clinicopathological parameters.
Methods: Formalin-fixed, paraffin-embedded tissue samples from 100 patients diagnosed with endometrial carcinoma were assessed for CPSF2 expression via immunohistochemistry. Expression levels

were scored semi-quantitatively, and patient data were retrospectively reviewed to correlate CPSF2 status with tumour type, grade and stage.
Results: Most endometrial carcinoma samples demonstrated varying degrees of CPSF2 immunoreactivity, and preliminary analyses suggest that its expression may be linked to specific pathologic features, including tumour stage and histological grade.
Conclusion: We report that CSF2 is frequently expressed in endometrial carcinoma. Nevertheless, the significance of CPSF2 expression, including potential prognostic implications and underlying biological mechanisms require larger prospective studies and mechanistic analyses will help clarify the clinical relevance of CPSF2 in endometrial carcinoma.

Funding: Research project, University of Prishtina, Kosovo No. 2/963. 15.11.2023

E-PS-11-090
Prognostic implications of microsatellite instability and p53 expression in endometrial carcinomas: an immunohistochemical study
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Background & Objectives: The study of microsatellite instability (MSI) and mutations of the TP53 gene is part of the new molecular classification of endometrial carcinomas (EC) adopted by the latest edition of the WHO classification of tumours of the female genital tract. Our work aimed to evaluate, through immunohistochemistry, the microsatellite status and p53 expression in a series of EC and to determine their clinico-pathological features.
Methods: This was a retrospective descriptive study involving 76 cases of EC collected at the pathology department of FarhatHached Hospital over seven years (2014-2020). Immunohistochemical analysis was performed using a tissue microarray (TMA) block with p53, MLH1, MSH2, MSH6, and PMS2 antibodies.
Results: The average age of the patients was 58.9 years. The majority of cases were EC (89.5%), with low-grade tumours (48.7%) and early FIGO stage (69.8%). Microsatellite instability was found in 35.5% of cases. Abnormal p53 expression was observed in 11.8% of cases. MSI patients were older and had endometrioid tumours in 96.7% of cases, although no significant association was found. Overexpression of p53 was statistically correlated with advanced age (p=0.010), non-endometrioid type (p=10^-3), high-grade FIGO (p=10^-3), and advanced FIGO stage (p=0.001). The survival rates (overall survival and relapse-free survival) of MSI/p53-wild type patients were reduced compared to those of the MSS/p53-wild type group (p=0.767; p=0.990). The overexpression of p53 decreased both overall survival (p=10^-3) and relapse-free survival (p=0.003) and was identified as an independent poor prognostic factor for overall survival.
Conclusion: The study of the microsatellite status and p53 expression allowed us to determine three subgroups in our series: the MSS/p53-wild type subgroup had the most favourable prognosis, the MSI/p53-wild type subgroup had an intermediate prognosis, and the MSS/p53-abnormal subgroup had the poorest prognosis. This "immunohistochemical" classification brought us closer to the molecular classification of EC, emphasizing the role of immunohistochemistry in prognostic studies of EC.

E-PS-11-091
Endometrial sampling in women aged 40 and under: an institutional experience of an increasing caseload
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Background & Objectives: The incidence of endometrial sampling of women under 40 has steadily increased in our institution over recent years, requiring significant pathology resources. We aimed to audit practices regarding endometrial sampling in this age group. To compare the incidence, indications, and significant findings of endometrial sampling in women aged 40 and under in our institution between two time periods, ten years apart, to better understand the core reasons for the increase observed. To examine whether indications for endometrial sampling are in keeping with current guidelines, and whether the risk of neoplasia/preneoplasia is changing in our younger patients over time.
Methods: All endometrial biopsies in women aged 40 and under were identified from Cork University Hospital pathology department electronic records database using search codes for endometrial biopsies for 2008-2012 (T1) and 2018-2024 (T2). Clinical details, macroscopic, and microscopic reports were analysed. All data was recorded and analysed using Microsoft Excel.
Results: 2582 cases were identified, 271 cases from T1 (21% of total number sampled), and 2311 (19% of total number sampled) cases from T2. T1 had an average of 54.2 cases per year, T2 had an average of 330.1 cases per year. The average age in T1 was 35.5 and 34.8 in T2. No significant difference between sampling indications were identified. The most common indication was AUB (76% of T1, 74% of T2). A small but non-statistically significant difference in diagnosis of ATH/EIN and endometrial carcinoma was identified (0% ATH/EIN, 0% endometrial carcinoma in T1, 1% ATH/EIN, 1% endometrial carcinoma in T2).
Conclusion: A small, non-statistically significant increase in the incidence of ATH/EIN and endometrial carcinoma was observed between time periods. Relative stability compared with a large increase in overall number sampled suggests consistency in management of these women. The continuing increase in cases may reflect a growing baseline population in our region.

E-PS-11-092
Heterogeneity in mesonephric adenocarcinoma: clinicopathological and immunohistochemical analysis of two cases
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Background & Objectives: Mesonephric carcinomas of the uterine cervix are rare tumours believed to originate from mesonephric remnants. We present two cases of mesonephric adenocarcinoma in patients from different age groups.
Methods: **First Case:** A 40-year-old female patient presented with spotting-type bleeding. Ultrasound revealed no abnormalities in the vagina, cervix, uterus, or adnexa. Pelvic examination identified uterine prolapse and cystocele. The patient underwent cervical amputation due to uterine prolapse, which led to the diagnosis of mesonephric adenocarcinoma. A subsequent total hysterectomy was performed, and no residual tumour was detected.
Second Case: A 75-year-old female patient presented with postmenopausal bleeding at an external centre and underwent curettage. Histopathological evaluation of both the initial and repeat curettage samples confirmed the diagnosis of mesonephric adenocarcinoma, leading to a decision for hysterectomy.
Results: In the first case, examination of the cervical amputation specimen revealed back-to-back acini lined with low cuboidal cells containing intraluminal eosinophilic secretions, surrounded by desmoplasia. The acini exhibited invasive features within the muscle layer. Immunohistochemically, the tumour cells were positive for GATA-3 and PAX8 but negative for CD10 and the oestrogen receptor.

In the second case, examination of the curettage and hysterectomy specimens showed similar acinar structures, along with papillary formations containing true fibrovascular cores with hierarchical branching, lined by cuboidal/columnar cells. Immunohistochemical analysis demonstrated negativity for the oestrogen receptor, positivity for GATA-3, PAX8, CD10, and TTF-1, wild-type p53 expression, and patchy p16 positivity.
In both cases, the invasive appearance of these structures ruled out mesonephric remnants. The combination of oestrogen receptor negativity, wild-type p53 expression, and p16 negativity helped exclude endometrioid-type adenocarcinoma and serous carcinoma. No sarcomatous component was present.
Conclusion: Mesonephric adenocarcinoma is a rare cervical tumour that requires both morphological and immunohistochemical differentiation from benign mesonephric remnants and other, more common cervical tumours.

E-PS-11-093
Identification of new diagnostic and therapeutic targets in endometrial carcinoma
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Background & Objectives: Endometrial carcinoma (EC) originates from the epithelial lining of the endometrium and is histologically classified into Type I (low-grade, favourable prognosis) and Type II (high-grade, poor prognosis). Molecular classification defines four prognostically significant subgroups: POLE-mutated, microsatellite instability (MSI), low copy number, and high copy number tumours. The PTEN gene, frequently mutated in EC, plays a key role in the PI3K/Akt signalling pathway, regulating tumour growth, invasion, and apoptosis. Additionally, alterations in glycosylation significantly influence tumour progression by modulating cell adhesion, migration, and proliferation. This study aims to characterize changes in surface glycoconjugates in EC and correlate them with the molecular classification, as well as to investigate alterations in the PI3K/Akt/PTEN pathway and their association with protein sialylation.
Methods: Formalin-fixed, paraffin-embedded EC biopsy samples were analysed using lectin histochemistry to assess alterations in surface glycoconjugates. Lectins specific for distinct carbohydrate motifs (ECL, PNA, PSA, UEA, SNA, LCA, MAL, RCA, AAL, PHA) were utilized to obtain a comprehensive glycosylation profile. Immunohistochemistry was performed to evaluate PI3K/PTEN/AKT pathway activity, focusing on PTEN expression and phosphorylated AKT.
Results: PTEN expression was higher in microsatellite stable tumours compared to MSI tumours. AKT strong positivity in invasive front foci was observed in 31%, suggesting a role in invasion and progression. Weak diffuse AKT positivity was more frequent in G3 tumours, indicating its involvement in early carcinogenesis or less aggressive tumours. SNA positivity (α2,6-sialylation) predominated, while MAL expression (α2,3-sialylation) was weak, emphasizing the role of sialylation in EC pathogenesis.
Conclusion: The observed AKT positivity at invasive fronts and the predominance of α2,6-sialylation suggest a potential role of glycosylation in EC progression. These findings provide new insights into EC tumour biology and may inform future diagnostic and therapeutic strategies. Further research using additional lectins is needed to confirm the correlation between glycosylation patterns and molecular characteristics of EC.

Funding: VEGA 1/0646/25. Alterations in the placental tissue glycocode related to maternal glucose metabolism affecting the course of pregnancy

E-PS-11-094
High-grade serous carcinoma arising from a bilateral micropapillary serous borderline tumour: a rare case of malignant transformation
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Background & Objectives: Serous borderline tumours (SBTs) of the ovary are non-invasive epithelial neoplasms with generally favourable outcomes. However, progression to high-grade serous carcinoma (HGSC) is extremely rare, especially following micropapillary variants. We present a unique case of HGSC developing three years after the initial diagnosis of bilateral micropapillary-type SBT with microinvasion.
Methods: A woman in her 60s underwent total hysterectomy and bilateral salpingo-oophorectomy for bilateral ovarian masses. Histopathological evaluation revealed bilateral micropapillary-type serous borderline tumours with microinvasion. The patient received adjuvant chemotherapy and was followed for a period. During follow-up, elevated CA-125 levels and ascites were noted, but she was later lost to follow-up. Three years after the initial diagnosis, she presented with abdominal distension and pain. Imaging revealed an omental "cake-like" appearance. Diagnostic laparoscopy and biopsy confirmed extensive infiltration of high-grade serous carcinoma.
Results: While the progression of SBTs to low-grade serous carcinoma is a recognized phenomenon, transformation into HGSC remains exceedingly uncommon and raises important questions regarding the pathogenesis and molecular evolution of these tumours. The micropapillary subtype and microinvasive foci in this case may represent early indicators of potential aggressive transformation.
Conclusion: This case highlights a rare but significant clinical course where a micropapillary serous borderline tumour with microinvasion progressed to high-grade serous carcinoma over a prolonged interval. It underscores the importance of long-term surveillance and consideration of the micropapillary pattern as a potential risk factor for malignant transformation.

E-PS-11-095
New rodent models of atypical implantation and placentation: cons and pros
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Background & Objectives: Elucidating pathogenesis of placenta accreta spectrum (PAS) is the key foundation for improving the pregnancy outcome of PAS patients clinically. Appropriate animal models could facilitate comprehensive research on the pathogenesis of PAS. We investigated the possible role of adipocyte clusters in uterine scar in PAS development.
Methods: In the right horn of the uterus of the Sprague-Dawley rats (n=10) was inserted a strip of autologous fat tissue. On the left horn, a full-thickness surgical incision of uterine wall was made and stitched (control). Three weeks after the operation, males were put in the cages with these females. The gross pathological and histopathological examination of implantation and placentation in both horns was carried out on the 16th day of pregnancy.
Results: In the right horn, 3-4 embryos have been found at the site of the incorporated adipose tissue in 7 cases. In the control left horn, no implantion was found at the incision site. The number of embryos in the right horn was significant higher than in the control left in all observations ($p<0.05$). The placenta of foetus implanted in adipose site were atypical and different from the normal placenta. Signs of

invasion of the foetal vessels in the metrial gland were detected in several observations.
Conclusion: Our developed rat model can be useful for research on pathogenesis of PAS and the effect of uterine scar adipocytes on PAS development or caesarean scar pregnancy.

Funding: The work was carried out within the framework of FSBSI. "Petrovsky National Research Centre of Surgery", 119991 Moscow, Russia, No. 123030700105-0 (FURG-2023-0046)

E-PS-11-096
Atypical polypoid adenomyoma: a diagnostic masquerader in young women with abnormal uterine bleeding
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Background & Objectives: Atypical polypoid adenomyoma (APA) is a rare benign uterine lesion composed of atypical endometrioid glands and fibromuscular stroma, often accompanied by squamous morules. It commonly affects women of reproductive age and may mimic atypical hyperplasia or low-grade endometrioid carcinoma on biopsy. This case series aims to emphasize the diagnostic challenges of APA and the importance of histopathological and immunohistochemical evaluation in avoiding overtreatment.
Methods: We retrospectively analysed three cases of APA diagnosed between 2022 and 2024. Clinicopathological features, radiological findings, and immunohistochemical profiles (ER, PR, p63, CD10) were reviewed. All cases were diagnosed on endometrial sampling and/or hysterectomy specimens.
Results: The first case involved a 49-year-old woman with abnormal uterine bleeding. Hysterectomy revealed a 0.8 cm APA in the myometrium, along with mucinous cystadenoma in the ovary and leiomyoma. The second and third cases were younger women (26 and 34 years) presenting with heavy bleeding. Endometrial curettage specimens revealed irregular, crowded endometrioid-type glands with squamous morules embedded in fibromuscular stroma, consistent with APA. All cases showed diffuse ER and PR positivity in both glands and stroma. p63 expression was confined to squamous morules, and CD10 highlighted the periglandular stromal component. None of the patients showed evidence of malignant transformation or recurrence during short-term follow-up.
Conclusion: APA poses significant diagnostic challenges, particularly on limited biopsy material where it can mimic premalignant lesions. Recognition of its characteristic morphology, supported by a focused immunohistochemical panel, is essential for appropriate diagnosis and management. This is especially important in reproductive-age women, where fertility preservation is a key consideration.

E-PS-11-097
Wrong hormonal status during hysterotomy can cause problems with uterine scar formation
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Background & Objectives: Preventing and treating caesarean scar defects is important task to decrease pregnancy complications. Animal models are an important tool for pre-clinical trials of methods and drugs aimed at the prevention and treatment of pregnancy complications. Our objective was to investigate how the sexual cycle phase during surgery affects the quality of healing after a thorough incision of the uterine wall.
Methods: Surgical incision (10 mm in length) were carried out on both uterine horns of Sprague-Dawley rats in different phases of estrous cycle: proestrus (n=5), estrous (n=5), metestrous (n=5) and diestrous (n=5). The incision on the right horn was stitched, but the incision on the left horn was left unsealed. On the 5th and 10th day after the operation, gross pathology and histopathology examinations were performed.
Results: By 5th day after surgery, the animals operated in the estrous phase had the damaged area covered with fat tissue on both sutured and unsutured horns. The wound space was filled by connective tissue. The operated rats in the diestrus had an unsealed incision of left horn and the incision of right horn wasn't covered with adipose tissue. By 10 days after the operation, the greatest delay in healing was observed in animals operated in the diestrous phase. The best healing was found in rats operated in the estrous phase. The attachment of adipose tissue to the damaged area was dependent from estrous phase in which was carried out the operation and correlated with healing quality. The parameters of the healing after the surgery in the metestrus and the proestrus were intermediate between the parameters for the estrus and the diestrus.

Conclusion: The level of sex hormones affects the healing of the uterine wound and the scar formation. The important role of visceral fat tissue in the healing efficiency of the uterine wound was discovered.

Funding: The work was carried out within the framework of FSBSI "Petrovsky National Research Centre of Surgery", 119991 Moscow, Russia, No. 123030700105-0 (FURG-2023-0046)

E-PS-11-098
Single nucleotide polymorphisms associated with cervical cancer susceptibility in Georgian women
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Background & Objectives: Cervical cancer (CC) is the third most common malignancy in women worldwide. Genome-wide-association studies (GWAS) have identified multiple single nucleotide polymorphisms (SNPs) that are associated with an increased risk of cervical cancer. In this study, we aimed to investigate the association between 13 SNPs and overall cervical cancer risk in Georgian population.
Methods: 50 patients diagnosed with cervical cancer and 50 healthy women had enrolled in this study. We genotyped 10 SNPs rs11263763, rs7726159, rs6897196, rs2853672, rs148261157, rs7579014, rs687289, rs635634, rs231775, rs2304204. These SNPs are described in association with different gynaecologic tumours and are mapped to cancer-related genes: HNF1B, TERT, BCL11A, ABO, CTLA4, IRF3. TaqMaq assays were used for the investigation.
Results: Our analysis, which utilised the GraphPad Prism 9.3.1 software package showed that there was a significant association of rs7579014 (BCL11A G/A), rs7726159 (TERT C/A) and rs687289 (ABO T/A) SNP risk genotypes with cervical cancer risk in Georgian population (p=0.02, p=0.04 and p=0.02, respectively). At the same time no significant association was found with other studied SNPs. Among them are CTLA4 and IRF polymorphysms, previously found to increase CC risk in other population groups.
Conclusion: These results are preliminary with a small sample size and relatively few SNPs analysed. However the tendency has been identified and it allows planning further investigations.

Funding: This study was supported by Shota Rustaveli National Science Foundation of Georgia (grant #FR-21-17599)

E-PS-12 E-Posters Haematopathology

E-PS-12-001
Primary Rosai Dorfman disease of bone: a case series
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Background & Objectives: Rosai Dorfman disease (RDD) is a histiocytic disorder which predominantly involves nodal sites with uncommon extranodal presentation. Primary osseous RDD is very rare and it is reported in 2-8% of cases. In this case series we are describing three cases of primary RDD in bone, in which the diagnosis has been confirmed by the novel marker cyclin D1.
Methods: NA
Results: Case 1 is a 16-year-old female who presented with right knee pain for 6 months with metaphysial lytic lesions in distal femur and proximal tibia on MRI. Case 2 is an 11-year-old male with a raised tender scalp lump for 1 year with well-defined lytic lesion is noted left occipital bone. Case 3 is a 14-year-old with a painful scalp lump for 3months. Radiologically, a lytic lesion is observed in the scalp occipital region. All three patients were previously healthy.
Histologically, sheets of large histiocytes with emperipolesis is noted in all three cases which showed S100 positivity along with diffuse strong nuclear Cyclin D1 positivity. Case 2 and 3 showed prominent sclerotic areas. Predominant plasma cell infiltration is seen in Case 1 while case 2 and 3 showed predominant neutrophil infiltration.
All three patients were treated with surgery and case 1 was initially treated with steroids. To date all three patients do not show evidence of extraoeesous RDD.
Conclusion: RDD should be considered as a differential diagnosis in bone lesions with inflammatory/histiocytic infiltrate or with fibrosis. Prominent stromal fibrosis in extranodal RDD can lead to misdiagnosis. Osteomyelitis, Langerhan cell histiocytosis and Erdhein Chester are differential diagnosis which cannot be reliably differentiated with S100. Therefore, Cyclin D1 is a useful marker in RDD.

E-PS-12-002
Primary cutaneous peripheral T-cell lymphoma with follicular helper T-cell phenotype: an indolent phase of a systemic disease?
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Background & Objectives: Primary cutaneous peripheral T-cell lymphoma with T-follicular helper cell phenotype (pcPTCL-TFH) is uncommon, and was proposed as a lymphoma subtype (M. Battistella, Arch Dermatol 2012). It's characterised by persistent skin disease without nodal involvement, although circulating cells and bone marrow involvement can occur. Recently, targeted mutational analyses have revealed overlapping profiles with primary nodal peripheral T-cell lymphoma with a T-follicular helper cell phenotype (nPTCL-TFH), raising questions about the classification of these cases.
Methods: We present a case of pcPTCL-TFH with overlapping genetic features and peripheral blood involvement, characteristic of nPTCL-TFH.
Results: An otherwise healthy 82-year-old woman presented with asymptomatic erythematous papulo-nodular lesions on extremities and face, showing an autoinvolutive and recurrent course for weeks. No constitutional syndrome, lymphadenopathies or visceromegaly were present. Histopathology revealed an atypical lymphohistiocytic infiltrate in the mid and deep dermis with granulomatous features, paired with an atypical lymphoid population of medium-sized cells with monocytoid appearance and plasma cells aggregates. Immunohistochemical studies showed a predominant T-cell component with TFH phenotype closely related to cellular aggregates expressing B-cell markers. Monoclonal expansions were confirmed for both the B (FR1/FR2/FR3) and T (TCRγ/TCRβ) cell components. The p.G17V mutation in the *RHOA* gene was also detected. Complete staging studies, including bone marrow biopsy, showed no nodal or visceral involvement. The diagnosis of PTCL-TFH with cutaneous involvement was made. NGS studies confirmed the same *RHOA* mutation an identified 3 *TET2* mutations and a *DNMT3A* mutation. A minimal population (0.11%) of atypical T-cells with surface CD3 loss and CD4+/PD1+/CD200+ in peripheral blood was detected. The patient was treated with CVP (cyclophosphamide, vincristine and prednisone) scheme, with no response, being alive with disease limited to the skin after 24 months of follow-up.
Conclusion: The present case raises the questions of how to classify and manage such lymphomas according to the current classifications and therapeutic tools.

E-PS-12-003
Littoral cell angioma: a surprising tumour of spleen
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Background & Objectives: Littoral cell angioma (LCA) is a rare, benign vascular neoplasm unique to the spleen, characterized by the proliferation of vascular channels exhibiting a hybrid endothelial-histiocytic phenotype. It is often discovered incidentally. This report presents a case of LCA and highlights its diagnostic challenges.
Methods: A 50-year-old male with a past history of right calf pain and a previously identified popliteal lymph node enlargement on MRI and ultrasound presented without current complaints. Subsequent MRI revealed a 45x36 mm splenic mass exhibiting no elevated FDG uptake on PET/CT.
Results: Macroscopic examination of the enlarged spleen (160 mm in diameter) revealed a solitary, well-circumscribed, blackish-brown lesion measuring 7.5×7×6.5 cm. The lesion displayed a spongy, haemorrhagic, and encapsulated appearance on cross-section. Microscopically, the lesion was located in the red pulp and comprised anastomosing, blood-filled vascular channels resembling hypertrophic splenic sinuses. These channels were lined by a single layer of plump or elongated endothelial cells with abundant eosinophilic cytoplasm, lacking cellular atypia or necrosis, and no mitotic figures were observed. Immunohistochemical analysis demonstrated positivity for CD31, CD68, and Langerin, and negativity for CD34, CD8, SMA, and HHV-8. The Ki-67 proliferation index was low. Finally, the diagnosis of LCA was made.
Conclusion: The differential diagnosis of LCA includes hemangiomatosis, hamartoma, angiosarcoma, lymphoma, sarcoidosis, splenic cyst, inflammatory pseudotumor, sclerosing angiomatoid nodular transformation, and metastasis. In this case, the microscopic features of the tumour, characterized by monolayer-lined vascular channels with plump, cuboidal or elongated cells lacking atypia, necrosis, or mitotic figures, along with the immunohistochemical profile (CD31+, CD68+, Langerin+), supported the diagnosis of LCA. Pathologists should consider rare splenic tumours and integrate macroscopic, histomorphologic, and immunohistochemical findings with clinicoradiologic data for accurate diagnosis.

E-PS-12-004
Light chain deposition disease: a series of diagnostically challenging cases
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Background & Objectives: Light chain deposition disease (LCDD) constitutes a rare disease defined by abnormal deposition of non-amyloid monoclonal chains in organs and tissues leading to their dysfunction. Despite the well-established renal involvement, reports of extrarenal manifestations are scarce. We present 3 cases of LCDD diagnosed at unexpected sites, aiming to underscore the need for clinicopathological vigilance.
Methods: We retrieved three cases of extrarenal LCDD from the archives of our Pathology Department over a period of 5 years (2020-2024) and reviewed the histochemical and immunohistochemical stained sections.
Results: Among 3 patients, 2 were female and 1 male. The male patient was a 65-year-old with known steatohepatitis, who underwent liver biopsy due to increased liver stiffness on elastography. The second case was a 46-year-old female with multiple subcutaneous nodules and papules and clinical suspicion of systemic autoimmune disease, who underwent skin punch biopsies. Finally, a female patient of 62 presented with dyspnea; PET/CT revealed a hypermetabolic nodule in the left upper lobe. Lung segmentectomy was performed. Histological examination in all cases revealed amorphous deposits, positive on PAS and Masson trichrome stains, and negative for Congo red stain. These were accompanied by histiocytic, lymphocytic and plasma cell infiltrates. Immunoreactivity to kappa light chains was established in two cases, whereas lambda depositions were identified in the case involving skin. Diagnosis of LCDD was set. No evidence of renal involvement was present. Bone-marrow biopsy was conducted in all patients, and plasma cell neoplasm was diagnosed in two.
Conclusion: LCDD is an underdiagnosed entity, usually unsuspected by clinicians, especially when it concerns unusual sites. Clinical and laboratory findings may be nonspecific, demanding a high level of awareness on part of the pathologists. Furthermore, the fact that LCDD may be the first manifestation of a plasma cell neoplasm or other lymphoproliferative disease emphasizes the crucial need for early diagnosis and treatment.

E-PS-12-005
Paediatric-type follicular lymphoma: case report
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Background & Objectives: Paediatric-type follicular lymphoma (PTLF) is a relatively rare neoplasm, first recognized as a distinct entity in the 2016 WHO classification. Despite its characteristic high-grade histology, it differs from that found in adults due to its clinical behaviour and excellent prognosis.
Methods: We report a case of PTFL diagnosed in a 5-year-old male patient with no significant medical history and B symptoms who was admitted to the Oro-maxillo-facial surgery department with a slowly growing and apparently unique lymph node developed in the right submandibular region. All preoperative laboratory tests were normal. The removed lymph node measuring 2.5 cm × 1.5 cm × 1.5 cm was sent for histopathology.
Results: The lymph node was completely processed, and microscopically, under low-power microscope, the lymph node structure was partially destroyed, replaced by follicles of variable size with regular contour, packed, closely arranged with attenuated/disappeared mantle zone. At high magnification, the follicles were composed of centrocyte-like cells mixed with centroblasts and with persistence of a starry sky appearance. These cells expressed CD20, PAX5, CD79a and CD10, BCL6, with a high Ki-67 index (60-70%). Bcl-2 and MUM1 were negative. CD23 and CD21 highlight the dendritic follicular cell network, IgD confirms attenuation of the mantle zone. The diagnosis of PTCL was developed based on clinical and paraclinical data, i.e. nodule architecture and immunophenotype of cells of follicular structures. For therapeutic management, pET-CT examination was performed, which revealed multiple lymph nodes less than 2 cm located laterocervically and submandibularly, without compression phenomena on surrounding structures.
Conclusion: Based on the above imaging and pathologic findings, the diagnosis of PTFL in this case requires molecular confirmation by immunoglobulin (IG) gene rearrangement. To avoid misdiagnosis, differential diagnosis plays a crucial role in clinical practice.

E-PS-12-006
Idiopathic multicentric Castleman disease in a tertiary hospital: a diagnostic challenge
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Background & Objectives: Multicentric Castleman disease (MCD) was first described in 1978 and is classified into subgroups based on aetiology: human herpesvirus 8 (HHV8)-associated, POEMS syndrome-associated, or idiopathic. Clinically, it is characterized by generalized lymphadenopathy, hepatosplenomegaly, renal dysfunction, and laboratory abnormalities such as hypergammaglobulinemia and elevated C-reactive protein.
Methods: This is a retrospective observational study of cases diagnosed as idiopathic multicentric Castleman disease (iMCD) by the Pathology Department of our institution between 2014 and 2024. The study exclusively included lymph node excision samples, excluding fine-needle biopsy specimens.
Results: Initially, nine cases of iMCD were identified; however, two were excluded after completing the clinical assessment, as they were found to be HHV8-associated in HIV-positive patients. The remaining seven cases included four males and three females, with a median age of 59 years. All cases met the major histopathological diagnostic criteria established by the NCCN Clinical Practice Guidelines in Oncology. Histopathological analysis revealed that 57.1% (4 cases) corresponded to the plasmacytic subtype, 28.6% (2 cases) to the hyaline-vascular subtype, and 14.3% (1 case) presented a mixed pattern.
Among all cases, six patients (85.7%) received anti-IL6 therapy with siltuximab. The only untreated patient died 42 days after diagnosis. Among the treated patients, one died (16.7% of treated cases), with the number of treatment cycles ranging from 6 to 52. In three cases, treatment was discontinued due to poor tolerance, two of whom had the hyaline-vascular histopathological subtype. Additionally, one patient showed no response after four treatment cycles and was subsequently diagnosed with progression to low-grade follicular lymphoma upon histological re-evaluation.
Conclusion: iMCD is a rare entity, often underdiagnosed due to its morphological variability and heterogeneous clinical presentation. Despite its uncertain aetiology, treatment with anti-IL6 siltuximab and the establishment of standardized histopathological diagnostic criteria have contributed to improved diagnostic accuracy and, consequently, better prognosis.

E-PS-12-007
Onions, Lollipops and HHV8: a recipe for Castleman disease, with a side of Kaposi Sarcoma in a HIV-negative patient
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Background & Objectives: Human Herpesvirus 8-associated Multicentric Castleman disease is a rare lymphoproliferative disorder characterized by recurrent episodes of systemic inflammation. Pathogenesis is driven by dysregulated cytokine activity, particularly human and viral interleukin 6. Additionally, these individuals have a significantly increased risk of developing concurrent Kaposi Sarcoma. Definitive diagnosis requires histopathologic confirmation through lymph node biopsy.
Methods: The patient was admitted to the Haematology Department of the Emergency City Hospital in Timisoara, Romania, presenting with fever, night sweats, palpitations, weight loss, and general deterioration. The symptoms had appeared approximately three months prior, with gradual progression. Clinical examination revealed bilateral lymphadenopathy in the cervical and inguinal regions. Laboratory tests showed elevated C-reactive protein, elevated IL-6, pancytopenia, hypergammaglobulinemia, hypoalbuminemia, hyponatremia, and HIV negative serology. CT imaging revealed generalized lymphadenopathy and splenomegaly. Further excisional biopsy of the inguinal lymphadenopathy was performed.
Results: Microscopic examination using Haematoxylin-eosin staining revealed a spindle cell proliferation with slit-like vascular spaces and moderate atypia. The remaining lymphoid tissue presented atrophic germinal centres, onion ring and lollipop follicular architecture, consisting of hyalinized penetrating vessels and thickened mantle zones. Additionally, hyperplastic follicles with plasma cell aggregates were observed. Immunohistochemical staining with the following antibodies: anti-HHV8, anti-CD34, anti-CD31, anti-D2-40, anti-Ki-67 was performed and the diagnosis of Human Herpesvirus 8 associated multicentric Castleman disease, concomitant with Kaposi sarcoma was established. The patient is currently undergoing oncological treatment.
Conclusion: Human Herpesvirus 8-associated Multicentric Castleman Disease is predominantly observed in HIV-positive patients, but there is evidence of its occurrence in HIV-negative individuals, presenting distinct epidemiological and pathological characteristics. Early and precise diagnosis is essential, as the disease can progress rapidly and may lead to severe or fatal outcomes.

E-PS-12-008
Lactylation in B-cell lymphomas: a novel epigenetic signature?
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Background & Objectives: Lactylation, a newly identified post-translational modification, introduces a novel layer to epigenetic regulation. Cancer cells often undergo metabolic reprogramming, like the Warburg effect, producing excess lactate. Lactate-driven lactylation can alter gene expression, promoting tumour growth. Here, we investigate lactylation-related genetic alterations in B-cell lymphomas.
Methods: Next-generation sequencing data from cBioPortal (5,245 samples, 5,139 patients across 17 studies) were analysed, covering both low-grade and aggressive B-cell lymphomas. We performed a literature review identifying 57 lactylation-related genes. After filtering for somatic mutations and queried gene profiles, we included 3,779 samples (3,752 patients). Further selection incorporating copy-number alterations (CNA) resulted in 170 samples (128 patients). Patients were grouped by genetic alterations; survival analysis (Kaplan-Meier) and Chi-square tests compared altered versus unaltered groups.
Results: *CREBBP* (10%), *SF3B1* (7%), and *EP300* (4%) were the most frequently altered genes. Including CNAs revealed additional alterations in *HDAC2, ABCF1, ATAD3A, LARS2,ALDOB*, and *H2AZ2* (3–4%), while SF3B1 alterations were 1.6%. Genetic alterations of lactylation-related genes across B-cell lymphomas, were detected in more than 40% of high-grade B-cell lymphomas, follicular lymphoma, and germinal centre B-cell-type diffuse large B-cell lymphoma (GCB-DLBCL); approximately 20% in activated B-cell-type DLBCL (ABC-DLBCL), Burkitt lymphoma, primary central nervous system DLBCL, chronic lymphocytic leukaemia (CLL), and marginal zone lymphoma; and less than 10% in mantle cell lymphoma. *CREBBP* and *SF3B1* mutations were mutually exclusive, while *EP300* alterations co-occurred with *CREBBP*. Initial survival analysis showed a non-significant benefit for lactylation-related alterations in aggressive lymphomas. However, the integration of mutations with CNAs revealed a statistically significant survival advantage in patients with alterations ($p=0.003$).
Conclusion: Our findings underscore lactylation's emerging role in regulating cancer-associated gene expression, potentially surpassing traditional DNA methylation. Integrating mutation and CNA analyses was essential for identifying clinically relevant alterations, especially in GCB-derived lymphomas. This study positions lactylation as a promising epigenetic-driver and therapeutic target in B-cell lymphomas.

E-PS-12-009
Intravascular lymphoma: a case series about a silent killer
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Background & Objectives: Intravascular lymphoma is a rare extranodal non-Hodgkin lymphoma with a poor prognosis. Its diagnosis is challenging due to its clinical presentation. Most reported cases are B-cell lymphomas, although T-cell variants have also been described. The estimated incidence is approximately 0.09 cases per million people. This study presents a clinicopathological review of nine patients diagnosed at our hospital over the past 20 years.
Methods: We conducted a retrospective review of patients diagnosed with intravascular lymphoma by biopsy or autopsy between 2004 and 2022. Nine patients met the inclusion criteria, and their clinical data, biopsies, immunohistochemical studies, and molecular analyses were reviewed.
Results: A biopsy confirmed the diagnosis in 78% of cases, while 22% were diagnosed postmortem. Fever of unknown origin (FUO) was the most common presentation (78%), followed by skin lesions (22%). All cases showed intravascular infiltration of large lymphocytes with vesicular nuclei, prominent nucleoli, and a discohesive growth pattern. Anaplastic and immunoblastic morphologies were observed in 11% each, while 78% had conventional morphology. Among FUO cases, 78% were classified as the classical subtype, and 22% as the cutaneous subtype.
Immunophenotyping showed that 78% expressed B-cell markers (CD20, CD79a), while 22% had a T-cell phenotype (CD30+, ALK-). Among B-cell cases, 40% were CD5+ and 60% CD5-. Germinal centre and non-germinal centre phenotypes were found in 43% and 57% of cases, respectively. Clonality studies (IGH and TCR) were performed in 44% of patients, detecting clonality in 22%.
All living patients received treatment; however, 72% died due to disease-related complications, while 28% remain alive.
Conclusion: Intravascular lymphoma is an aggressive neoplasm with an exclusive intravascular distribution, predominantly exhibiting a B-cell phenotype. It primarily affects elderly patients without gender predisposition. Its rarity and nonspecific clinical presentation make diagnosis complex, requiring close clinicopathological correlation.

E-PS-12-012

Sclerosing angiomatoid nodular transformation of spleen: case report in cancer staging

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Background & Objectives: Sclerosing angiomatoid nodular transformation (SANT) is a rare, benign vascular lesion of the spleen. It reveals itself morphologically and phenotypically as a nodular red pulp vascular proliferation surrounded by fibrous tissue.
The aim of this study is to report a case diagnosed in the context of a cancer staging process.
Methods: A 59-year-old female patient who underwent caudal pancreatectomy for a neuroendocrine tumour was admitted suspected of having splenic metastasis, eligible for total splenectomy.
Results: Gross findings revealed a firm, whitish subcapsular nodular spleen lesion measuring 1.5cm and demonstrating a stellate central scar. Histopathological examination showed angiomatoid nodules composed of slit-like, ectatic, and irregularly shaped vascular channels, surrounded by concentric layers of collagen and fibrinoid material, with red blood cells within and outside the lumina. The lesion centre was essentially fibrotic. Immunohistochemical analysis revealed a population of phenotypically variable blood vessels, including sinusoids (CD31 and CD8 positive), capillaries (CD31 and CD34 positive) and veins (CD31 positive).
Conclusion: According to the World Health Organization Classification of Tumours (5th ed.), SANT is often asymptomatic and mostly detected incidentally by imaging studies in middle-aged adults. The definition is a circumscribed lesion composed of multiple angiomatoid nodules containing blood vessels as seen in splenic red pulp, with intervening fibrosclerotic stroma. It has been suggested for the pathogenesis that a disruption of the local microcirculation could be caused by a fibrotic stromal proliferation, leading to transformation of red pulp into angiomatoid nodules. Molecular studies support either its reactive nature or the presence of a benign neoplasm. Although IgG4-related disease and EBV infection have been previously linked to this entity, they are not supported by current studies.
Since knowledge is limited, additional effort could be made to understand its nature and whether reactive or neoplastic processes are related to its origin.

Funding: Educorp - State University of Campinas

E-PS-12-014

Thyroid MALT Lymphoma with Extreme Plasmacytic Differentiation and Dense Fibrosis Mimicking IgG4-Related Disease

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Background & Objectives: Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) of the thyroid typically arises in the setting of chronic lymphocytic thyroiditis. This hematolymphoid neoplasm can show extensive plasmacytic differentiation. We present a case of thyroid MALT lymphoma with extreme plasmacytic differentiation and unusually dense fibrosis, mimicking IgG4-related disease of the thyroid gland. We discuss the morphologic features and immunohistochemical workup of this uncommon presentation of MALT lymphoma.
Methods: A 59-year-old female with longstanding Hashimoto's thyroiditis on thyroxine presented with a diffuse goiter and compressive symptoms. She underwent a total thyroidectomy, which revealed a large, multinodular thyroid.
Results: Gross examination of the thyroid gland revealed a firm, homogenously pale tan-whitish cut surface with vague lobularity. Histology revealed diffuse replacement of thyroid parenchyma by dense fibrosis and a dense plasma cell infiltrate. The degree of fibrosis was marked in some areas, mimicking IgG4-related disease of the thyroid gland. Residual atrophic thyroid follicles and focal lymphoepithelial lesions were identified. Despite the morphologic resemblance to IgG4-related disease of the thyroid gland, immunohistochemistry for IgG and IgG4 showed no increased IgG4-positive plasma cells or IgG4:IgG ratio. In-situ hybridization for kappa and lambda light chains demonstrated a monotypic, kappa-restricted plasma cell proliferation. Lymph nodes from both central neck compartments also exhibited kappa-restricted plasma cell aggregates, supporting disease involvement. Clinical, biochemical and radiological findings did not support multiple myeloma or plasmacytoma. The final diagnosis was thyroid MALT lymphoma with extensive plasmacytic differentiation.
Conclusion: We report an uncommon histomorphological appearance of thyroid MALT lymphoma mimicking IgG4-related disease of the thyroid gland. Judicious use of ancillary investigations including in-situ hybridization for immunoglobulin light chains is crucial to further interrogate thyroid specimens with dense plasmacytic infiltrate. Other lymphomas with plasmacytic differentiation should also be considered. Accurate diagnosis and classification are essential for treatment and prognostication.

E-PS-12-015

Composite nodal T-follicular helper cell lymphoma and marginal zone lymphoma – a case report of a rare disease

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Background & Objectives: Nodal T-follicular helper cell lymphoma (nTFHL) is a group of mature T-cell neoplasms comprising angioimmunoblastic-type, follicular-type and not otherwise specified (NOS), with their normal counterpart being TFH cells within lymphoid follicles. Generalised lymphadenopathy is the most common clinical presentation, but myriad features related to immune dysregulation can be seen. Histologically, this is reflected by the frequent presence of a prominent B-cell lymphoproliferative response and reactivation of Epstein-Barr Virus (EBV) within large B-immunoblasts. While the association between nTFHL and B-cell neoplasms has been widely documented, composite marginal zone lymphoma (MZL) occurring in nTFHL is rare. Here, we present a case of an 82-year-old female with metastatic lung adenocarcinoma who developed a right elbow soft tissue mass which was diagnosed as extranodal MZL. Following localised radiotherapy with radiological resolution of disease, she then developed multiple subcutaneous masses in the left arm and right thigh, including new hilar and lower paratracheal lymphadenopathy. Excision of a left arm lesion revealed a diagnosis of composite MZL and nTFHL-NOS. The mechanistic association between nTFHL and B-lymphoproliferations and the related diagnostic challenges are discussed.
Methods: N/A
Results: N/A
Conclusion: N/A

E-PS-12-016

Critical analysis and summary of the study on 10-colour flow cytometry in Multiple Myeloma (MM)

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Background & Objectives: This study aimed to evaluate the clinical utility of **10-colour flow cytometry** in identifying immunophenotypic aberrations in clonal plasma cells (cPCs) of multiple myeloma (MM) patients, with a focus on diagnostic and therapeutic monitoring applications.
Methods:

- **Gating Strategy:** Plasma cells were isolated using CD45/SSC (low CD45, moderate side scatter) and CD38/CD138 (high expression) markers.
- **Markers Analyzed:** Surface antigens (CD19, CD56, CD117, CD81, CD27) and cytoplasmic immunoglobulin light chains (cKappa/cLambda) were assessed in **118 MM patients** (pre- and post-treatment) and **40 healthy controls**.

Results: A clonal plasma cell population was identified in **99.2% of MM patients**, demonstrating high sensitivity for malignancy detection.**Immunophenotypic Aberrations in MM vs. Normal Plasma Cells:CD19**: Rarely expressed in MM (2.4% positive) compared to normal plasma cells.**CD56**: Overexpressed in **87.6% of MM cases** (aberrant marker of malignancy).**CD81**: Heterogeneous expression (58.3% ±).**CD117 and CD27**: Low positivity rates (17.6% and 22.6%, respectively), distinct from normal plasma cell profiles.

Conclusion: 10-colour flow cytometry effectively identifies cPCs, distinguishes malignant from normal plasma cells, and provides valuable insights for MM diagnosis and treatment monitoring.

E-PS-12-017
Mantle cell lymphoma in a 14-year-old patient with Nijmegen breakage syndrome: a rare case report
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Background & Objectives: Mantle cell lymphoma is a subtype of B-cell lymphoma that is relatively common in adults but extremely rare in the paediatric population. Nijmegen breakage syndrome is a genetic disorder associated with impaired DNA repair and a predisposition to malignancies, particularly lymphoproliferative diseases. We present a unique case of a paediatric Nijmegen breakage syndrome patient who developed two distinct lymphoproliferative disorders in the lungs: lymphomatoid granulomatosis, a rare but known complication in immunodeficient individuals, and mantle cell lymphoma, an entity almost unheard of in children. By presenting this case, we aim to highlight the possibility of MCL in the paediatric population and share our insights into the diagnostic process of such a rare case.
Methods: A 14-year-old female with a known diagnosis of Nijmegen breakage syndrome presented with cough and dyspnea. Chest X-ray revealed bilateral infiltrates. After excluding infectious and other non-malignant causes, a biopsy of the pulmonary lesions was performed. The final diagnosis was established through histopathological examination using H&E and Giemsa stains, a panel of immunohistochemical markers, fluorescence in situ hybridization, and molecular pathology techniques.
Results: Histopathological examination revealed two distinct morphological patterns: dispersed large cells (CD30+, CD20+, LMP+) in a T-cell-rich background with blood vessel wall infiltration, and dense infiltrates of small lymphocytes (CD20+, CD5+, cyclin D1+). Clonality of the lymphoid population was confirmed by multiplex PCR. The diagnosis of mantle cell lymphoma was further supported by fluorescence in situ hybridization, which detected the t(11;14)(q13;q32) IGH/CCND1 translocation. Next-generation sequencing using Archer VariantPlex and FusionPlex Lymphoma panels revealed no additional genetic abnormalities in the tumour.
Conclusion: The final diagnosis was a coexistence of mantle cell lymphoma and lymphomatoid granulomatosis in a paediatric patient with Nijmegen Breakage Syndrome. This case highlights the complexity of lymphoproliferative disorders in immunodeficient patients and reports the exceptionally rare occurrence of mantle cell lymphoma in a child.

E-PS-12-018
Myelofibrosis-induced erythropoietin-resistant anaemia due to renal osteodystrophy
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Background & Objectives: We present a case of myelofibrosis secondary to renal osteodystrophy caused by primary hyperparathyroidism (PHPT), a rare clinical entity. The pathogenesis involves prolonged stimulation of bone marrow stromal cells by elevated parathyroid hormone (PTH) levels, resulting in fibrosis and abnormal bone remodelling. PHPT, characterized by elevated PTH levels due to parathyroid adenoma or hyperplasia, can lead to haematological abnormalities such as pancytopenia, anaemia, and splenomegaly through collagen deposition in the bone marrow. Early detection and treatment are critical, as myelofibrosis may be reversible in some cases.
Methods: The patient's clinical history, laboratory findings, and imaging studies were systematically analysed. Myelofibrosis was confirmed via bone marrow biopsy. Imaging modalities, including MRI and CT, were utilized to identify the underlying cause of PHPT.
Results: A 19-year-old woman with end-stage renal disease on hemodialysis for 6 years presented with erythropoietin-resistant anaemia. Laboratory analyses revealed hypercalcemia and significantly elevated PTH levels. Imaging confirmed a parathyroid adenoma as the cause of PHPT. Parathyroidectomy resulted in significant improvement in laboratory parameters; however, the bone marrow fibrosis persisted during follow-up. Bone marrow biopsy revealed hypo-grade 3 nonuniform, patchy peritrabecular myelofibrosis with increased osteoclastic and osteoblastic activity. In the context of hyperparathyroidism resulting from long-standing chronic kidney disease and the absence of other underlying causes, the bone marrow findings were consistent with non-malignant myelofibrosis secondary to hyperparathyroidism and renal osteodystrophy.
Conclusion: Myelofibrosis secondary to PHPT is rarely documented, particularly in paediatric populations. This case highlights that PHPT can cause haematological complications, including erythropoietin-resistant anaemia, even in early life stages. Early detection and treatment are essential, as myelofibrosis may be reversible. PHPT should be considered in the differential diagnosis of myelofibrosis, especially in paediatric cases.

E-PS-12-019
Myeloid sarcoma, a diagnostic challenge: the experience of a tertiary hospital
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Background & Objectives: Myeloid sarcoma (MS) is a rare tumour with a highly variable immunophenotypic profile. Therefore, its differential diagnosis is wide and it is often misdiagnosed, especially in cases without known history of acute myeloid leukaemia (AML). The

aim of this study is to analyse these diagnostic difficulties, revising our collection of cases.
Methods: In the last ten years, 8 cases of MS have been diagnosed in our department, one of them without any available material left. A wide panel of immunohistochemistry was performed for all cases. Finally, clinical, histological and immunophenotypic characteristics have been compiled.
Results: In our case series, skin is the most often involved organ (20%), followed by lymphoid tissues, soft tissue, thyroid and gastrointestinal tract. Histologically, almost all cases showed diffuse architecture effacement by a dense proliferation of intermediate sized cells with irregular nuclear contours, occasional nucleoli and atypical mitoses. Immunohistochemically, all cases were positive for CD45, CD43, CD68, and Lysozyme. Almost all cases were positive for CD4 (87,5%), CD163 (85%), Myeloperoxidase (62,5%), and CD117 (62,5%). Meanwhile, CD34, CD7, CD56, and CD15 were less commonly positive (37,5%). Only one case showed co-expression of TdT and CD38. The rest of antibodies (CD20, CD79a, PAX-5, CD3, and CD8) were always negative. Clinically, only one of the eight cases had a prior diagnosis of AML.
Conclusion: MS is a rare disease with heterogeneous immunohistochemical characteristics. In our series, most of the cases lacked a previous diagnosis of AML, making the diagnosis even more challenging. Therefore, a broad differential diagnosis is essential. Our results highlight the importance of a wide and adequate immunohistochemistry study, which can be helpful in ruling out other entities, and reduce misdiagnoses caused by aberrant expression of B, T or NK-cell markers.

E-PS-12-020
Revisiting the classification of histiocytic and dendritic cell neoplasms: a retrospective review based on the 2022 WHO update
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Background & Objectives: Histiocytic and dendritic cell neoplasms represent a distinct and diverse group of tumours originating from monocytic or dendritic cell precursors. The WHO5 Classification of Hematolymphoid Tumours introduces a hierarchical classification structure. The aim of this study is to revisit the histiocytic and dendritic cell neoplasms diagnosed at a tertiary care centre to reclassify according to the most recent (2022) WHO classification.
Methods: We reviewed all hematolymphoid malignancies diagnosed according to the 4th edition of the WHO from 2015 to 2023 at our centre. The cases were then reclassified using the 2022 update of the WHO classification. Demographic data, including the site of involvement (nodal vs extra-nodal) was collected.
Results: Forty-nine (4.08%) were initially diagnosed as histiocytic/dendritic cell neoplasms according to the 4th edition of the WHO classification. Upon reclassification, these cases were divided into two groups: histiocytic/dendritic neoplasms (Group 1, n=38, 77.55%) and stroma-derived mesenchymal tumours (Group 2, n=11, 22.44%). Group 1 included Langerhans Cell Histiocytosis (LCH, n=27), Rosai-Dorfman Disease (RDD, n=6), Xanthogranuloma (n=3), Histiocytic Sarcoma (n=2), Plasmacytoid Dendritic Cell Neoplasm (n=1). Group 2 consisted of stroma-derived neoplasms of lymphoid tissues: Follicular Dendritic Cell Sarcoma (FDCS, n=8), Cytokeratin-positive Interstitial Reticulum Cell Sarcoma (CIRCS, n=2), Littoral Cell Angioma (n=1).
A majority of cases in both groups were extra-nodal (Group 1: 72%, Group 2: 80%). All cases in Group 2 were adult patients (mean-38 years), while most cases in Group 1 were paediatric (63.15%, mean-15 years). All Group 2 cases were male. Tumours involving the skin (n=13) and bone (n=6) were all classified in Group 1, while all gastrointestinal tumours (n=4) were classified in Group 2. Both CIRCS cases involved the gastrointestinal tract. At nodal site, RDD(n=6), LCH(n=4), and FDCS(n=2) were diagnosed.
Conclusion: Histiocytic and dendritic cell neoplasms represent a distinct and diverse group of tumours of extranodal site.

E-PS-12-021
Systemic chronic active Epstein-Barr virus disease: three case report
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Background & Objectives: Chronic active Epstein–Barr virus disease (CAEBV) is a rare condition characterized by persistent systemic inflammation and clonal proliferation of EBV-infected T or NK cells. It predominantly affects East Asian and indigenous Central and South American populations. Diagnosis requires four criteria to be met: mononucleosis-like symptoms lasting over three months, EBV-DNA viral load >10,000 IU/mL, EBV-infected T/NK-cell infiltration in peripheral blood or tissues, and exclusion of known immunodeficiency, autoimmune disorders or malignancies.
Methods: A retrospective review of three CAEBV cases analysed age, sex, origin, affected organs, EBV copy number, T/NK lymphocyte infection, progression to lymphoma/leukaemia, and survival time.
Results: The median age was 22 years. All patients were men, one from Africa and two from South America. Liver involvement was present in all, while two had bone marrow and lung involvement. One patient had an end-stage chronic kidney disease, which made the therapeutic approach very challenging. This patient suffered from a digestive bleeding and died. Autopsy also revealed multiple organ involvement by CD3- expressing lymphocytes along with EBV RNAs detected by in situ hybridization. Another patient developed EBV-associated T/NK-cell lymphoma/leukaemia (with ARID1A and STAT3 mutations), and another developed EBV+ T-cell lymphoma (withDDX3X and STAT3 mutations). Interestingly, different mutations of unknownsignificance in SETD2 gene were detected in two cases of CAEBV. The median survival time was 24 months. Allogeneic Stem Cell Transplantation is considered the only curative option; however, none of our patients was able to receive it.
Conclusion: CAEBV, which follows a variable course, often leading to hematologic malignancies, should be suspected in Asian and Central American patients with persistent fever, systemic symptoms, and positive EBV serology. This study underscores the importance of early diagnosis and further research into disease progression and treatment. Untreated, CAEBV disease carries a high mortality rate. However, determining the optimal time to start treatment remains a challenge.

E-PS-12-022
Gaucher's disease-case report
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Background & Objectives: Gaucher disease is a lysosomal storage disease caused by genetic mutations in GBA gene. The main characteristic is a deficiency of the enzyme ß-glucocerebrosidase. The consequence of the deficit of the enzyme is the accumulation of

glucocerebroside in macrophages which becomes specific cells-Gaucher cells which infiltrate bone marrow, liver, spleen and lymph nodes.
Methods: Histopathological diagnoses imply the detection of Gaucher cells-large lipid-laden macrophages, sized 20-100μm. Cytoplasm is pale, "wrinkled tissue paper" like and nucleus is small eccentrically placed. Diagnosis is confirmed according to clinical symptoms, laboratory findings, bone marrow biopsy and genetic testing.
Results: We have received a mail patient aged 35 years with the clinical symptoms of hepatosplenomegaly, pancytopenia and osteopenia. Bone marrow biopsy reveals clustered and dispersed large macrophages with pale, "wrinkled tissue paper" cytoplasm and small eccentrically placed nucleus, which account about 40-50% of bone marrow cellularity. Immunohistochemistry was positive in CD68, CD163, Lysozome, HLADR, Fascin (week), CD14 (week). The main differential diagnoses in bone marrow consider Niemann-Pick disease, sea-blue histiocytosis, leukaemia or myelodysplastic syndromes. Genetic analysis was positive and indicated to type 1 with the mutation in CYP2D6 gene with phenotypic intermediate metabolizer activity.
Conclusion: The prompt and correct diagnoses is essential considering the treatment for those diseases is a different and for some types of Gaucher disease there is adequate treatment if we start on time.

E-PS-12-023
MALT lymphoma of the dura: a report of two cases with emphasis on histopathological features
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Background & Objectives: Primary dural lymphoma is a rare type of primary central nervous system lymphoma that often mimics meningioma or other dural-based lesions on imaging. Most cases are extranodal marginal zone lymphomas. We report two cases of primary dural MALT lymphoma with distinct histopathological features.
Methods: Two female patients, 60 and 48 years old, presented with neurological symptoms - facial hypoesthesia and upper lip ptosis in the former, and persistent bilateral headache in the latter. MRI imaging revealed dural-based extra-axial lesions, leading to craniotomy followed by surgical resection.
Results: Histopathology in both cases showed a diffuse infiltration of sclerotic meningeal tissue by small lymphoid cells with round to irregular nuclei, some exhibiting monocytic morphology and a subset demonstrating plasmacytic differentiation. There were also some regressive and colonized lymphoid follicles. Immunohistochemistry confirmed CD20 and BCL2 positivity, with CD10, CD5, CD3, CD23, and cyclin D1 negativity; plasma cells with monotypic light chain expression were identified. The first case exhibited scattered intermediate to large atypical cells with vesicular chromatin, not forming sheets, and the proliferation index (Ki-67) varied between 20% and 60% (vs. 10% in the other case). Systemic involvement was ruled out and a diagnosis of MALT lymphoma of the dura was rendered.
Conclusion: MALT lymphoma of the dura may exhibit significant histopathological variability, often posing diagnostic challenges, particularly with diffuse large B-cell lymphoma. While scattered large lymphoid cells may be present, this does not significantly impact prognosis or treatment response. Both patients achieved stable disease following treatment - rituximab plus radiotherapy in the first case and rituximab alone in the latter.

E-PS-12-024
Chronic myeloid leukaemia blast phase with concurrent t(9;22) and inv(16): a rare case of clonal evolution
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Background & Objectives: Chronic myeloid leukaemia (CML) is characterized by the t(9;22)(q34.1;q11.2) translocation, resulting in the Philadelphia (Ph) chromosome and BCR::ABL1 fusion gene. Progression to blast phase (CML-BP) is often associated with additional cytogenetic abnormalities such as extra Ph chromosome, trisomy 8, isochromosome 17q, or trisomy 19. Rarely, CML-BP acquires aberrations commonly seen in de novo acute myeloid leukaemia (AML), including t(8;21), t(15;17), and inv(16)/t(16;16). The coexistence of Ph and inv(16) in CML is extremely rare, with few reported cases.
Methods: We present a 31-year-old Portuguese-speaking male with no significant past medical history who presented with fever, gastrointestinal symptoms, and massive splenomegaly.
Results: Laboratory studies revealed hyperleukocytosis and thrombocytosis. Peripheral blood flow cytometry demonstrated left-shifted myeloid maturation with 19.4% CD34+ myeloblasts. Bone marrow biopsy showed marked hypercellularity (98%) with granulocytic hyperplasia, eosinophilia, and 10% blasts by CD34 immunostaining, while differential count of aspirate smears revealed approximately 13% blasts. The variation in blast percentages may reflect sampling differences and the effects of hydroxyurea. FISH of peripheral blood was positive for BCR::ABL1 fusion gene, specifically the p210 transcript. Bone marrow karyotyping revealed 46,XY,t(9;22)(q34.1;q11.2)[6]/46,idem,inv(16)(p13.1q22)[14], consistent with CML-BP with rare clonal evolution involving inv(16). Molecular genetic testing on bone marrow was negative for FLT3 and c-KIT mutations.
Conclusion: De novo AML with inv(16) is associated with a favourable prognosis, however older age and FLT3 and KIT mutations are associated with a worse outcome. Inv(16) presence in CML-BP typically portends an aggressive clinical course marked by rapid progression and treatment resistance. Most reported cases have resulted in poor outcomes, underscoring the need for novel therapeutic strategies and vigilant disease monitoring. This case highlights the rare coexistence of acquired (Ph chromosome) and secondary chromosomal abnormalities (inv(16)) in CML-BP. Recognizing such combinations is crucial for understanding disease biology, guiding prognosis, and tailoring treatment, especially in distinguishing these cases from conventional CML-BP.

E-PS-12-025
A case of occult mastocytosis
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Background & Objectives: Systemic mastocytosis (SM) is characterised by the extracutaneous infiltration of morphologically and/or immunophenotypically aberrant mast cells (MCs) into at least one organ system, usually involving the bone marrow (BM). The condition is primarily driven by a somatic gain-of-function mutation in *KIT* and presents with a broad clinical spectrum.
Methods: Histology, immunohistochemistry and molecular pathology were performed.
Results: We report the case of a 61-year-old female patient who presented to the Department of Haematology for further clarification of an IgA lambda paraprotein found in routine examinations. BM biopsy revealed a discrete infiltration of lambda monotypic plasma cells with concomitant CD56 expression and scattered MCs with an aberrant immunophenotype (partial CD25 and CD2 expression) and 40% spindle cell morphology, comprising approximately 5% of the BM cellularity. The patient's history included eosinophilic colitis with intestinal cramps, food intolerance and episodes of flushing symptoms following alcohol consumption, raising the suspicion of intestinal involvement by SM. Colonoscopy showed several flat, white-yellowish lesions with prominent infiltrates of eosinophilic granulocytes and dense aggregates of atypical MCs. Further testing revealed slightly elevated tryptase levels and evidence of a *KIT*

D816V mutation, establishing the diagnosis of SM with an associated haematological neoplasm (SM-AHN, WHO 2022). Given her stable general condition, treatment with famotidine and desloratadine was initiated and clinically followed. Laboratory tests showed slightly persistent elevated tryptase, IgA levels and IgA lambda paraprotein.
Conclusion: To our knowledge, plasma cell disorders associated with SM are rare, leading to the diagnosis of a SM-AHN of non-myeloid lineage. The discrete MC infiltration of the BM with simultaneous extensive intestinal involvement is another unusual finding. Thus, the presence of prominent eosinophilic infiltrates on endoscopic biopsies should raise the suspicion of occult SM, especially in patients with peripheral eosinophilia and concomitant haematological abnormalities.

E-PS-12-026
EBV-positive mucocutaneous ulcer: a comparison of histological and clinical findings of four cases from Istanbul University-Cerrahpasa with the literature
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Background & Objectives: EBV-positive mucocutaneous ulcer (EBV-MCU) is a rare, recently described entity associated with immunodeficiency and immune dysregulation. It primarily affects the elderly due to immunosenescence but is also common in patients receiving immunosuppressive therapy. Microscopically, it presents with polymorphic infiltration and Reed-Sternberg-like cells, making differentiation from other EBV-positive lymphoproliferative (EBV-LP) diseases challenging.
Methods: Four EBV-MCU cases (2016–2024) from the Pathology Department archive of Istanbul University-Cerrahpasa were reviewed. H&E slides, IHC, and EBER in situ hybridization analyses were performed. 26 papers total of 235 cases (2010–2025) were reviewed for comparison.
Results: The mean age of the patients was 48 years (16, 43, 47, 78). Two were female, and two were male. Three lesions were located in the oral cavity, while one was in the anal canal. The youngest patient had systemic lupus erythematosus and was under immunosuppressive therapy, whereas the 78-year-old patient's condition was likely due to immunosenescence.
Microscopic examination revealed ulcer bases with heterogeneous inflammatory infiltrates. Atypical large cells were CD30-positive (4/4), CD20-positive (2/4), PAX5-positive (2/2), and MUM1-positive (2/2). EBER was positive in all cases. CD3-positive band-like T cell infiltration limiting the infiltration was present (4/4). The Ki-67 proliferative index was 10–25% in three patients and over 50% in one.
Compared to the literature (mean age: 67.3 years), our series had a younger mean age due to the inclusion of a paediatric case, which is rare. Only nine paediatric EBV-MCU cases have been reported. Despite this, none of our cases were HIV-positive. In contrast, the literature reports six HIV-positive cases, five of whom were under 60.
Conclusion: EBV-MCU is a benign disease that can resolve spontaneously or with immunosuppressive drug cessation. Misdiagnosis may lead to overtreatment, especially in immunosuppressed patients. Pathologists should recognize this entity when evaluating EBV-LP cases.

E-PS-12-027
Next-Generation Sequencing study of low grade B lymphomas after one year of implementation: usefulness as a diagnostic, prognostic and therapeutic tool
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Background & Objectives: The incorporation of Next-Generation Sequencing (NGS) in the study of lymphomas represents an advancement in their diagnosis and management. This innovative approach provides a detailed analysis of each patient's genetic profile, facilitating essential information for precise diagnosis, particularly in low grade lymphomas, personalized treatment, and identification of markers that can be monitored in liquid biopsy studies of minimal residual disease, ultimately improving the clinical outcomes. In 2024, this technique was implemented in our department, in collaboration with the Haematology Department.
Methods: NGS was performed in 16 paraffin-embedded low grade lymphomas: 5 marginal zone lymphomas, 5 follicular lymphomas, 5 small lymphocytic lymphomas and 1 mantle cell lymphoma. The NGS panel used was developed by the international Liverpool Lymphoid Network consortium (ThermoFisher Scientific), and based on amplicon technology that includes 60 relevant genes to both B and T lymphomas. In parallel, one case was analysed in peripheral blood.
Results: Out of the 16 samples, 15 were informative. Mutations were found in 87.6% of the cases. In 84.6% of them, mutations with prognostic utility were identified, in 46.2% had diagnostic utility and in 7.7% were useful for selecting targeted therapy.
In two cases, the technique was essential to support the diagnosis of marginal zone lymphoma over other types. In one patient with Richter's syndrome, clonal evolution between sequential biopsies was demonstrated, and in the case where both paraffin and liquid biopsy samples from the same patient were analysed, the same mutation was detected.
Conclusion: NGS in lymphomas is a useful tool for identifying diagnostic and prognostic biomarkers, as well as mutations related to resistance to targeted therapy, influencing therapeutic decisions and patient monitoring.
The collaboration between the Departments of Pathology and Haematology, has facilitated the implementation of NGS in lymphomas in our hospital, presenting it as an option to consider for implementation in other centres.

E-PS-12-028
Diagnostic challenges in HHV8 positive diffuse large B-cell lymphoma: a case report
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Background & Objectives: HHV8-positive diffuse large B-cell Lymphoma (DLBCL) is a rare and aggressive subtype of lymphoma caracterized by a monoclonal proliferation of HHV8 infected lymphoid cells that resemble plasmablasts. Its diagnosis can be challenging due to its overlap with other hematologic malignancies particularly with plasmablastic features. We report this case to highlight the diagnostic difficulties associated with HHV8-positive DLBCL and to emphasize the importance of considering this diagnosis in patients presenting with necrotic lymphadenopathy.
Methods: A 66-year-old male presented with cervical lymphadenopathy that had progressively enlarged over the course of one year. A first biopsy was performed.
Results: This biopsy showed large lymphoid cells with a plasmacytoid appearance and nuclear debris. A wide panel of antibodies was used, and the diagnosis of Kikuchi necrotizing lymphadenitis in its pseudotumoral form was made. Corticosteroid treatment was initiated and we noted further enlargement of lymph nodes. A second biopsy of the cervical lymph node was performed and processed in our laboratory. Histological analysis revealed sheets or confluent clusters of large

atypical cells with plasmablastic morphology with effacement of the lymph node normal architecture. Mitotic activity was high. Immunohistochemical analysis revealed positive staining for EMA, MUM1, and HHV8, while the tumour cells were negative for CD3, CD20, CD138, CD30, PAX5, and OCT2. These findings were consistent with a diagnosis of HHV8-positive DLBCL.
Conclusion: HHV8-positive DLBCL can present significant diagnostic challenges. Plasmablastic lymphoma and other histologically similar entities, including plasmablastic myeloma and reactive plasmacytic proliferations, must be considered in the differential diagnosis. The combination of clinical presentation, histological findings, immunohistochemistry, and HHV-8 detection is critical for accurate diagnosis.

E-PS-12-029
A rare case of intestinal T-cell lymphoma masquerading as B-cell lymphoma: a diagnostic pitfall
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Background & Objectives: Enteropathy-associated T-cell lymphoma (EATL) is a rare, aggressive malignancy originating from intraepithelial T cells in patients with celiac disease, most commonly affecting the small intestine. It often presents with gastrointestinal symptoms and has a poor prognosis. In some cases, its morphology can resemble B-cell lymphomas, leading to potential misclassification without detailed immunophenotypic analysis.
Methods: We report the case of a patient who presented with acute abdominal pain and peritonitis, requiring an enterectomy. Histopathological examination revealed a massive transmural lymphocytic proliferation, infiltrating the intestinal wall and extending through the serosa into the mesentery. The tumour was composed of small mononucleated cells with scant clear cytoplasm, indented centrocytic nuclei, and scattered larger cells with centroblastic, immunoblastic, plasmacytoid, and monocytoid morphology. Based on these findings, an initial diagnosis of extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) was considered, pending immunohistochemical confirmation.
Results: Immunohistochemistry showed strong positivity for CD79a, but the absence of CD20, PAX5 and CD19 argues against a B-cell lineage, which contradicts the initial suspicion of MALT lymphoma. The strong positivity for CD3 and CD7, combined with CD2 negativity, suggests a T-cell neoplasm. The lack of BCL6 and MUM1 expression argues against a germinal centre or activated B-cell phenotype, while Cyclin D1 negativity excludes mantle cell lymphoma.
The immunohistochemistry results indicate a T-cell lymphoma, ruling out the initial diagnosis of MALT lymphoma. The absence of B-cell markers (CD20, PAX5, CD19) and the strong expression of T-cell and cytotoxic markers support the reclassification as Enteropathy-associated T-cell lymphoma.
Conclusion: This case highlights the importance of recognizing T-cell lymphoma, such as EATL, as a diagnostic consideration in gastrointestinal tumours with atypical morphology.
The initial misclassification as a B-cell lymphoma underscores the need for comprehensive immunohistochemical analysis that was crucial in establishing the correct diagnosis and guiding appropriate management.

E-PS-12-030
Cutaneous clues to a hidden malignancy: CD10-positive Hairy cell leukaemia presenting with Sweet syndrome
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Background & Objectives: Hairy cell leukaemia (HCL) is a rare indolent B-cell neoplasm that may trigger systemic inflammatory responses; however, its association with Sweet syndrome (SS) is rare and underrecognized. SS, an acute febrile neutrophilic dermatosis, may occur idiopathically or as a paraneoplastic manifestation, particularly in hematologic malignancies.
Methods: A 33-year-old woman with history of anxiety and endometriosis, chronic fatigue and drenching night sweats for one year presented with one-month history of painful, erythematous plaques and papules on the extremities, fever and severe arthralgia. Laboratory studies revealed microcytic hypochromic anaemia, leukopenia with absolute neutropenia, monocytopenia, and markedly elevated inflammatory markers, with normal liver and renal function. Autoimmune and infectious serologies, including ANA, hepatitis C, and HIV, were negative. CT imaging showed necrotic hilar and mediastinal lymphadenopathy and mild splenomegaly, raising concern for malignancy.
Results: Skin biopsy demonstrated a dense neutrophilic dermal infiltrate with suppurative liquefactive necrosis, consistent with Sweet syndrome. Peripheral blood smear revealed rare lymphoid cells with abundant cytoplasm and fine, circumferential villous projections, raising suspicion for HCL. Bone marrow flow cytometry identified monotypic CD20+ B-lymphocytes lambda light chain restricted, co-expressing CD11c, CD25, CD103 (subset), and CD10 (subset). Bone marrow biopsy and immunohistochemistry showed normocellular marrow (70%) with interstitial infiltration by CD20-positive/CD79a-positve B-lymphocytes with abundant cytoplasm (80% of marrow), CD10-positive (subset), negative for Cyclin-D1, LEF-1 and SOX-11. PCR detected BRAF V600E mutation, confirming the diagnosis. Although CD10 expression is uncommon in HCL, reported cases demonstrate similar morphological features to CD10-negative HCL. CD10-positive HCL may be associated with unfavourable prognosis.
Conclusion: This case underscores the importance of recognizing SS as a potential early or residual marker of hematologic malignancy. Recognition of atypical cutaneous findings in the context of systemic inflammation is critical for guiding timely hematopathologic evaluation. Recognizing the dermatologic signatures of hematologic disease may enable timely diagnosis and intervention, ultimately improving patient outcome.

E-PS-12-031
The importance of bone marrow biopsy in the diagnosis of splenic lymphoma
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Background & Objectives: Splenic lymphomas are rare B-cell malignancies involving the spleen and bone marrow. Bone marrow biopsy plays a crucial role in diagnosis, as splenectomy may not be available for every case.
Methods: Between 2010 and 2024, 56 cases of splenic lymphomas (splenic marginal zone lymphoma,red pulp lymphoma(hairy cell leukemia,splenic diffuse red pulp small B-cell lymphoma), mantle cell lymphoma)bone marrow biopsies have been reviewed based on their clinical and pathological data from Istanbul University-Cerrahpasa.
Results: The study included 33 male and 24 female patients (mean age:65, range 40–86). Splenomegaly was reported in 51 cases (140–290 mm). Twelve had B symptoms, and 20 had lymphadenopathy. Thrombocytopenia was observed in 35 cases, anaemia in 38, leukopenia in 15, pancytopenia in 9, and leukocytosis in 17. Paraproteinemia was detected in 6 patients.
Flow cytometry showed CD5 negativity in 15/19 cases, CD20 positivity in 17/17, and CD23 positivity in 9/15. Bone marrow cellularity ranged from 30% to 100%; 43 cases were hypercellular, and 12 were

normocellular for age. The marrow infiltration pattern was interstitial in 40 cases, nodular in 37 (9 paranodular/7 internodular), and intrasinusoidal in 34.
Reticulin fibrosis was grade 0 in 16 cases, grade I in 12, grade I–II in 14, grade II in 7, and grade II–III in 5. Morphologically, cells were mature in 47/48 cases; 6 also had medium-sized cells, and 1 had only medium-sized cells.
Splenectomy was performed in 27 cases (20 SMZL, 5 RPL, 2 MCL), with bone marrow biopsy diagnosing 11/20SMZL, 2/5 RPL, and 2/2 MCL cases. Although splenic lymphoma was suggested in the bone marrow of 12/27 cases, splenectomy was required for diagnosis. A correct diagnosis was obtained from bone marrow in 15 cases.
Conclusion: Splenic lymphomas often involve the bone marrow with diverse infiltration patterns, cell morphologies, and immunohistochemical profiles, making it a key diagnostic tool.

E-PS-12-032
Mastocytosis: morphological and immunohistochemical examination
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Background & Objectives: The term "mastocytosis" encompasses a group of rare diseases characterized by tumorigenic proliferation of clonal mast cells (MCs) and infiltration of one or more organs. Mastocytosis is separated from the group of myeloproliferative disorders as a nosological entity in the 5th edition of the WHO. Cutaneous mastocytosis (CM) usually manifests during the first year of life. Systemic mastocytosis (SM) is a group of hematologic oncohematologic diseases based on proliferation of tumour-associated mast cells (MCs) with involvement of one or more organs. Bone marrow (BM) trepanobiopsy is a mandatory examination in newly diagnosed mastocytosis, regardless of its form. The criterion for diagnosis is the formation of multifocal accumulations of MC in the BM (more than 15 cells) and/or in organs other than the skin. Other criteria for mastocytosis include the presence of a mutation in codon 816 of the KIT gene, elevated serum tryptase levels above 20 ng/mL, and aberrant expression of CD2 and/or CD25 by immunochistochemistry (IHC).
Clinical and morphologic analysis of patients with different forms of mastocytosis from viewpoint of modern classification (WHO, 2024).
Methods: Mastocytosis cases diagnosed in 2021-2024 were retrospectively analysed using histological and immunohistochemical methods with determination of CD117, CD25 expression based on data from the database of the Pathological anatomy department of the Clinical Institute ("MONIKI").
Results: Mastocytosis was diagnosed in 16 patients, age range 2.9 - 74 years, median age - 46 years, female:male ratio= 1.8:1. In all cases, mastocytosis was associated with cutaneous manifestations. Systemic mastocytosis was diagnosed in 7/16 patients by bone marrow trephine biopsy including IHC. As of 01.01.2025, all patients are alive.
Conclusion: Most patients with CM remain in an indolent stage for many years. However, in our population, in 44% cases SM was found with aggressive course. That's why bone marrow biopsy with IHC and molecular analysis is necessary for all patients.

E-PS-12-033
Histopathological and immunohistochemical features of inguinal region lymphomas: a singlecentre experience
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Background & Objectives: Lymph nodes located in the inguinal region are among the most important components of the lymphatic system and can be sites of either primary or secondary lymphoma involvement. The most common type observed is follicular lymphoma (FL), followed by diffuse large B-cell lymphoma (DLBCL), Hodgkin lymphoma (HL), and mantle cell lymphoma (MCL). Lymph nodes in the inguinal region, particularly those previously affected by inflammatory processes, may exhibit architectural alterations, leading to diagnostic challenges.
This study aims to clarify whether inguinal lymphoma cases differ from those in other regions, as well as to define their morphology and immunophenotype.
Methods: The clinical and demographic characteristics, as well as the histopathological, immunohistochemical, and genetic features, of 18 lymphoma cases diagnosed from inguinal lymph node excision materials in our department between 2020 and 2024 were recorded.
Results: Among the cases, 50% (9 cases) werediagnosed with follicular lymphoma (FL), 44.4% (8 cases) with diffuse large B-cell lymphoma (DLBCL), and 5.5% (1 case) with Hodgkin lymphoma (HL). Bcl-6 gene rearrangement detected in 4 of theDLBCL cases. CD23 positivity was observed in 2 Grade 2 FL cases, whereas none of the DLBCL casesexhibited CD23 positivity.
The gender distribution, age range, and frequency of histopathological subtypes in our cases were found tobe consistent with the literature. However, differingfrom previous reports, CD23 positivity, which is commonly observed in Grade 1 follicularlymphomas, was detected in Grade 2 cases in ourstudy.
Conclusion: Follicular lymphomas exhibiting CD23 positivityremain a subject of debate in the literature. Theclinical significance of this finding has not yet beenclearly established and requires further studies forvalidation.

E-PS-12-034
Clinicopathological characteristics of plasmablastic lymphoma: a retrospective single-centre analysis
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Background & Objectives: Plasmablastic lymphoma (PBL) is a rare and aggressive large B-cell lymphoma, typically associated with immunosuppression, particularly HIV. However, increasing evidence suggests its occurrence in immunocompetent individuals as well. This study aims to characterize the clinicopathological and immunophenotypic features, treatment responses, and survival outcomes.
Methods: A retrospective review was conducted on 66 patients diagnosed with PBL at a single tertiary centre between 2006 and 2024. Demographic, clinical, pathological, and laboratory data were analysed. Immunohistochemical markers, HIV status, and survival data were evaluated.
Results: The median age was 65 years (range: 19–95), with a male predominance (69.7%). The most common tumour sites were bone and soft tissue (n=14), head and neck (n=13), and nodal regions (n=13). Other affected sites included the gastrointestinal tract (n=11), medullary region (n=7), spleen (n=4), and testis (n=3), with one case involving renal involvement. Immunohistochemistry showed frequent expression of CD138 (80.7%), MUM1 (91.5%), and CD38 (76.9%), while CD20 was negative in 88.9% of cases. MYC and EBER positivity were seen in 62.5% and 61.7%, respectively. Only 10% of 20 tested patients were HIV-positive. Bone marrow involvement was seen in 28.6%, and 54.5% were diagnosed at clinical stage IV. High Ki-67 proliferation index (mean 74.3%) and elevated LDH levels (mean 1229 IU/L) reflected aggressive disease. Despite

treatment in 76.2% of cases, the objective response rate was only 20%. The median survival time was 26.2 months.
Conclusion: In conclusion, PBL demonstrates a highly aggressive clinical course with poor response to conventional therapies. Although commonly linked to immunodeficiency, our data emphasize that a significant proportion of PBL cases arise in immunocompetent individuals. High proliferative index, MYC and EBER expression, and frequent extranodal involvement reflect the unique biology of PBL and underscore the urgent need for improved therapeutic strategies.

E-PS-12-035
Nodular lymphocyte predominant Hodgkin lymphoma: a clinicopathologic appraisal based on a single institution experience of North India
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Background & Objectives: Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) is a rare indolent lymphoma traditionally considered a subtype of Hodgkin lymphoma, accounting for <5% of Hodgkin lymphoma with an incidence of approximately 0.1-0.2/100.000/year, even lesser in Asia. NLPHL however differs from Classic Hodgkin lymphoma (CHL) with the tumour cells expressing B-cell antigens and hence, is now regarded as a B-cell lymphoma. Most patients present with early-stage disease and display an excellent prognosis.
Objective: To chronicle the clinic-pathological profile of NLPHLs diagnosed and treated at our centre.
Methods: All cases diagnosed as NLPHL over a period of 5 years at a tertiary cancer centre were explored. The relevant clinical details and survival data were obtained from hospital electronic medical records and analysed.
Results: Of the 36 patients included in the study, the median age of presentation was 45 years with 3 patients (8.33%) less than 18 years of age. age. Male to female ratio was 2.27:1, with predominant nodal presentation except one. Clinical stage of the patients was as such: Stage I (19.4%), Stage II (27.7%), Stage III (27.7%), and Stage IV (25%). Bone marrow was involved in a single case. The closest differential was CHL, with immunohistochemistry markers such as CD20, PAX5, and LCA proving handy in accurately diagnosing NLPHL. On a median follow-up of 18 months (1-58 months), 5 patients expired and the 3-year overall survival rate was 79.1±8.7%.
Conclusion: NLPHL has varied histological patterns with close differentials like Lymphocyte-rich CHL, T-cell/histiocyte-rich large B cell lymphoma, EBV-positive Diffuse large B cell lymphoma, and Progressive transformation of germinal centres. The chemotherapeutic regimen for NLPHL is different and has a more favourable prognosis than its mimickers. Therein lies the significance of histopathological and immunohistochemical expertise, especially on core biopsy samples, in veracious detection of this rare entity, paving the way for precise therapeutic management.

E-PS-12-036
Classical Hodgkin lymphoma with marked necrotising granulomatous reaction: diagnostic difficulty
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Background & Objectives: Hodgkin lymphoma (HL) is a lymphoid malignancy characterised by the presence of large mononuclear and multinucleated neoplastic Hodgkin and Reed-Sternberg cells surrounded by lymphoid and non-lymphoid inflammatory cells. The incidence of necrotizing granuloma is 1.8% and the incidence of necrotizing granuloma in HL has been reported in studies to be 9%. Granulomatous reaction may easily mask the presence of lymphoma. Therefore, the differential diagnosis should be made very carefully.
Methods: An excisional biopsy of the lymphoid nodule was performed. The specimen was formalin fixed and paraffin embedded. The sections were stained with routinary haematoxylin and eosin staining. Immunohistochemistry was performed.
Results: A 26-year-old female presented with a painless, palpable mass in the right cervical region. Ultrasonography showed multiple atypical lymphadenopathies in the right cervical region segment 3-4a, the largest measuring 40 mm. Disrupted lymph node structure and multiple necrotic epithelioid granuloma-like formations were observed on haematoxylin and eosin staining. In addition, these granuloma-like changes were separated from the lymphocyte-rich stroma. Scattered large multinucleated Hodgkin and Reed-Sternberg cells were seen in these areas. Epithelioid cells expressed CD68. High expression of CD30 and MUM1 was seen in the Hodgkin and Reed-Sternberg cells, and weak expression of PAX5 was identified. Based on the combination of histological examination and immunohistochemical results, classic HL was diagnosed.
Conclusion: Lymphoma is one of the potential underlying causes of granuloma. In particular, some prominent granulomatous lesions may mask the changes in lymphoma. Immunohistochemical staining can be used to exclude infectious changes during the clinicopathological diagnosis process. In young patients with lymph node granulomatous lesions, HL should be excluded first.

E-PS-12-037
MISREAD Network Project: a multicentre retrospective study for the identification of undiagnosed cases of idiopathic multicentric Castleman Disease based on suggestive histological findings
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Background & Objectives: Idiopathic multicentric Castleman disease (iMCD) is a rare disorder marked by abnormal lymph node proliferation, mimicking various diseases, mainly lymphoma. Accurate diagnosis is crutial to avoid mismanagement. The MISREAD Project aims to identify undiagnosed iMCD cases by reviewing previous lymph node biopsies using newly published diagnostic and grading criteria from the Spanish Haematopathology Group.
Methods: This retrospective multicentre study identifies lymph node biopsies with CD-like features through searches in pathology databases (Laboratory Information System) using predefined keywords (Castleman, plasmacytosis, regressive centres, and follicular hyperplasia). Fine-needle aspiration biopsies and cases with conditions excluding

iMCD were excluded. Reviews focus on histological grading, clinical history, and outcomes. The study has two phases: Phase 1 (review and checklist development by two hospitals) and Phase 2 (checklist implementation across 15 centres).
Results: In Phase 1, 66 cases were reviewed (39 in Centre-A, 27 in Centre-B); 1case (1,5%) met both histological and clinical criteria for iMCD, and was previously missdiagnosed as reactive follicular hyperplasia NOS.
The phase 2 is ongoing. Systematic biopsy review applying the standardized checklist is being applied during the next months. Findings from this expanded cohort will be evaluated once data collection and review are completed.
Conclusion: Accurate iMCD diagnosis requires accurate histological criteria application. Without proper grading, diagnoses may be overlooked, as seen in 1,5% of cases in Phase 1. Phase 2 will assess nationwide diagnosis improvements using the checklist, enhancing iMCD detection and clinical decisions.

E-PS-12-039
Molecular heterogeneity in paediatric Langerhans cell histiocytosis: BRAF V600E and KRAS mutational spectrum with VE1 immunohistochemical concordance analysis
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Background & Objectives: Paediatric Langerhans cell histiocytosis (LCH) is a rare clonal neoplastic disorder of Langerhans-type cells. The BRAF V600E mutation is a key oncogenic driver, while KRAS mutations are emerging as alternative pathogenic events. This study explores the clinicopathological and molecular features of paediatric LCH, focusing on the concordance between BRAF V600E mutation and VE1 immunohistochemical expression.
Methods: We conducted a retroprospective analysis of 10 paediatric LCH cases. Clinical and pathological data were reviewed. Histological diagnosis was established according to WHO criteria and confirmed by CD207 (Langerin, Ventana) immunoreactivity. VE1 monoclonal antibody (Ventana) was used to assess BRAF V600E expression. Molecular testing was performed via real-time PCR using TheraScreen BRAF and KRAS (Qiagen) assays. Statistical analyses included Fisher's exact and Mann-Whitney U tests, with $p < 0.05$ considered significant.
Results: The cohort comprised 10 patients (7 males, 3 females; median age: 6 years, range: 1–11), all with osseous involvement. BRAF V600E mutations were identified in 6 cases (60%), KRAS mutations in 3 (30%), and 1 case (10%) was wild-type. Langerin was positive in all cases, validating the diagnosis of LCH. VE1 immunohistochemistry demonstrated 100% sensitivity and specificity for BRAF V600E mutational status, with moderate to strong cytoplasmic immunoreactivity exclusively observed in BRAF-mutated cases. No VE1 immunoreactivity was seen in KRAS-mutated or wild-type cases. No statistically significant differences in age distribution ($p = 0.48$) or gender predominance ($p = 1.00$) were observed between BRAF- and KRAS-mutated cohorts.
Conclusion: Our findings demonstrate perfect concordance between VE1 immunohistochemical profile and BRAF V600E mutational status, validating its utility as a reliable surrogate biomarker in paediatric LCH. The identification of KRAS mutations in 30% of cases underscores the molecular heterogeneity of this entity and suggests potential alternative therapeutic targets for BRAF-negative patients, warranting further investigation.

E-PS-12-040
Histiocytic sarcoma. A rare tumour review in the last 10 years
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Background & Objectives: Histiocytic sarcoma (HS) is a rare and aggressive malignant neoplasm showing morphological and immunophenotypic features of macrophages. HS occurs in lymph nodes or extranodal sites, most commonly the gastrointestinal tract, spleen, soft tissue, skin, and CNS. It can be localized or disseminated. It represents a diagnostic challenge due to its prevalence and overlapping features with other hematolymphoid disorders and its diagnosis is usually by exclusion of different entities.
The objective is to review the cases diagnosed in our hospital in the last 10 years.
Methods: We retrospectively studied cases diagnosed as HS at Hospital Universitario de Cruces between 2014 and 2024. We reviewed clinical data and histopathological and immunohistochemistry findings.
Results: Four cases of HS were identified, all affecting adult patients, 2 were women, the mean age was 53, and the median was 54. Two were diagnosed in the gastrointestinal tract (ileum and rectum), and the others in the oral cavity and the lung. Histologically all of them were characterized by large, pleomorphic cells with abundant eosinophilic cytoplasm and vesicular nuclei. Immunohistochemistry (IHC) played a crucial role in confirming the diagnosis, with tumour cells that expressed CD68, CD163, CD4, lysozyme, and vimentin whereas lacking markers of dendritic CD1a, epithelial (CK AE1/AE3), lymphoid (CD3, CD10) and other lineages (HMB45, Melan-A). The proliferation index (Ki-67) ranged from 10% to 20%. Two cases had necrosis (<50% of the tumour) and vascular invasion but this was not reported in other cases. Two patients deceased one year after the diagnosis and the others are still alive.
Conclusion: - Histiocytic sarcoma remains a rare and aggressive entity that requires a thorough histopathological and immunohistochemical approach for accurate diagnosis.
- Due to its rarity, case series like this contribute to a better understanding of its clinicopathological spectrum and may aid in future diagnostic and therapeutic strategies.

E-PS-12-041
Aberrant expression of epithelial marker in a follicular dendritic cell sarcoma: a case report highlighting diagnostic pitfalls
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Background & Objectives: Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm originating from specialized antigen-presenting cells normally located in the germinal centres of lymphoid tissue. A subset of FDCS cases has been reported in association with Castleman disease, a lymphoproliferative disorder involving follicular dendritic cells. We report an unusual case of FDCS arising in the setting of Castleman disease, marked by a spectrum of progressive morphologic changes—ranging from follicular dendritic cell (FDC) hyperplasia and dysplasia to neoplasia—and an aberrant immunophenotypic profile.
Methods: Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm originating from specialized antigen-presenting cells normally located in the germinal centres of lymphoid tissue. A subset of FDCS cases has been reported in association with Castleman disease, a lymphoproliferative disorder involving follicular dendritic cells. We report an unusual case of FDCS arising in the setting of Castleman disease, marked by a spectrum of progressive morphologic changes—ranging from hyperplasia and dysplasia to neoplasia—and an aberrant immunophenotypic profile.
Results: Histologic examination revealed a lymph node with partially preserved architecture encased in a fibrous capsule. Proliferative lymphoid follicles composed of atypical epithelioid FDCs

displayed marked nuclear pleomorphism, vesicular chromatin, prominent nucleoli, and occasional binucleation or multinucleation. These follicles were surrounded by small lymphocytes in an "onion-skin" arrangement, with prominent hyalinized vasculature. Immunohistochemically, the atypical FDCs were strongly positive for AE1/AE3, fascin, D2-40, and PD-L1, but negative for other epithelial markers (EMA, CK7, CK20). Focal positivity for FDC markers, including CD21, CD23, and CD35, was also observed. CD20 staining highlighted surrounding concentric mantle zone lymphocytes.
Conclusion: This case represents a rare instance of FDCS arising in a background of Castleman disease with associated FDC hyperplasia and dysplasia. Aberrant expression of epithelial marker may complicate the diagnosis by mimicking metastatic carcinoma, emphasizing the importance of comprehensive histologic and immunophenotypic evaluation.

E-PS-12-042
B-lymphoblastic leukaemia with co-occurrence of BCR::ABL1 p190/p210, t(12;21) ETV6-RUNX1, and ETV6 exon 5 deletion: a case report
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Background & Objectives: B-cell acute lymphoblastic leukaemia (B-ALL) is an aggressive hematologic malignancy in adults. The most prevalent genetic alteration is the BCR::ABL1 p210 fusion. However, the simultaneous presence of BCR::ABL1 p190 and additional rearrangements, such as t(12;21)(p13;q22) ETV6::RUNX1, is exceptionally rare. This co-occurrence suggests underlying molecular reprogramming and increased clonal heterogeneity in B-ALL. Given its clinical and therapeutic implications, comprehensive molecular characterization is essential.
Methods: A 52-year-old female patient presented with lower limb cellulitis. Laboratory findings revealed marked hyperleukocytosis (217,300/mm³) with 83.6% circulating blasts. Flow cytometry confirmed a diagnosis of common B-ALL. RT-qPCR identified the concurrent expression of BCR::ABL1 p210 and p190 transcripts. The presence of the t(12;21) ETV6-RUNX1 translocation and a 57 bp deletion in exon 5 of the ETV6 gene was detected through RT-PCR, capillary electrophoresis, and in silico analysis. The patient was initiated on the GRAAPH treatment protocol in combination with dasatinib. After the second induction cycle, molecular remission for the BCR::ABL1 p190 transcript was achieved, enabling allogeneic hematopoietic stem cell transplantation.
Results: The molecular characterization of B-ALL provides critical prognostic and therapeutic insights. The co-occurrence of BCR::ABL1 p190/p210, observed in fewer than 10% of cases, has been associated with adverse outcomes due to its high oncogenic potential. The t(12;21)(p13;q22) ETV6-RUNX1 translocation is exceedingly rare in adults, with an unclear prognostic significance. Additionally, the exon 5 deletion in ETV6 may impair hematopoietic differentiation and proliferation, potentially contributing to a more unfavourable disease course.
Conclusion: The co-occurrence of BCR::ABL1 p190/p210 in B-ALL is an uncommon event that may significantly influence leukemogenesis and treatment response. Its association with t(12;21) ETV6-RUNX1 and ETV6 exon 5 deletion suggests increased clonal complexity. Given the clinical and therapeutic implications of these genetic alterations, comprehensive molecular profiling with prognostic relevance is crucial for optimizing treatment strategies and patient management.

E-PS-12-043
Marginal zone lymphoma of the liver: pathology and molecular profiling of three cases
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Background & Objectives: Marginal zone lymphoma (MZL) is a B-cell non-Hodgkin lymphoma that typically arises in mucosa-associated lymphoid tissue (MALT). While MZL can involve various extranodal sites, primary hepatic MZL lymphoma is exceedingly rare, with only a few reported cases. This study aims to characterize the clinical, pathological, and genetic features of hepatic MZL.
Methods: We retrospectively analysed three cases of hepatic MZL diagnosed at our reference centre. Clinical and histopathological data were reviewed. Molecular studies included whole-exome sequencing (WES), targeted sequencing using a custom B-cell lymphoma panel, and fluorescence in situ hybridization (FISH) analysis for *MALT1–IgH* rearrangement using a break-apart probe.
Results: We identified three cases of primary hepatic MZL. One patient had Sjögren's disease. All cases presented with a liver mass as the primary manifestation. One patient also exhibited enlarged cervical and axillary lymph nodes on further imaging. Histopathological examination of the liver showed a nodular to diffuse infiltration of small to medium-sized lymphocytes, with focal lymphoepithelial lesions involving interlobular bile ducts. Immunophenotyping showed a B-cell phenotype consistent with MZL ($CD20^+/CD5^-/CD23^-$). One case demonstrated lambda light chain restriction. Bone marrow involvement was absent in all patients. Notably, one patient developed an indolent systemic T-cell lymphoproliferative disorder. FISH analysis in two cases showed no evidence of the *MALT1–IGH* t(14;18)(q32;q21) translocation. Sequencing data identified mutations in *KMT2D* (p.Q1213H), *PRDM1* (p.L144Rfs, p.S405L), *KLF2* (c.75+1G>A), *NFKBIA* (p.E40K, p.A4T), and *NOTCH1* (p.P1410S).
Conclusion: The mutational landscape of hepatic MZL in our series included alterations in the NOTCH pathway (*NOTCH1*), transcription factors (*KLF2*), and epigenetic regulators (*PRDM1*, *KMT2D*), but no *PTPRD* mutations were detected. This profile overlaps more with nodal and splenic MZL than with MALT lymphomas, reinforcing the biological heterogeneity of MZL. The characterization of primary hepatic MZL remains limited, but its biology appears to be linked to antigen stimulation and BCR signalling.

E-PS-12-044
Myeloid sarcoma localized in the stomach as a progression of chronic myelomonocytic leukaemia
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Background & Objectives: Myeloid Sarcoma (MS) is an aggressive and highly heterogeneous haematological malignancy characterized by myeloid blasts in an extramedullary location, occurring either before or after leukaemia diagnosis. The occurrence of MS in association with myelodysplastic/myeloproliferative neoplasms is rare. In this report, we present the case of an 80-year-old woman who exhibited extramedullary localization of MS following a diagnosis of chronic myelomonocytic leukaemia (CMML).

Methods: A gastric biopsy was performed due to suspicion of gastric carcinoma. Formalin-fixed paraffin-embedded (FFPE) tissue was routinely prepared, and a comprehensive immunohistochemical panel, including CD68 PGM1, CD68 KP1, CD163, CD14, CD45, myeloperoxidase (MPO), CD15, CD34, CD117, CD3, CD20, CD2, CD25, CD30, ALK, CD138, CK AE1/AE3, CK7 and S100, was applied.
Results: Microscopic examination of the gastric mucosa revealed atypical small to medium-sized elements with blastic features. These characteristics included scant cytoplasm, irregular nuclear profiles, and fine chromatin with indistinct nucleoli. Immunohistochemical analysis indicated a histiocytic phenotype (CD68 PGM1+, CD68 KP1+, CD163+, CD14-/+) with CD15 and CD45 positivity, and a high proliferation index (Ki-67: 90%). The neoplastic cells tested negative for MPO, CD34, CD3, CD20, CD2, CD117, CD25, Tryptase, CD30, ALK, CD138 and S100. A diagnosis of MS secondary to CMML was established, and the patient died shortly after histopathological diagnosis.
Conclusion: Diagnosis of extramedullary myeloid sarcoma is challenging in routine practice. This case highlights a rare manifestation of disease progression in CMML, seldom reported in gastric biopsies.

E-PS-12-045
Comparative analysis of mediastinal lymphomas diagnosed at a tertiary medical centre over a 25-year period
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Background & Objectives: Mediastinal lymphomas represent a diagnostic challenge due to overlapping morphologic and immunophenotypic features, particularly between classical Hodgkin lymphoma (CHL), primary mediastinal large B-cell lymphoma (PMBCL), diffuse large B-cell lymphoma (DLBCL), and mediastinal gray zone lymphoma (MGZL). This study aims to comparatively evaluate these subtypes based on cases diagnosed over a 25-year period in a single tertiary centre.
Methods: We retrospectively analysed 40 cases (10 per entity) diagnosed between 2000–2025 at Cerrahpasa Medical Faculty. Histopathologic and immunohistochemical features were re-evaluated using archival slides and pathology reports.
Results: Reed-Sternberg (RS) or RS-like cells were seen in all CHL and MGZL cases, frequently binucleated with prominent eosinophilic nucleoli, but not in DLBCL or PMBCL. Prominent inflammatory background was typical for CHL (10/10) and MGZL (9/10), while rare in DLBCL (1/10) and PMBCL (2/10). Fibrosis was frequent in PMBCL (8/10) and CHL (7/10). CD30 was positive in all CHL and MGZL, and in most PMBCL (9/10), but rare in DLBCL (2/10). CD15 was seen mainly in CHL (9/10). CD20 was expressed in all DLBCL and PMBCL, variably in MGZL (6/10), and rarely in CHL (2/10). High Ki-67 (>70%) was common in DLBCL (9/10), PMBCL (8/10), MGZL (7/10), but less frequent in CHL (3/10). EBV was positive in 4/10 CHL and 2/10 MGZL.
Conclusion: Despite overlapping features, certain histologic and immunophenotypic patterns can help distinguish between mediastinal lymphoma subtypes. While RS morphology, CD30&CD15 positivity and inflammatory background favour CHL and MGZL, strong B-cell markers and high proliferation index support DLBCL and PMBCL diagnoses.

E-PS-12-046
Clinicopathological profile of tonsillar diffuse large B-cell lymphoma NOS, in younger patients: a six-year single-centre study
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Background & Objectives: Diffuse Large B-Cell Lymphoma (DLBCL) of the tonsil represents a distinct entity among extranodal lymphomas with unique clinicopathological features. This study aims to characterize tonsillar DLBCL in younger patients (aged <50 years) and compare their profile with older counterparts, focusing on cell-of-origin classification and its potential prognostic implications.
Methods: We retrospectively analysed 50 consecutive cases of primary tonsillar DLBCL diagnosed at our department between January 2019 and December 2024. Cases were classified into germinal centre B-cell-like (GCB) and non-germinal centre B-cell-like (non-GCB) subtypes using the Hans algorithm (CD10, BCL6, MUM1).BCL2 and c-MYC immunostaining and EBER in situ hybridization were performed for all cases. Clinical and pathological data were statistically analysed (significance: $p < 0.05$).
Results: Among the 50 patients, 13 (26%) were under 50 years of age, with a mean age of 34.0 years (range: 15–46). The younger cohort showed a male predominance (61.5%) that was less pronounced than in older patients (≥50 years: 73.0% male). Notably, the GCB subtype was significantly more frequent in younger patients (61.5%) compared to older individuals (16.2%; $p = 0.002$). In contrast, the non-GCB subtype predominated in patients aged ≥50 years (78.4% vs. 38.5% in younger patients). Three double-hit cases (MYC and BCL2 co-expression) were identified exclusively in older patients. EBER was negative in all cases. The annual incidence of cases remained stable over the study period, ranging from 5 to 13 cases per year.
Conclusion: Tonsillar DLBCL in younger patients displays a distinct molecular profile, with a significantly higher prevalence of the GCB subtype. This age-related molecular heterogeneity may reflect divergent pathogenic pathways and has potential prognostic implications, given the generally more favourable outcomes associated with the GCB phenotype. These findings underscore the importance of age-adapted diagnostic and therapeutic strategies in the management of tonsillar DLBCL.

E-PS-12-048
Blastic plasmacytoid dendritic cell neoplasm with unusual morphologic, phenotypic and cytogenetic features
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Background & Objectives: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare haematological malignancy characterized by the formation of cutaneous tumours and subsequent/simultaneous leukemic manifestations. Most of these haematological diseases exhibit chromosomal abnormalities and previous studies have detected BPDCN displaying an 8q24 rearrangement of the *MYC* locus. Herein, we describe two cases of BPDCN with *MYC* rearrangement.
Methods: Between 2024 and 2025, two cases of BPDCN were diagnosed from incisional skin biopsies. Formalin-fixed paraffin-embedded (FFPE) tissues underwent immunohistochemical analysis, including markers such as CD123, CD4, CD45, CD56, S100, CD207, CD34, CD117, and MYC. Furthermore, fluorescence in situ hybridization (FISH) was performed using a commercially available probe to identify the 8q24 rearrangement of the *MYC* gene.
Results: The patients were 83 and 75 years old. Skin biopsies showed a diffuse infiltrate in the dermis composed of large, atypical cells with round vesicular nuclei and centrally located nucleoli (immunoblasts). Both cases tested positive for CD123, CD4, CD45 and exhibited high expression of MYC (>90%) along with a high proliferation rate (Ki-67: 90%). CD56 was positive in only one of the cases. Additionally, CD34, CD117, MPO, and CD15 were negative. FISH analysis of tissue sections from the skin lesions confirmed *MYC* rearrangement. Both

patients experienced rapid clinical deterioration and died shortly after diagnosis.
Conclusion: These two cases highlight the complexities of diagnosing BPDCN due to unusual morphological (immunoblastoid vs. myelo-/lymphoblastic) and immunophenotypic features (CD56 negativity vs. CD56 positivity). Interestingly, neoplastic cells demonstrated intense and diffuse c-MYC immunohistochemical expression and harboured *MYC* rearrangement, consistent with previous reports of BPDCN immunoblastic variants and their aggressive clinical course. Therefore, these unique morphological and cytogenetic features in BPDCN should be recognized for diagnostic and prognostic purposes.

E-PS-12-049
Thinking out of the bone: extramedullary multiple myeloma in uncommon locations
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Background & Objectives: Extramedullary involvement by multiple myeloma (MM) is rare, typically emerging during relapse and carrying a poor prognosis. It most frequently involves the skin and soft tissues, but it can rarely affect other organs. The main differential diagnosis is with solitary plasmacytoma, which has a different management and better prognosis.
Methods: We report two cases of extramedullary disease in two rare locations. The first case is of a 68 year old male, in remission from MM, who presented with a painful lesion in the right testicle measuring 53cm3, associated with biochemical relapse of MM. The patient accepted intervention with right orchiectomy.
The second case concerns a 72 year old male with MM diagnosed 3 years prior, in remission. A month after suspending lenalidomide, the patient presented with a painful mass in the right preauricular region measuring 6cm. A CT scan showed a well delimited lesion in the superficial lobe of the parotid gland, which was submitted to a Fine Needle Aspiration (FNA).
Results: In the first case, the testicular parenchyma was almost completely obliterated by sheets of plasmacytoid cells, with occasional Dutcher bodies, immunohistochemistry positive for CD56 and CD138; lambda light chain restriction was noted (by in situ hybridization).
In the second case, the FNA cytology revealed a sheet of plasmacytoid cells positive for CD138, CD56 and MUM1, with lambda light chain restriction and a high Ki-67 index.
Conclusion: These cases highlight both the importance of correlation with the patient's clinical information and the necessity of considering rare diagnoses due to their impact on patient management and outcomes.

E-PS-12-050
Clinicopathological and molecular diversity of large B-cell lymphoma across extranodal sites: a comparative analysis of 160 cases from the tonsil, stomach, and mediastinum
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Background & Objectives: Large B-cell lymphoma (LBCL) frequently arises in extranodal sites, particularly the gastrointestinal tract, exhibiting site-specific biological and molecular profiles. This study compares the clinicopathological, immunophenotypic, and molecular features of DLBCL across three distinct extranodal locations, with emphasis on cell-of-origin classification and age-related patterns.
Methods: We retrospectively analysed 160 cases of primary extranodal DLBCL diagnosed between 2019-2024 (50 tonsillar, 88 gastric, 22 mediastinal). Cell-of-origin classification utilized the Hans algorithm (CD10, BCL6, MUM1). Immunohistochemical assessment included BCL2, c-MYC, PD-L1, CD30, and CD23. EBER in situ hybridization was performed for all cases. Comparative statistical analyses were performed between the different anatomical sites, with a p-value < 0.05 considered.
Results: Median age varied significantly across sites: tonsillar (65 years), gastric (60 years), and mediastinal (36 years; $p < 0.001$). Male predominance characterized tonsillar (56.0%) and gastric (54.2%) cases, while mediastinal DLBCL, consistent with primary mediastinal large B-cell lymphoma (PMBCL), predominantly affected females (68.4%; $p = 0.02$). The GCB subtype was significantly enriched in younger patients across sites, particularly in tonsillar DLBCL (61.5% in <50 years vs. 21.6% in ≥50 years; $p = 0.03$). Non-GCB phenotype predominated in older patients (78.4% in tonsillar, 77.0% in gastric DLBCL aged ≥50 years). Three double-hit cases (MYC/BCL2 co-expression) were identified exclusively in older patients. EBER positivity was observed in 4 gastric cases (4.8%) but was negative in all tonsillar and mediastinal cases. Mediastinal DLBCLs demonstrated typical PMBCL features with younger age and female predominance.
Conclusion: LBCL demonstrates distinct site-specific and age-dependent clinicopathological profiles. The significant enrichment of GCB subtype in younger patients, particularly in tonsillar DLBCL, suggests age-related molecular heterogeneity with divergent pathogenic mechanisms. PMBCL exhibits a unique demographic profile, while gastric DLBCL shows occasional EBV association. These findings underscore the importance of anatomical site and patient age in DLBCL molecular stratification and support site-adapted and age-adapted diagnostic and therapeutic approaches.

E-PS-13 E-Posters Head and Neck Pathology

E-PS-13-001
Clinicopathological correlations in medication-related osteonecrosis of the jaw: a retrospective histopathological study
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Background & Objectives: Medication-related osteonecrosis of the jaw (MRONJ) is a severe complication associated with antiresorptive and antiangiogenic therapies, particularly in patients with malignancies. Histopathological features of MRONJ remain underexplored and unstandardized, limiting their clinical utility. This study aimed to investigate the correlation between clinical variables and histopathological parameters in MRONJ cases to identify potential prognostic indicators.
Methods: Among 101 MRONJ cases diagnosed between 2013 and 2025 and archived in the Department of Oral Pathology at Gazi University, 32 cases associated with malignancy-related medication use were retrospectively selected. Demographic, clinical, and radiographic data were recorded. Variables such as soft tissue changes, inflammation, haemorrhage, presence of microorganisms, bone resorption, proportion of viable bone, cement line integrity, and presence of osteoclasts were assessed. Histochemical stains were applied to further characterize microorganisms. Statistical analyses were performed to assess correlations between clinical and histopathological findings.
Results: The most frequent clinical trigger was tooth extraction, and the most commonly used drug was zoledronic acid. All cases showed classic features of osteonecrosis; Actinomyces was detected in 62.5% of cases. Inflammation was higher in male patients ($p < 0.0001$), those with metastases ($p < 0.0001$), and following tooth extraction ($p < 0.0001$). Denosumab use was linked to increased inflammation ($p = 0.0008$) and osteoclast activity ($p = 0.0287$) compared to zoledronic acid. Actinomyces presence correlated with metastasis, tooth

extraction, and inflammation ($p < 0.05$). The type of primary tumour and treatment regimen significantly influenced bone vitality and inflammatory response. Notably, age was the only variable significantly correlated with all histopathological parameters, suggesting a potential role of advanced age in disease severity.
Conclusion: Histopathological findings in MRONJ correlate with key clinical variables. Age, drug type, metastasis, and local risk factors may influence disease severity. These findings support the potential prognostic value of histopathology and underscore the need for standardized evaluation criteria in MRONJ.

E-PS-13-002
The mystery of long-standing pleomorphic adenoma
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Background & Objectives: Pleomorphic adenoma is the most common benign salivary tumour, rarely undergoing malignant transformation. Carcinoma ex pleomorphic adenoma (CEPA) is a rare malignancy that affects the major and less frequently, minor salivary glands. Recent studies suggest that apocrine changes within pleomorphic adenoma may represent a premalignant stage and intraductal carcinoma is a preinvasive lesion of CEPA. We present a case of a 53-year-old patient with 20-year-evolving pleomorphic adenoma of genian region with areas of low-grade apocrine intraductal carcinoma, highlighting the importance of thorough diagnostic evaluation of benign tumours.
Methods: A 53-year-old man presented with a painless, firm, slow-growing nodular tumour located in the left cheek, involving its entire thickness. Ultrasound evaluation shows a solid, well-demarcated vascularized lesion located at a depth of 3 mm. The tumour formation was surgically removed and was sent to the pathological anatomy laboratory for histopathological and immunohistochemical evaluation.
Results: Macroscopic examination reveals a well-demarcated nodular tumour formation, encapsulated with a lobulated contour that presents a solid, multinodular, white-gray appearance on section with brown-haemorrhagic and yellowish areas. The tumour formation is in contact with the surgical resection margin macroscopically. Microscopic evaluation shows a nodular tumour proliferation consisting of three elements: predominantly chondromyxoid stroma, epithelial and myoepithelial elements. The epithelial component presents a tubular or cribriform architecture, with reduced cellular pleomorphism with eosinophilic nucleoli and reduced mitotic activity. Immunohistochemistry was performed for CK7, CK5, p63, p53, GCDFP15 and androgen receptor, which were positive, confirming the presence of areas of apocrine intraductal carcinoma, as well as SOX10 which was negative in the carcinoma area.
Conclusion: This case highlights the potential for malignant transformation of long-standing pleomorphic adenomas. The histopathological and immunohistochemical approach is important for an accurate diagnosis, since early recognition of malignant components affects the clinical management and prognosis of the patient.

E-PS-13-003
Reclassification of squamous cell carcinomas of the tongue according to the 8th edition of the TNM classification: prognostic impact of the new T stage
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Background & Objectives: Tongue squamous cell carcinoma (TSCC) is a common and aggressive form of oral cavity cancer, often diagnosed at advanced stages with poor prognosis. The 8th edition of the TNM classification introduces updated criteria, especially concerning tumour size and depth of invasion (DOI). This study aimed to reclassify the T stage of TSCC using the new TNM classification and assess the prognostic impact of DOI.
Methods: We analysed 67 cases of TSCC diagnosed at Salah Azaiez Institute between 2012 and 2018. Tumours were reclassified according to DOI, and survival analysis was performed using Log Rank test.
Results: The mean age of patients was 68 years [49–98], with a male-to-female ratio of 0.9. Tobacco use was reported in 35% of cases, and alcohol use in 25%. The mean tumour size was 27mm (range 8–64).
Re-evaluation of the T stage based on the 8th edition of TNM led to the upgrading of 22 cases, with no downgrades. Specifically, 20 of 27 cases initially classified as T1 with a DOI >5mm were reclassified as T2, and 10 of 29 cases initially classified as T2 with a DOI >10mm were reclassified as T3. Two cases initially classified as T3 with a DOI >10mm were upgraded to T4a.
Survival analysis revealed that DOI>10mm and T3-T4 stages were significantly associated with lymph node metastasis and 5-year disease-free survival ($p=0.000$ and $p=0.005$, respectively). In multivariate analysis only DOI was independently associated with lymph node metastasis (OR 11.8, CI [3.2-43.3]).
Conclusion: In conclusion, the 8th edition of the TNM classification has a significant impact on the reclassification of TSCC, with DOI emerging as a key prognostic factor in staging and patient outcomes. This new classification allows better risk stratification and more rigorous mentoring of OTC who were earlier considered at risk-free.

E-PS-13-004
Unusual case of sinonasal carcinosarcoma on inverted papilloma – case report
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Background & Objectives: Sinonasal (Schneiderian) papillomas are benign epithelial neoplasms and the most common tumours of the nasal cavity and paranasal sinuses. These lesions are well known for their tendency to recur and malignant transformation.
Malignancies arising in sinonasal papillomas are rare and almost always described as in situ or invasive squamous cell carcinoma. An exceedingly rare situation is the coexistence of carcinomatous and sarcomatous components.
Methods: We report the case of a 42-year-old male who presented with recurrent nasal obstruction, bleeding and an enlarging sinonasal mass in the left nasal vestibule.
Our pathology department received a piecemeal resection of the tumour. The blocks were sectioned and stained with Haematoxylin and eosin, and blank slides were prepared for immunohistochemical stains.
Results: Histopathological examination revealed a lesion that exhibited a biphasic morphology, with areas demonstrating moderately differentiated squamous cell carcinoma and regions showing a spindle cell component. Immunohistochemical analysis revealed strong positivity for CK34bE12 and p40 in the squamous cell carcinoma areas, confirming their epithelial origin. The sarcomatous component was positive for vimentin, desmin, h-caldesmon and actin, suggesting mesenchymal differentiation. Additionally, both components were negative for S100 and CD34. The transition from the inverted papilloma to the malignant

components was evident, with dysplastic epithelium at the periphery of the papilloma, indicating a stepwise progression to carcinoma and sarcoma.
Conclusion: This case underscores the importance of thorough histopathological and immunohistochemical evaluation in diagnosing rare malignancies like sinonasal carcinosarcoma, particularly in the context of pre-existing inverted papillomas. It also highlights the potential for malignant transformation in these lesions, necessitating vigilant follow-up in patients with Schneiderian papillomas.

E-PS-13-005
Mesenchymal chondrosarcoma: an illustrative case
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Background & Objectives: Malignant small round blue cell tumours encompass a diverse group of aggressive neoplasms with overlapping histological features, complicating diagnosis. This report presents a case of mesenchymal chondrosarcoma (MCS) in a 6-year-old female, emphasizing diagnostic challenges and differential considerations.
Methods: An incisional biopsy from the left maxillary alveolar bone revealed soft, cream-tan tissue fragments. Histopathological examination demonstrated undifferentiated small round blue cells with hyperchromatic nuclei, scant cytoplasm, and slit-like vascular spaces resembling staghorn vessels. Abrupt transitions to mature hyaline cartilage were noted. Immunohistochemical studies revealed strong NKX3.1 staining in the undifferentiated component and S100 positivity in the cartilaginous component. SATB2 was weakly positive in the undifferentiated cells but absent in the cartilage. Pancytokeratin and desmin were negative. These findings supported a diagnosis of MCS, with molecular testing for HEY1::NCOA2 fusion recommended for confirmation.
Results: MCS is a rare sarcoma comprising 2-10% of all chondrosarcomas, with 20-30% occurring in the head and neck, particularly affecting young individuals. It exhibits biphasic histology with undifferentiated mesenchymal cells and mature cartilage. Diagnosing MCS is challenging when the cartilaginous component is absent in limited biopsies, leading to potential confusion with Ewing's sarcoma, desmoplastic small round cell tumour, small cell osteosarcoma, and rhabdomyosarcoma. NKX3.1, a novel marker, is absent in these differentials, aiding distinction. The HEY1::NCOA2 gene fusion further supports diagnosis, particularly in cases lacking characteristic cartilage.
Conclusion: Due to its aggressive nature, MCS requires long-term follow-up. Craniofacial tumours in paediatric patients tend to have better outcomes post-surgical resection and chemotherapy. This case highlights the importance of integrating histology, immunohistochemistry, and molecular studies for accurate diagnosis and appropriate management of MCS.

E-PS-13-006
Laryngeal salivary duct carcinoma with pagetoid spread: a very rare case report
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Background & Objectives: Paget disease is a rare carcinoma characterized by an intraepithelial growth of neoplastic cells originating in the skin or representing the intraepithelial spread of an underlying visceral carcinoma. It usually is located in the breast or apocrine-rich areas.
Methods: Here, we present a rare case of laryngeal salivary duct carcinoma (SDC) with pagetoid spread in a 71-year-old male. The patient had a 2-year history of hoarseness and new-onset stridor, which led to the decision to perform a tracheostomy, followed by a laryngeal biopsy. Further imaging revealed a 1.5 cm soft tissue lesion in the neck that infiltrates thyroid tissue, which was also biopsied, with no other masses identified elsewhere. Both biopsies were sent for histopathological examination with a one-week interval.
Results: The first biopsy revealed intraepithelial carcinoma cells, with no additional lesions identified in the subepithelium, aside from some inflammatory cells. The second biopsy from the neck mass demonstrated neoplastic infiltration consisting of cells with eosinophilic cytoplasm and large, round, and pleomorphic nuclei, organized in irregular clusters within a desmoplastic stroma. Immunohistochemical analysis showed positivity for cytokeratin 7, EMA, CEA, and androgen receptor, while cytokeratin 20, p40, TTF-1, PAX8 and S100 were negative. Identical immunohistochemical findings were observed for both biopsies. Laryngoscopic findings showing submucosal mass localized in the subglottic area and histopathological findings supported a diagnosis of laryngeal SDC.
Conclusion: This case is particularly intriguing and rare for several reasons. Paget's disease in the head and neck region is exceedingly uncommon, with the majority of reported cases involving the oral mucosa. Additionally, SDC, typically associated with major salivary glands, was found in the minor salivary glands of the larynx in this instance. To the best of our knowledge, this represents the first documented case of laryngeal SDC with pagetoid spread in the literature.

E-PS-13-007
Molecular characterization and biomarkers in salivary gland carcinomas through NGS: diagnostic and therapeutic implications
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Background & Objectives: Salivary glands carcinomas shows genotypic diversity, complicating their management in advanced cases. Next-generation sequencing (NGS) allows for the detection of genetic alterations, improving accurate diagnoses and offering therapeutic targets. Since 2020, our service has implemented NGS in advanced cases of salivary gland carcinoma.
Methods: We analysed ten paraffin tissue samples: five adenoid cystic carcinomas (AdCC), three ductal carcinomas (SDC), one myoepithelial carcinoma (MECA), and one epithelial-myoepithelial carcinoma (EMC). We used three custom panels: Oncomine™ Precision Assay (50 genes) for five cases, Oncomine™ Focus Assay (52 genes) for four cases and Oncomine™ Dx Express Test (46 genes) for one case. Three cases underwent NGS at an external laboratory (Foundation One, FOne). Immunohistochemical biomarkers (Her-2, PDL-1, androgen receptors, and c-kit) and fluorescence in situ hybridization (FISH) were performed.
Results: Molecular alterations were detected in two cases with diagnostic utility: EMC (*HRAS* and *PIK3CA*) and SDC (*FGFR1*). The three analysed cases with FOne, showed diagnostic alterations: two AdCC (*MYB* and *NOTCH-1*, respectively) and one SDC (*PTEN, TP53* and *NOTCH-1*). We did not detect these genes because they were not included in our panels.
FISH detected a *MYB* fusion in a AdCC case. Immunohistochemical staining detected two CD117+ cases (AdCC), five androgen receptors+ cases (three SDC and two AdCC), of which four received antiandrogenic treatment; one PD-L1 CPS 6 (AdCC), treated with Pembrolizumab, and one HER2+++ (SDC), without related treatment. In cases without alterations, the treatments included RT-chemotherapy and tyrosine kinase inhibitors.

Conclusion: NGS is valuable for identifying molecular alterations, improving diagnostic accuracy and offering therapeutic targets, with treatment options. It is important to highlight the need of a broad panel that includes the main genes involved in salivary glands carcinomas. Our study found that small percentage of cases showed significant results for the diagnostic process, while immunohistochemical biomarker studies had a greater impact on therapeutic decision-making.

E-PS-13-008

Cytomegalovirus sialadenitis: a diagnostic mousetrap

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Background & Objectives: Sialadenitis is the inflammation of the salivary glands. It can be caused by various infectious, obstructive, and auto-immune processes. Cytomegalovirus (CMV) sialadenitis is extremely rare and occurs mainly in immunocompromised patients.
Methods: A 32-year-old healthcare worker woman presented with a left submandibular tumour-like mass. Imagery showed a pseudotumour appearance. Therefore, a fine-needle aspiration was carried out, the specimen contained small lymphoid-like cells and large cells with abundant, granular cytoplasm and a large nucleolated nucleus. The exact type of these cells could not be determined and a biopsy proved to be necessary for a definitive diagnosis.
Results: The biopsy showed atrophic salivary tissue, with a few residual acini dissociated by a dense lymphoplasmacytic infiltration, without a recognizable lymphoid follicle or an obvious lymphoepithelial complex; several salivary epithelial cells contained granular basophilic cytoplasm and a large intra-nuclear inclusion of the CMV type; there were no granulomas or giant cells.
An immunohistochemical study was performed using antibodies to CD3, CD20, and CK; CK identified acini and salivary ducts without a lymphoepithelial complex; the lymphoid cells were polymorphic with a predominance of T lymphocytes (CD3+), which are thought to be reactive to CMV infection.
These findings prompted a more in-depth investigation, which ultimately revealed that the patient was HIV-positive.
Conclusion: The deceptive imagery and cytological appearance make this pathological entity easily mistaken for benign or malignant tumours. Therefore, the patient's immune status is a crucial factor in diagnostic orientation, and biopsies should be widely considered even after a fine-needle aspiration. Although rare, this entity should be included in the differential diagnosis of suspicious submandibular masses, particularly in immunocompromised patients.

E-PS-13-009

Watch carefully! Perineural invasion in adenoid cystic carcinoma proves once again to be a negative prognostic marker for metastasis even without local recurrence post-R0 resection. A case report

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Background & Objectives: Adenoid cystic carcinoma (ACC) of the parotid gland is a rare and aggressive malignancy, representing approximately 1% of head and neck cancers, with MYB-NFIB fusion gene playing a crucial pathophysiological role. ACC has a propensity for perineural invasion (PNI) – parotidean tumours particularly along facial nerve branches – complicating detection and management as they are mostly clinically indolent. Despite unclear mechanisms linking PNI to distant metastasis, PNI is a recognized negative prognostic marker. This presentation aims to discuss a rare case of ACC that, following an R0 resection and radiotherapy, presented with delayed extensive metastases but no local recurrence, underscoring how critical clinical history and robust surveillance are.
Methods: A 54-year-old female patient initially presented with facial asymmetry due to a tumour in the right parotid gland. The patient underwent surgical excision of the tumour, facial nerve and lymph nodes (jugulo-carotid chain and spinal levels III/IV). Pathology confirmed ACC, staged IVA pT4aN0M0, with perineural invasion (PNI) and no lymphovascular invasion (LVI), achieving clear margins (R0). Post-surgery, adjuvant radiotherapy was administered. Three years later, the patient experienced acute abdominal symptoms. Imaging revealed metastatic masses in the lungs, liver, stomach, intestines, colon, and bones. An emergency laparotomy confirmed a perforated gastric ulcer and multiple peritoneal masses, which were biopsied for origin confirmation and corroboration with the initial diagnosis of ACC.
Results: Histopathological examination showed well-circumcised nodular tumours consisting of metastatic lesions with cribriform pseudoglandular pattern; cysts surrounded by cuboidal and, at the periphery, myoepithelial cells, with monomorphic small round nuclei, infrequently larger/hyperchromic/discretely vesicular; low mitotic activity. Immunohistochemistry was consistent with metastatic ACC: CK7 positivity (ductal component); p63 positivity (myoepithelial cells); CK20 and TTF1 negativity.
Conclusion: Due to its significance as prognostic marker of delayed distant metastatic behaviour, documenting PNI is crucial for the clinical management and surveillance of ACC patients, even after achieving local disease control.

E-PS-13-010

Low grade fibromyxoid sarcoma arising in the parotid gland - a pitfall in salivary gland cytopathology

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Background & Objectives: Low grade fibromyxoid sarcoma (LGFMS) is a rare malignant neoplasm, most commonly found in the extremities or trunk. In the literature, we found reports of 49 head and neck LGFMS, 3 in the parotid gland. These neoplasms have spindle and deceptively bland cells, often with an alternating myxoid and collagenous background. We report the clinicopathologic features of one case of LGFMS in the parotid gland.
Methods: A 58-year-old woman previously been submitted 5 years ago to a superficial parotidectomy elsewhere with unknown diagnosis, presented with a *de novo* hard, painful and palpable nodule on the same location. Fine needle aspiration citology (FNAC) of the lesion was followed by total parotidectomy.
Results: FNAC revealed a hypocellular lesion composed of bland spindle cells dispersed in a chondromyxoid-like matrix. A diagnosis biphasic neoplasia compatible with pleomorphic adenoma (PA) was established. On the surgical specimen the findings were of a multinodular myxoid-yellowish tumour with gross infiltration of the salivary gland and soft tissues. Histological evaluation revealed dispersed neoplastic spindle cells with poorly defined cytoplasm and no atypia

in a collagenous and myxoid stroma with hypocellular and hypercellular areas. The neoplastic cells were MUC4 positive and fluorescence in situ hybridization (FISH) revealed *FUS* gene rearrangement. A final diagnosis of LGFMS was made.
Conclusion: This case demonstrates that LGFMS is a difficult diagnosis, especially in citology and in uncommon locations like the head and neck, where other matrix-rich tumours like PA are commonly found. High suspicion for a myxoid mesenchymal neoplasm is necessary to properly choose complementary studies like immuno-histochemistry and FISH analysis.

E-PS-13-011
Ewing-like sarcoma of the oral cavity: a rare diagnostic challenge
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Background & Objectives: Ewing-like sarcomas are a subset of undifferentiated round cell sarcomas that pose significant diagnostic challenges due to their histological and immunophenotypic overlap with other malignancies. Metastases to the oral cavity are extremely rare, comprising only 1% of orofacial malignancies, with the lung being the most common primary site. Distinguishing metastatic Ewing-like sarcoma from primary oral tumours is critical for appropriate management.
Methods: A 64-year-old female with multiple comorbidities, including a history of lung adenocarcinoma with multiple metastases presented with intraoral ulcerative, haemorrhagic mass. Chest and neck CT scans were followed by palliative surgical excision of the intraoral mass. Histopathological and immunohistochemical analyses, including markers CK7, CK20, Vimentin, CD99, CD34, TTF-1, CD56, Ki-67, Synaptophysin, SATB2 and TLE-1 were performed.
Results: CT scans revealed a multilobulated parenchymal-density mass in the left central hilar region along with an osteolytic lesion in the horizontal branch of the left mandible with infiltration of adjacent structures. H&E examination demonstrated diffuse, infiltrating atypical cells arranged in trabeculae, sheets, and small clusters with frequent atypical mitoses. Immunohistochemical analysis revealed CD99, CK7, synaptophysin, CD56, SATB2 and TLE-1 positivity. BCOR::CCNB3 fusion testing was unavailable, limiting further molecular characterization.
Conclusion: Although rare, oral cavity metastases should be considered in patients with a history of lung malignancy. A thorough immunohistochemical workup is crucial for distinguishing Ewing-like sarcoma from other malignancies. This case underscores the importance of recognizing atypical metastatic patterns and employing a systematic diagnostic approach for accurate classification and optimal patient care.

E-PS-13-012
Anatomopathological diagnosis of tumours of the oral cavity: a retrospective study of 10 years, from 2013 to 2023
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Background & Objectives: Oral cavity tumours present with a wide range of clinical and histopathological features, posing challenges in diagnosis and treatment. This study provides a comprehensive overview of oral cavity tumours over a decade from 2013 to 2023 at the University Hospital Centre of Marrakech and proposes a standardized diagnostic report template to enhance diagnostic accuracy and therapeutic strategies.
Methods: This retrospective study reviewed a total of 98 cases of oral cavity tumours diagnosed over a 10-year period at the CHU of Marrakech. The tumours were categorized based on their clinical presentations and histopathological findings. To improve diagnostic consistency and quality, a new report template was developed based on the recommendations of the College of American Pathologists (CAP).
Results: The analysis of 98 cases revealed a diverse range of clinical and histopathological presentations. Based on this, the proposed report template, grounded in the latest recommendations from the College of American Pathologists (CAP) in 2023, aims to standardize diagnostic reporting. This approach is expected to lead to more accurate diagnoses and optimized therapeutic strategies.
Conclusion: This study emphasizes the importance of standardizing diagnostic reporting for oral cavity tumours. By implementing the proposed CAP-based report template, the quality of diagnoses and therapeutic strategies at the CHU of Marrakech can be significantly improved, ultimately leading to better patient outcomes.

E-PS-13-013
Expression of immune checkpoint regulators PDL-1, VISTA, LAG3, TIM3, Nectin-2 and CD8 in adenoid cystic carcinoma
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Background & Objectives: Adenoid cystic carcinoma (ACC) is characterized by frequent recurrence and metastasis, highlighting the need for novel therapeutic strategies, especially immunotherapies. This study aimed to evaluate the molecular characteristics of ACC cases and assess the expression of immune checkpoint markers PD-L1, VISTA, LAG3, and TIM3, as well as CD8 and Nectin-2 in tumour-infiltrating lymphocytes (TILs), to explore potential targets for immunotherapy.
Methods: We performed immunohistochemical staining for PD-L1, VISTA, LAG3, TIM3, CD8, and nectin on 27 ACC cases diagnosed between 2019 and 2025. TILs were semi-quantitatively assessed in the most densely infiltrated areas. Expression was considered high when ≥4% of TILs were positive for PD-L1, VISTA, and CD8, and >1% for LAG3, TIM3, and nectin. Retrospective molecular analyses included testing for c-erbB-2 and androgen receptor expression, microsatellite instability, BRAF, KRAS, and EGFR mutations, and gene fusions (NTRK, RET, ALK, ROS1), as well as MET amplification.
Results: Of the 27 cases (14 female, 13 male; age 34–74), high PD-L1 expression was seen in one case, VISTA in 15, TIM3 in 8, and LAG3 in 6. CD8 was highly expressed in all cases. Nectin-2 expression in TILs was absent, though a unique PDL-1 positive case showed tumour cell expression. No cases showed c-erbB-2, androgen receptor positivity, microsatellite instability, or relevant gene fusions. One case each had a BRAF exon 11 G469E mutation, a KRAS exon 2 mutation, and a BRAF V600E mutation.
Conclusion: Co-expression of VISTA, TIM3, and LAG3 was observed in 3 cases, despite no significant molecular mutations. These findings support the potential role of immune checkpoint markers in ACC and suggest that better biomarkers are needed to understand immune evasion and resistance, paving the way for personalized immunotherapy.

E-PS-13-014
Beyond HPV: the role of invasion pattern and stromal signals in oral cavity squamous cell carsinoma
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Background & Objectives: The Worst Pattern of Invasion (WPOI) has emerged as a critical histopathological parameter in oral cavity squamous cell carcinomas (OCSCC), with significant prognostic and therapeutic implications. This study evaluated the relationship between WPOI and various clinicopathological and microenvironmental features in patients with oropharyngeal carcinoma.
Methods: A retrospective cohort of 53 patients diagnosed with OCSCC was analysed. WPOI was classified into low-risk (types 1–3) and high-risk (types 4–5) categories. Associations between WPOI and key variables—including p16 status (as a surrogate for HPV association), perineural invasion (PNI), lymphovascular invasion (LVI), tumour budding, tumour-infiltrating lymphocytes (TILs), stroma-tumour ratio (STR), depth of invasion (DOI), tumour differentiation, nodal metastasis, and recurrence were evaluated using Pearson's chi-square test. Survival outcomes were assessed via Kaplan-Meier analysis with log-rank tests for statistical significance. Histopathologic parameters were evaluated in haematoxylin and eosin-stained sections.
Results: The cohort included 53 patients (26 male, 27 female) with a median age of 63.84 years (range: 41-86). High-grade WPOI showed statistically significant correlations with several adverse pathological features: perineural invasion ($p = 0.0002$), lymphovascular invasion ($p = 0.0020$), high tumour budding grade ($p < 0.0001$), stromal predominance (>50% stroma; $p = 0.0006$), poor differentiation ($p = 0.0404$), and cervical lymph node metastasis ($p = 0.0068$). However, no significant associations were found between WPOI and p16 status ($p = 0.452$), TIL density (20% cutoff; $p = 0.317$), or anatomical subsite ($p = 0.189$). Survival analysis demonstrated significantly worse outcomes for high-WPOI cases (log-rank $p = 0.0039$), while higher tumour budding showed a trend toward increased nodal metastasis ($p = 0.0166$).
Conclusion: WPOI strongly correlates with adverse features (PNI, LVI, stromal response, tumour budding) and poor survival in OCSCC, reflecting critical tumour-host interactions. These findings support integrating WPOI into routine pathology reporting and risk stratification, offering valuable HPV-independent prognostic information.

E-PS-13-016
Oropharyngeal/tonsillar NUT carcinoma – an important differential diagnosis to non-keratinizing squamous cell carcinoma
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Background & Objectives: NUT carcinoma is an uncommon and highly aggressive malignant tumour which may arise in a wide range of anatomical locations. Rare primary NUT carcinomas of the oropharynx may be misdiagnosed as HPV-associated non-keratinizing (NK) squamous (SCC) or undifferentiated cell carcinoma. We present a case of NUT carcinoma originating from the left posterior oropharyngeal wall/left tonsil, with cervical nodal metastases, which displayed morphological features overlapping with NK-SCC, both on cytology and histomorphologically.
Methods: Histology from the oropharyngeal tumour showed nests of medium-sized neoplastic cells with surrounding inflammation and central necrosis. The tumour cells displayed monotonous nuclei, increased nuclear-to-cytoplasmic ratios, vesicular nuclei, prominent nucleoli, and brisk mitotic activity. No keratinization was identified. An enlarged left level 2 cervical lymph node underwent fine-needle aspiration biopsy, which contained tumour cells arranged in syncytial crowded sheets and occasionally dispersed singly, with scattered atypical, keratinized and non-keratinized tumour cells, with necrotic and karyorrhectic debris in the background.
Results: On immunohistochemistry (IHC), the tumour cells in both the oropharynx tumour and cervical lymph node showed p63/p40 expression and focal p16 positivity. Given the tumour origin, relatively monotonous appearance of the cells, and lack of distinct light microscopical squamous differentiation, an impression of metastatic HPV-associated NK-SCC was entertained. However, the absence of block-positive p16 expression prompted further IHC testing, and we detected diffuse speckled nuclear positivity for NUT in the tumour cells in both sites.
Conclusion: Oropharyngeal NUT carcinoma is a rare neoplastic event entity that can be easily missed and misdiagnosed as other more common cancers of the oropharynx. Given the highly aggressive nature and poor prognosis compared to oropharyngeal HPV-associated NK-SCC, this distinction is of utmost clinical importance. Awareness that NUT carcinoma may arise in the oropharynx and applying IHC for NUT is critical in avoiding this mistake.

E-PS-13-018
The periostin immunoexpression in histological preparation of 100 nasal polyps
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Background & Objectives: Periostin is an extracellular matrix protein that contributes to the remodelling of the upper respiratory system in chronic rhibosinusitis (CRS). Our aim is to investigate the periostin in nasal polyps (NPs).
Methods: NPs from 100 patients were studied. The positivity and intensity of periostin immunoexpression was evaluated. Detection of periostin was performed with the rabbit polyclonal anti-periostin anti-rabbit antibody from Abcam International Inc. (Cambridge, UK, ab14041) at a dilution of 1:100.
Results: The immunostaining score was calculated for each case using H-score with values ranging from 0 to 300 and was calculated by multiplying the percentage of positively stained cells by the staining intensity using the following formula: [1× (% weakly positive area) + 2× (% moderately positive area) + 3× (% strongly positive area)]. The results were then divided into three categories, <100, 100-200 and >200. 58% of the selected patients were male and 42% female. From the histopathological data, 70% of nasal polyps belonged to the oedematous, 20% to the adeno-cystic (ductal) and 10% to the fibrous type respectively. Periostin was expressed in all samples. The total mean immunostaining score was 136,1. 10% of nasal polyps had > 200, 68% 100- 200 and 22% <100 H-score.
Conclusion: Periostin is highly expressed in chronic Th2 inflammation such as asthma and its overproduction in the nasal mucosa is reported to contribute to polyp formation (Stankovic KM, 2008). Periostin is involved in inflammatory procedures in nasal polyps and appears to be a novel molecular biomarker for the categorization of CRS into at least 2 distinct molecular endotypes. Based on our study, periostin may serve as a new target for future therapeutic interventions in CRS with nasal polyps.

E-PS-13-020
Salivary gland tumour with ductal differentiation: A rare malignancy with HMGA2: WIFI fusion mimicking secretory carcinoma
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Background & Objectives: Salivary gland neoplasms are a diverse group of tumours with ductal and myoepithelial differentiation and varying stromal features. Their overlapping histological and immunohistochemical characteristics can challenge pathologists in making accurate diagnoses. Recent studies have explored their molecular characteristics for diagnostic purposes. Notably, the HMGA2:WIF1 fusion was identified in pleomorphic adenomas of the parotid gland, which resemble canalicular adenomas and have a greater risk of recurrence and progression to carcinoma. Secretory carcinoma, a rare tumour featuring the ETV6-NTRK3 fusion, and its differential diagnosis includes mucoepidermoid carcinoma, salivary duct carcinoma, pleomorphic adenoma, and acinic cell carcinoma. This study aims to highlight a case of salivary gland tumour initially diagnosed as secretory carcinoma, later identified as a different malignancy due to molecular analysis
Methods: A 75-year-old woman with a slow-growing mass in the left parotid gland underwent a left subtotal parotidectomy. Imaging showed a multilobulated lesion measuring 1.4 x 2.4 x 2.2 cm. Histology revealed an epithelioid neoplasm extending beyond the capsule, with duct formation and eosinophilic secretions. Immunohistochemistry showed strong CK7, Sox10, and patchy mammaglobin positivity, initially diagnosed as secretory carcinoma. However, molecular testing identified the HMGA2-WIF1 fusion, reclassifying the diagnosis to an HMGA2 rearrangement salivary gland tumour, consistent with a benign ductal adenoma or pleomorphic adenoma.
Results: The HMGA2-WIF1 fusion reclassified the tumour from secretory carcinoma to a salivary gland tumour with an HMGA2 rearrangement, resembling a benign ductal adenoma or pleomorphic adenoma. This molecular finding clarified the diagnosis, which would have otherwise been missed
Conclusion: This case underscores the importance of molecular testing in diagnosing salivary gland tumours, particularly when histological and immunohistochemical findings are ambiguous. The HMGA2-WIF1 fusion reclassification highlights the need for combining histological, immunohistochemical, and molecular approaches to accurately diagnose these challenging tumours. Molecular profiling can prevent misdiagnosis and guide appropriate treatment, improving patient outcomes

E-PS-13-022
High grade sinonasal adenosquamous carcinoma with focal ciliated and apocrine features
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Background & Objectives: Sinonasal Adenosquamous carcinoma is rare. Further clinicopathologic studies should be considered.
Methods: 48-year-old Chinese female nonsmoker nondrinker presented with facial pain and intermittent epistaxis. No occupational exposure to leather or wood dust was present. Patient had history of Asthma and Graves disease on Carbimazole. Nasal endoscopy showed mass involving inferior turbinate long the nasal floor. MRI showed tumour epicentre at the medial wall of left maxillary sinus infiltrating into the nasal cavity. Patient underwent left maxillectomy and left level I-V lateral neck dissection. Histology showed poorly differentiated non-keratinizing carcinoma with formation of nests and islands with areas of comedonecrosis. Focal squamous differentiation with keratinization in some solid nests and areas of glandular lumina formation with focal ciliated and apocrine features were seen. No goblet cells or sinonasal papilloma component seen. Tumour infiltrated into subcutaneous tissue through the maxillary wall (pT3). Perineural invasion was noted. No lymph node metastases were seen. Resection margins were close.
Results: Immunostaining profile:
AE1/3- moderate to strong positive staining
P40- positive in squamous areas
Androgen Receptor- patchy positive within solid nests and areas of apocrine differentiation
GATA3, Desmin, NKX2.2, NUT and p16 were negative.
SMARCA4 (BRG1) and SMARB1 (INI1) were intact.
Conclusion: High Grade Sinonasal carcinoma with glandular and squamous differentiation are rare. Unusual features such as presence of Ciliated tumour cells as well as apocrine differentiation were seen. The differential considered included apocrine adenocarcinoma of minor salivary gland origin however GATA3 was negative. Postresection patient received proton beam (radiation) therapy and is currently disease free at 3 months follow up. PET scan did not show any evidence of metastasis. The prognosis of Adenosquamous carcinoma, in general, has been found to be worse than that for conventional Squamous Cell Carcinoma (SCC) or HPV associated SCC. These cases should be studied further for appropriate classification, further refining treatment and prognostication.

E-PS-13-023
Case report: GNAQ mutation in a blue nevus of the nasal cavity
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Background & Objectives: A common blue nevus typically presents as a blue-black macule or papule, often found on the extremities. Histologically, it is made up of elongated melanocytes containing cytoplasmic melanin within the dermal collagen in the mid and upper dermis. Molecular profiling of a common blue nevus may identify GNAQ or GNA11 mutations and immunohistochemistry (IHC) is often positive for SOX10, HMB45, MelanA/MART1, and S100. Here, we describe a case of a blue nevus of the nasal cavity in a 25-year-old female which was found to have a GNAQ Q209L variant.
Methods: The clinical, microscopic, immunohistochemical, and molecular features were reviewed. Next-generation sequencing (NGS) had been performed using the Ampliseq for Illumina NGS panel on the Illumina MiSeq instrument.
Results: This patient had a longstanding and increasingly firm pigmented lesion on the right caudal medial septum on the mucocutaneous junction. Histologically, the lamina propria to the deep margin contained a heavy melanocytic pigmentation of macrophages and a fascicular proliferation of spindled and epithelioid cells, also with pigmentation. There were intervening bands of thick collagen. IHC showed positivity of the spindled cells for SOX10 and MelanA/MART1, with focal HMB45 staining, and low Ki67 labelling (<2%). BRAF IHC (for V600E mutation) was negative. Beta catenin IHC was normal. Molecular testing by NGS was positive for GNAQ variant Q209L (18% allele frequency). Activating variants in GNAQ, almost always present at Q209, occur in up to 83% of blue nevi and up to 46% of uveal melanomas.
Conclusion: This rare finding within the nasal cavity may have diagnostic and therapeutic implications, including the consideration of metastatic uveal melanoma, a tumour which often has activating GNAQ and GNA11 variants. To the authors' knowledge, this is the first study to characterize the molecular profile of a blue nevus within the nasal cavity, thereby broadening our understanding of these lesions.

E-PS-13-024
Assessment of tumour-infiltrating lymphocytes predicts the behaviour of oral tongue cancer: which cut-off to choose?
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Background & Objectives: The role of the tumour microenvironment in cancer prognosis has sparked interest among pathologists in recent years. Immune infiltrates around tumours have been worldwide studied. However, routine pathology reports do not assess the immune response in oral tongue carcinoma (OTC). Therefore, it is clinically important to identify histopathological criteria that can effectively evaluate the immune response. This study aims to evaluate tumour-infiltrating lymphocytes (TILs) in OTC to determine whether TILs is a prognostic factor, and to identify which cut-off point would be most useful.
Methods: We report 67 cases of OTC diagnosed at department of pathology B of Oncology Institute of Tunis during 8years. Lymphocytic infiltration was assessed according to the recommendations of the International Immuno-Oncology Biomarker Study Group (IIOBSG) for the evaluation of lymphocytes infiltrating solid tumours. To facilitate the interpretation of the results, TILs were classified into two categories using cut-off points of 30% and 60%.
Results: The distribution of TILs patterns showed that 75% of cases had TILs<30%, while 25% had TILs>30%. Survival analysis revealed that TILs>30% was associated with better overall survival(OS), although this was not statistically significant (p=0.36). The mean OS for TILs>30% was 85 months, compared to 74 months for TILs<30%. On the other hand, 94% of cases had TILs<60%, and 6% had TILs>60%. Survival analysis showed that TILs>60% was not associated with better prognosis. The mean OS for TILs >60% was 46 months, compared to 47months for TILs<60%.
Conclusion: In conclusion, this study represents the first evaluation of TILs in OTC in our institution. The method introduced by the IIOBSG can be used for the standardized determination of TILs in OTC. A cut-off of 30% is more reliable than a cut-off of 60%. Further studies with larger cohorts are required to validate these findings and clarify the role of TILs in OTC management.

E-PS-13-025
A Morphomolecular perspective on a rare phenomenon: malignant melanoma in the tonsil
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Background & Objectives: Malignant melanoma (MM), one of the deadliest skin cancers, may rarely occur in mucosa either as a primary or metastatic tumour. To date, less than 50 cases of primary/metastatic tonsillar MM have been reported.
Methods: Here, a case of malignant melanoma located in the right tonsil is presented.
Results: A 67-year-old man who had previously been diagnosed with acral lentiginous MM on the right heel presented with complaints of weight loss and difficulty in swallowing 16 years after the initial diagnosis. A 4.5 cm, black, indurated mass was detected on the right tonsil in physical examination. The patient underwent tonsillectomy. In microscopic examination, a tumour infiltrating the tonsil mucosa and submucosa with spindle and epithelioid morphology, containing brownish pigment was detected. The tumour was positive for HMB45, Melan-A, Sox10, and negative for Keratin. Then, next generation sequencing (NGS) was performed to reveal any mutations that might be targeted during therapy. However, no mutation was detected.
Conclusion: Considering the previous history of MM, the tumour in this case represents a metastatic lesion. Mucosal metastasis of skin melanoma, including metastatic tonsillar melanoma is rare. However, it should be kept in mind in differential diagnosis in cases diagnosed with melanoma, even in the long-term follow-up.

E-PS-13-027
Splenic metastasis of parotid acinic cell carcinoma
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Background & Objectives: Acinic cell carcinoma is a salivary gland neoplasm representing around 10% of all salivary gland malignancies, developing in the parotid gland in 85% of cases. Despite most cases having a favourable prognosis, as evidenced by mean 5-year-survival rates of approximately 95-97.2%, the prognosis worsens considerably with the presence of distant metastasis, dropping survival rates to around 22%. Acinic cell carcinoma most commonly metastizes via lymphatic spread and is more frequent in high-grade tumours.
Splenic metastases are rare and of hematogenous origin, as the spleen has no afferent lymphatic vessels. In this report we present a rare case of splenic metastasis of acinic cell carcinoma.
Methods: We report the case of a 53-year-old man with history of acinic cell carcinoma of the parotid gland for which he was surgically interventioned in 2018 and followed at the Instituto Português de Oncologia de Coimbra, with evidence of disease progression in 2024 in the form of lung and bone metastases, as well as a single splenic metastasis which was surgically excised.
Results: We received a surgical specimen of total splenectomy weighing 310g, measuring 13.5 x 10.5 x 4.5 cm with a smooth and continuous capsule. On cut section exhibits a heterogeneous nodule with 1.5 x 1.3 cm, with white and pink areas, tangential to the capsule.
On microscopic examination we observed an expansive nodule of acinic cells with central haemorrhage within the splenic parenchyma. The acinic cells showed diffuse and strong immunoreactivity to DOG1, focal, heterogenous staining for EMA and SOX-10, and no staining for p40.
Conclusion: As acinic cell carcinoma typically metastasize via lymphatic spread, this case is evidence of hematogenous spread to the spleen, highlighting the need for a more thorough staging process, particularly in the case of high-grade tumours.

E-PS-13-028
SMARCA4 deficient malignancies of the head and neck region: focusing on 6 new cases of SMARCA4 deficient carcinomas
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Background & Objectives: SMARCA4-deficient neoplasms are rare and highly aggressive malignancies characterized by inactivation or

loss of the SMARCA4 gene, which encodes BRG1, a core component of the SWI/SNF chromatin remodelling complex**.** These neoplasms exhibit a pattern-based association with specific cancer types rather than a random cancer distribution. In the head and neck (H&N), SMARCA4-deficient malignancies include SMARCA4-deficient sinonasal carcinoma and most of the teratocarcinosarcomas. Only one case of SMARCA4 deficient carcinoma was reported outside the sinonasal region.
Methods: Six cases of SMARCA4-deficient carcinomas of the H&N, were identified in the authors' archives. Their clinicopathological features were reviewed and documented. All cases with available tissue block were investigated by molecular genetic methods.
Results: The cohort consisted of six new cases localized in sinonasal (3/6) and non-sinonasal locations (3/6). The non-sinonasal tumours were present in the tongue, oral floor and the upper jaw submucosa, affecting 66- and 81-year old men and 61-years old woman, respectively. Lymph node metastasis were documented in two cases. Histologically, two cases were poorly differentiated malignancies with small cell morphology and one case showed morphology resembling salivary duct carcinoma. A novel fusion *SLC66A1::PLCB1 (exon 1::exon 31)* was found in one case, one case showed multiple copy number variations and in the third case had *KRAS* gene mutation.
Conclusion: The presence of SMARCA4-deficient carcinoma in the H&N outside the sinonasal tract is extraordinary**.** We present 3 cases of sinonasal SMARCA4-deficient carcinomas and three new cases outside the sinonasal tract widening the topographic distribution of SMARCA4-deficient carcinomas. These tumours are highly aggressive and are often diagnosed at an advanced stage. In the sinonasal region, they can mimic olfactory neuroblastoma, while in other head and neck sites, they may resemble neuroendocrine carcinoma. SMARCB1 immunohistochemistry is essential for evaluating poorly differentiated neoplasms throughout the head and neck to ensure accurate diagnosis.

Funding: This study was in part supported by study grant SVV 260652 from the Ministry of Education, Czech Republic, the Cooperatio Program, research area SURG, and the project National Institute for Cancer Research – NICR (Programme EXCELES, ID Project No. LX22NPO5102) - Funded by the European Union - Next Generation EU

E-PS-13-029

Human papillomavirus infection as a prognostic factor in carcinomas of the oral cavity

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Background & Objectives: Oral cavity squamous cell carcinomas account for 0.8% of cancers according to the North Tunisia Cancer Registry and affect more men than women. The main risk factors are alcohol and tobacco use. Human papillomavirus (HPV) infection is also a risk factor for squamous cell carcinoma (SCC). Its detection can be performed using various techniques. This study aims to determine whether p16 expression is a prognostic factor.
Methods: The is descriptive and retrospective study, including 60 cases of oral cavity SCC collected in Pathology Department B of the Salah Azaiez Institute over 11 years, from January 2012 to November 2022. It examines clinical features and histological features, alongside p16 expression determined by immunohistochemistry.
Results: The mean age of patients was 64 years [18-85], with a sex ratio of 2.75. Tumour locations were as follows: 23% lip, 12% cheek, 13% palate, 13% gum, and 38% tongue. p16 positivity was statistically correlated with gum location ($p = 0.023$). Alcoholic and/or tobacco use was present in 49% of cases. 18% of cases tested positive for p16, with intense staining in 80% of cells in 3 cases and in 100% of cells in the remaining 8 cases. Regarding patient follow-up, 20% had recurrences after treatment, with only one case of metastatic relapse, and 5% of patients died. P16 positivity was statistically associated with the absence of recurrence ($p<0.000$), but it was not correlated with lymph node metastasis or mortality.
Conclusion: HPV infection remains an emerging factor in squamous cell carcinoma of the oral cavity. However, in our country, it is still preceded by other major risk factors such as smoking and alcohol consumption. Our study demonstrates that HPV-infected patients have a better prognosis and fewer recurrences. Further investigations using other tools, such as PCR or in situ hybridization, should be conducted to confirm HPV infection.

E-PS-13-030

Immunohistochemical study of p16 in sinonasal carcinomas and correlation with anatomo- clinical and prognostic factors

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Background & Objectives: Sinonasal squamous cell carcinomas (SCC) are rare malignancies that arise in the nasal and paranasal regions, with a complex aetiology influenced by factors such as tobacco and alcohol use, as well as potential viral infections like Human Papillomavirus (HPV). However, the role of p16 expression, which is often linked to HPV infection, in sinonasal SCC remains poorly understood. This study explores the overexpression of the tumour suppressor protein p16 in sinonasal carcinomas and its correlations with clinical and prognostic factors.
Methods: This is a monocentric, descriptive, cross-sectional, and retrospective study that includes 32 Tunisian patients with sinonasal SCC, collected at the Pathology Department B of the Salah Azaiez Institute from 2010 to 2022. It examines clinical features (age, sex, tobacco/alcohol use, tumour characteristics) and histological features (subtypes, degree of keratinization), alongside p16 expression determined by immunohistochemistry.
Results: The average age at diagnosis was 60 years, with a male predominance. The tumour stage was advanced in 69% of cases, and the average tumour size was 48 mm. Tobacco use was observed in 37% of cases, and alcohol-tobacco use was noted in 19% of cases. In this study, 31% of cases were p16-positive. No association was found between p16 overexpression and age, gender, tobacco use, alcohol-tobacco use, tumour size, clinical tumour stage (T), presence of lymphadenopathy, or distant metastases. However, the histological types of adenoid cystic morphology and non-keratinizing subtypes were significantly associated with positive p16 expression ($p=0.006$, $p=0.03$).
Conclusion: p16 overexpression is statistically more commonly observed in adenoid cystic morphology and non-keratinizing squamous cell carcinoma. These results suggest that histological morphology may provide insight into p16 status and, by extension, HPV status. Further investigations using additional tools, such as PCR or in situ hybridization, should be conducted to confirm HPV infection.

E-PS-13-031

Aberrant expression of IRF1 promotes the proliferation and tumorigenicity of oral squamous cancer cells

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Background & Objectives: Interferon regulatory factor 1 (IRF1) is a transcription factor that belongs to the family of interferon regulatory factors. IRF1 plays regulatory roles in type I interferon production, lymphocyte development, and immune responses. Some studies show the antitumor properties of IRF1 in different cancer types. However, its tumour-promoting effects have also been reported. It is unclear what the expression profile and functional role of IRF1 are in oral squamous cell carcinoma (OSCC).
Methods: We initially examined the immunoexpression of IRF1 protein in 40 paraffin-embedded OSCC tissue samples, including tumour and non-cancer epithelial tissues, from our archives. Next, we performed the RNA-sequencing and western blot analysis of OSCC cell lines, including OECM-1, SAS, and HSC-3, comparing them to immortalized human oral keratinocytes (HOK). We further knocked down IRF1 expression in OECM-1, SAS, and FaDu cells to determine the potential of IRF1 to affect OSCC proliferation, migration, and invasion capability in vitro.
Results: IRF1 was primarily detected on the cell membrane and cytoplasm of OSCC cells, with increased nuclear staining in strong immunoreactivity. In thirty-three patients with paired normal and cancerous tissues, IRF1 showed greater positive expression in tumours than in normal epithelia. However, there was no significant difference between the survival times and IRF1 expression in 40 patients. A heat map showed the relative expression of *IRF1-3*, *IRF5-7*, and *IRF9* genes. Among *IRF* genes, only the *IRF1* gene was highly expressed in all three OSCC cells. Western blot analysis further indicated that OSCC cells exhibited a higher level of IRF1 proteins than HOK. Decreased cell proliferation in IRF1-knockdown OECM-1, SAS, and FaDu cells was found, and silencing IRF1 expression in those cells also reduced cell migration and invasion.
Conclusion: Our results suggest that IRF1 may serve as a prognostic biomarker associated with the tumorigenesis and aggressiveness of OSCC.

E-PS-13-032

Pd-L1 expression in head and neck squamous cell carcinomas (HN-SCC)

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Background & Objectives: PD-L1 molecule responsible for immune evasion, and p16, a surrogate marker of HPV. Study aimed to assess expression of PD-L1 in HN-SCCs. Authors studied PD-L1 expression in tumour and tumour infiltrating lymphocytes with clinico-pathologic parameters:age, gender, histologic subtype, histologic grade, nodal status, stage, lymphovascular and extranodal extension; & compared PD-L1 expression in HPV-positive and HPV-negative HN-SCCs using p16 immunohistochemistry.
Methods: IHC for PD-L1 was evaluated using combined proportion score (CPS). CPS ≥1:low positive,CPS ≥20:strong positive. CPS <1 or no expression in tumour or immune cells was scored as negative. Diffuse and strong nuclear and cytoplasmic expression of p16 in ≥70% tumour cells was considered positive (block) expression.
Results: Total 188 cases of HN-SCCs were included. Buccal mucosa(49%) was the commonest site.Of n=188 cases, 162(87%) showed PD-L1 positivity and 26(13%) did not show PD-L1 expression. In well-differentiated SCCs 69.6%(n=16) showed a CPS score >20, and in high-grade (moderate & poorly-differentiated SCC),66.1% (109)showed a CPS>20. 29 (17.1%) were low positive and 27(16.4%) were negative.A p-value of 0.894 was observed, suggesting no significant statistical correlation with PD-L1 expression with tumour grade. Among early stages (pT1&pT2), 47 (59.5%) were strong positive,15 (19.0%) were low positive and 17 (21.5%) were negative for PD-L1. Among advanced stage (pT3&pT4),78 (71.6%) were strong positive,17(15.6%) were low positive and 14 (12.8%) were negative for PD-L1 withp-value of 0.182 suggesting no significant statistical correlation between PD-L1 expression and tumour stage.Among 136 cases with p16 positivity, 91 were strongly positive for PD-L1,20 were low positive and 20 were negative for PD-L1 with no significant statistical correlation between p16 and PD-L1.
Conclusion: In current era of personalized cancer treatment & targeted immunotherapy role of PD-L1 is becoming relevant in management of HN-SCC.Studies with a bigger sample size are required to establish correlation of PD-L1 with clinico-pathological parameters and HPV association especially in Indian population.

E-PS-13-033

Craniofacial vascular malformation with *PIK3CA* activating mutation in a 15-year-old patient

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Background & Objectives: Vascular malformations are congenital anomalies arising from defects during vascular development. *PIK3CA* mutations, known to drive overactivation of the phosphoinositide 3-kinase (PI3K)/AKT pathway, have been implicated in a subset of vascular malformations, with potential therapeutic implications. We report a case of a 15-year-old male with a combined lymphatic and venous malformation harbouring an activating/oncogenic *PIK3CA* mutation, discussing its histopathological characteristics and clinical relevance.
Methods: A 15-year-old male presented with multiple polycystic lesions in the right frontal and orbital region. Biopsy of the lesions was performed, which was sent for histopathological examination, followed by targeted next-generation sequencing (NGS). Haematoxylin-eosin, histochemical, and immunohistochemical stained sections were examined. Molecular profiling was performed using the Oncomine Precision Assay on a Genexus Integrated Sequencer (CE-IVD).
Results: Microscopic examination revealed thin-walled lymphatic and venous-type vascular formations of various size and shape, within fibroadipose and striated muscle tissue. Lymphatic-type vascular formations were lined by a layer of podoplanin (D2-40)-positive endothelial cells. Venous-type formations exhibited a well-developed, continuous smooth muscle wall, whereas lymphatic-type formations had only focal smooth muscle fibres within their walls, as demonstrated by Masson's trichrome histochemical staining and caldesmon immunohistochemistry. No cytologic atypia, pleomorphism, or mitotic activity were observed. NGS analysis demonstrated an oncogenic *PIK3CA* p.H1047R (c.3140A>G) mutation, a hotspot variant in the kinase domain of the catalytic subunit of PI3K known to activate the PI3K/AKT pathway. This mutation has been reported in vascular malformations and is druggable with AKT (miransertib) and PI3K (alpelisib) inhibitors. No additional pathogenic variants were detected.
Conclusion: This case underscores the role of *PIK3CA* mutations in vascular malformations and their potential therapeutic relevance. Molecular profiling in vascular anomalies can guide therapeutic

decisions, offering new treatment avenues for patients with refractory or symptomatic lesions. Further research is needed to establish standardized molecular-driven treatment strategies for these conditions.

E-PS-13-035

EBV-positive mucocutaneous ulcer: a case report

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Background & Objectives: Epstein-Barr virus-positive mucocutaneous ulcer (EBVMCU) is a rare, indolent B-cell lymphoproliferative disorder, first described in 2010 by Stefan D.Dojcinov et al., characterized by solitary or multiple ulcers in the oral cavity, skin, gastrointestinal tract. It is often associated with immunosuppression, aging, or underlying immunodeficiency.
Methods: **Case report:** A 56-year-old woman presented with a persistent, non-healing ulcer on her buccal mucosa. The ulcer was approximately 1.5 cm in diameter, with a fibrinous base and irregular borders. The patient reported no significant medical history. An incisional biopsy was performed. Histopathological examination revealed a dense polymorphic inflammatory infiltrate including abundant lymphocytes, polyclonal plasma cells, scattered histiocytes, neutrophils and eosinophils. Among these, numerous large cells with vesicular nuclei, sometimes lobulated, and a prominent nucleolus were recognized, resembling Hodgkin-Reed Sterberg cells. These were positive to CD30, CD20, MUM-1 and EBV (LMP-1 protein) but negative to CD3, CD5, CD15 and Bcl-6. The histological findings in relation with the clinical information and the absence of lymphadenopathy, were compatible with an EBV-positive mucocutaneous ulcer. Further testing showed no evidence of systemic EBV-associated lymphoproliferative disorders.
Results: **Discussion:** EBVMCU is a challenging diagnosis due to its rarity and variable clinical presentation. The differential diagnosis includes lymphoma, squamous cell carcinoma, and other infectious or inflammatory processes. The diagnosis of EBVMCU may be a challenge to pathologists, as the presence of large pleomorphic cells are suggestive of malignant lymphoproliferative processes, such as classic Hodgkin lymphoma, DLBCL associated or not with EBV, anaplastic large cell lymphoma (ALCL) or lymphomatoid granulomatosis. The absence of a clear immunodeficiency state in this case is noteworthy, highlighting that EBVMCU can occur in immunocompetent individuals.
Conclusion: This case underscores the importance of considering EBVMCU in the differential diagnosis of persistent mucocutaneous ulcers, even in the absence of overt immunosuppression. Comprehensive histopathological and immunohistochemical evaluation is essential for accurate diagnosis.

E-PS-13-036

A pathological series of 30 ameloblastoma

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Background & Objectives: Ameloblastoma is defined as an odontogenic tumour. classified as benign, it behaves in a localy agressive maner and it's tendancy to recur. Pathology plays a key role not only in diagnosing but also prognosing by providing critical insights related to histological characteristics that can influence the treatment strategy .in this presentation we collected 30 cases from our pathology department from January 2023 to december 2024, we show case the distribution according to sexe, age, histological sub-types and other variables.
Describe the epidemiological and pathological profile of ameloblastoma.
Methods: For our describtive study, we collected a series of 30 cases including: 17 mandibulectomy specimens, 3 maxilectomies and 10 biopsies.
Results: - The males were commonly involved with a sex ratio of 1.72.
- The affected age group : 20 to 55 years old . mean age 35 yo.
- 05 cases of ameloblastoma unicystic type and 20cases of peripheral type.
- The histological types of ameloblatome found were:
follicular sub-type (22 cases), plexiform (3 cases), desmoplasic (2 cases), acanthomatous (2 cases).
metastatic ameloblastoma (1 case).
- No intravascular tumour emboli was found nor perineural invasion.
- 04 cases only involved spongy bone invasion.
- The R- classification resection results shows: -10 cases of R-2,06 cases of R-1 and 14 cases of R0.
Conclusion: Ameloblastoma is a frequent bone lesion, considering its radiological aspcets wich lacks pathognomonic features, it's diagnosis remains histological.

E-PS-13-040

Lymphoid stroma in a salivary gland pleomorphic adenoma case

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Background & Objectives: Pleomorphic adenomas (PAs) are common benign salivary gland tumours mostly situated in the superficial lobes of the parotid glands. We present a unique case of a PA with lymphoid stroma.
Methods: A 77-year-old female presented to the Oro-Maxillo-Facial Surgery Department, City Hospital of Timisoara, with a right parotid painless mass. A resection of the mass with tumour-free margins was performed. The patient was previously surgically treated for a synchronous squamous cell carcinoma of the gingivae of the left oral cavity.
Results: Macroscopically the tumour was a circumscribed 4.5/3/1.6 cm, white elastic mass with irregular capsule. The microscopic examination revealed a tumour with a mixture of myoepithelial cells, ductal cells and extracellular stroma. The stromal component was myxochondroid and rich in lymphoid cells. The histochemical examination with Periodic-Acid-Schiff (PAS) revealed positive stain within the lumen of ductal areas of the PA. Slides were stained immunohistochemically for CD20, CD3, CD8, and Multi (AE1/AE3) antibodies. The epithelial areas show a positive reaction for cytocheratins. In the lymphoid component, there were a population of cells positive for CD20, CD3 and CD8. The population of CD8 and CD3 positive cells was quantitatively richer than the CD20 positive one.
Conclusion: To best of our knowledge, this is the first case of PA with a lymphoid stromal component reported in the English language literature.

E-PS-13-041

Endoglin expression in vascular endothelial cells and its role in angiogenesis and pathogenesis of nasal polyps

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Background & Objectives: CD105/Endoglin, is a transmembrane glycoprotein and ancillary receptor of TGF-β, mainly expressed on

vascular endothelial cells. Antibodies against CD105 react preferentially with endothelial cells in tissues with active angiogenesis. Thus CD105 is a valuable angiogenic biomarker in the diagnosis and prognosis of cancer. CD105 is also related to inflammatory diseases: its expression is strongly upregulated in endothelial cells of inflammed tissues.Vascularity is a prognostic indicator of inflammation. Aim of this study is to evaluate the vascularity in histological preparation of 100 nasal polyp tissues.
Methods: Tissue from 100 operated patients was used for evaluation of the nasal polyp vascularity. The polyclonal anti-CD105 antibody was used. Then, the vascularity was assessed by counting CD105-stained vessels and calculating the Microvessel Density (MVD), through a Digital Image Analysis System, in order to obtain more objective results.
Results: CD105 was expressed in all tissue samples. Nasal polyps were associated with a high MVD, as revealed by CD105 immunostaining; the mean MVD value was 19,65.Of the total number of vessels counted in each section, the average number of small vessels was 90,45, while the average number of large vessels was 38,27.Moreover, the diameter of small vessels (min vessel area) ranged from 10 to 45 μm, with an average of 20,62 μm, while the diameter of large vessels (max vessel area) ranged from 87 to 1615 μm, with an average of 405,81 μm, respectively.
Conclusion: Recently, a significant association was found between CD105 expression and the size of nasal polyps, hypothesizing a role for CD105 and angiogenesis in the development of chronic rhinosinusitis with nasal polyps (CRSwNP). This study supports that CD105 expression in vascular endothelial cells may contribute to the angiogenesis and pathogenesis of nasal polyps.

E-PS-13-042

A challenging case of giant oral undifferentiated pleomorphic sarcoma uncovering a novel *SPECC1L::TERT* gene fusion

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Background & Objectives: Undifferentiated pleomorphic sarcoma (UPS) is a type of soft tissue sarcoma consisting of a patternless growth of pleomorphic bizarre tumour cells without identifiable line of differentiation. It can rarely involve the maxillo-facial region, constituting both a diagnostic and therapeutic challenge. Herein, we report a novel case of UPS of the oral cavity, characterized by exceptionally large size, aggressive clinical course and novel molecular finding, further deepening our knowledge about this entity.
Methods: Patient's clinical history was retrieved. Tissue samples were formalin-fixed and paraffin-embedded. Haematoxylin-eosin and immunohistochemical stainings (including CKAE1/AE3, CKMNF116, EMA, p63, p40, vimentin, SMA, SMMS-1, desmin, CD10, CD34, ERG, Melan-A, S-100, MDM2) along with RNA-based NGS were performed. A comprehensive literature review was conducted on public scientific databases (2002-present) to contextualize our findings.
Results: A 54-year-old woman presented with a rapidly enlarging, 10 cm oral mesenchymal neoplasm involving the left maxilla, unresponsive to neoadiuvant chemotherapy. Complete surgical excision was performed. Histopathology revealed a high-cellular, necrotic mass, composed of highly pleomorphic cells with brisk mitotic activity, arranged in a vaguely storiform pattern. Immunohistochemistry didn't show a specific lineage of differentiation, revealing an "only vimentin" positive phenotype; Ki-67 was 80%. RNA-based NGS found a novel gene fusion transcript: *SPECC1L::TERT*. After 6 months, patient is disease-free.
Conclusion: Only 53 oral UPSs have been reported so far. Male predominance, geographic predilection for middle-east Asia, history of trauma and aggressive course are common features. Differential diagnosis requires exclusion of other mesenchymal/non-mesenchymal neoplasms. Although complete surgical resection is critical, the role of chemotherapy remains undefined. Our case represents the largest documented oral UPS and, for the first time, NGS molecular evaluation was performed, with the discovery of *SPECC1L::TERT* gene fusion. While its functional implication requires further investigation, its identification provides new insights into the molecular pathogenesis of UPS, potentially informing future targeted therapies for this aggressive neoplasm.

E-PS-13-043

The role of chemokine receptors in salivary gland tumours

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Background & Objectives: Chemokine receptors (CRs) are G-protein-coupled-receptors that play a key role in the recruitment of immune cells, tumour progression and metastasis. Tumour cells exploit chemokine receptors to create a favourable microenvironment for immune evasion, angiogenesis, and therapy resistance. Data concerning chemokine receptors in salivary gland tumours are sparse. Therefore, we designed this study to comprehensively study the mRNA expression profile of 10 CRs in our cohort of salivary gland tumours.
Methods: We performed mRNA profiles of 10 CRs (CCR1, CCR2, CCR3, CCR4, CCR6, CCR8, CCR9, CXCR4, CXCR6, and CXCR7) of 70 paraffin-embedded salivary gland tumours by a semiquantitative realtime-PCR. Non-neoplastic lymphatic tissue specimens (tonsils, lymph nodes) known to express all the CRs were included as positive controls.
Results: The mRNA levels of the 10 CRs were detectable in nearly all included salivary gland tumours. Interestingly, no significant differences were observed between squamous and glandular tumours. However, hierarchical cluster analysis revealed two distinct tumour clusters: one characterized by high expression of the investigated CRs and the other by low expression. Moreover, survival analysis indicated that low expression of CCR6 and CCR10 was associated with shorter survival, confirming already published data.
Conclusion: Our data indicates that the expression patterns of the CRs are not influenced by the subtype of salivary gland tumour. Furthermore, we showed that hierarchical clustering identified two tumour groups based on CR expression, suggesting biological heterogeneity. Notably, low CCR6 and CCR10 expression correlated with reduced survival, highlighting their potential prognostic value. These findings warrant further investigation into the role of CRs as therapeutic targets.

E-PS-13-044

Palisading adenocarcinoma of the sublingual gland: a report of two cases of a recently described entity

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Background & Objectives: In recent years, a new tumour named palisading adenocarcinoma, which is characteristically and uniquely located in the sublingual gland and has a unique histological pattern, has been described. We would like to report two cases from more than one centre in Türkiye to better define the demographic and histopathological features of this particular type of carcinoma.
Methods: Two female patients, aged 39 and 54 years, presented with sublingual masses located in the floor of the mouth. MRI showed a mass not clearly demarcated from the normal sublingual gland for the first case and a well delineated mass for the second case. Macroscopically the mass dimensions were 3x3x2 cm and 2x2x1.8 cm. The capsule structure could not be clearly evaluated macroscopically in the first case. The second case was described as a well-circumscribed, solid encapsulated mass.
Results: Histopathological examination shows that both tumours are composed of 2 cell components. First and dominant component were consisted of cells with predominantly round, pale eosinophilic cytoplasm, prominent nucleoli and some nuclei has shown salt-pepper chromatin-like appearance. Secondary component was consisted of tubule forming cells and some irregular single infiltrating cells with small cytoplasm. Dominant component formed trabecular, mostly solid nests, palisading array around the nests and pseudorosette formation in some areas. While chromogranin, synaptophysin, S100, Sox10, INSM1 expression was not observed in the first component, CD56 was diffusely positive. Strong CK(AE1/AE3) positivity is observed in the ductal components and pale diffuse positivity in the other component. No mutation is observed in the Pan Cancer Fusion Panel containing 137 genes applied to the first case.
Conclusion: Our findings were strikingly similar with the previous cases and histopathological features support the claim that this is a new tumour entity.

E-PS-13-045
The lonely tumour of the salivary gland: sialolipoma, two case reports
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Background & Objectives: Sialolipoma is a rare benign tumour of the salivary gland, first described by Nagao et al. in 2001. According to the 2022 WHO Classification of Head and Neck Tumours, sialolipoma is the only mesenchymal tumour of the salivary gland. Accounting for approximately 0.3% of all salivary gland tumours, sialolipoma is a rare entity with only a limited number of reported cases in the literature. Here, we present two cases of sialolipoma diagnosed in our department to further contribute to the existing literature.
Methods: **Case 1:** A 59-year-old female patient presented in 2020 with a gradually growing, painless swelling on the right side of her face, present for nine years. Imaging studies revealed a well-defined, fat-containing lesion in the right parotid gland, measuring 31×44×14 mm. Gross examination of the excised specimen revealed a well-circumscribed, homogeneous yellow lesion measuring 44×31×10 mm, consistent with adipose tissue. Histopathological analysis demonstrated salivary glandular and ductal structures embedded within mature adipose tissue.
Results: **Case 2:** A 44-year-old male patient presented in 2024 with a swelling in the neck that had been present for 1.5 years. Radiological examination revealed a tumour-like lesion in the right parotid gland, measuring approximately 25×15 mm. Gross examination of the excised specimen revealed a tumour-like lesion with a homogeneous yellowish colour, measuring 42×32×22 mm, surrounded by a thin fibrous capsule. Histopathological analysis demonstrated enlarged ectatic vascular structures along with salivary glandular and ductal structures trapped within mature adipose tissue.
Conclusion: Sialolipoma is a rare and benign neoplasm of the salivary glands, classified as the only mesenchymal tumour in this region. There is limited information available about this tumour. Differentiation from pleomorphic adenomas with extensive lipomatosis and soft tissue lipomas is crucial for accurate diagnosis.

E-PS-13-046
Uncommon location, familiar pathology: papillary thyroid carcinoma in a thyroglossal duct cyst – case report and literature review
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Background & Objectives: Thyroglossal duct cyst (TGDC) is the most common congenital neck anomaly, yet it harbours malignancy in fewer than 1% of cases, predominantly papillary carcinoma. Other variants, including squamous, follicular, Hürthle cell, insular, or anaplastic carcinoma, are exceedingly rare, with no reported medullary carcinoma. Because TGDC typically mimics a benign cyst clinically, diagnosis is often established incidentally by histopathological examination.
Methods: We report the case of a 28-year-old female presenting with a 40×33×25 mm multilocular cystic mass located in the midline of the anterior cervical region, characterized by a smooth, intact wall and containing brownish-black fluid. The internal lining had a thickened, brownish papillary area measuring 20×20×10 mm. A simple excision was performed, removing only the cystic lesion without extending to surrounding structures.
Results: Microscopically, the cyst wall contained multiple foci of papillary and follicular tumour proliferations, along with numerous cystic spaces. These papillae, follicles, and cysts were lined by tumour cells displaying mildly eosinophilic cytoplasm and nuclei with features characteristic of papillary thyroid carcinoma: enlarged, overlapping, irregular contours, grooves, and a "ground-glass" appearance. Numerous reactive thyroid follicles lined by simple cuboidal epithelium were also observed. Immunohistochemically, the tumour cells were positive for cytokeratin AE1/AE3, CK7, TTF1, thyroglobulin, and PAX8, confirming their thyroid origin.
Conclusion: Papillary thyroid carcinoma arising within a TGDC is exceedingly rare, typically discovered incidentally after surgery, and generally demonstrates a favourable prognosis. With approximately 250 such cases reported in the literature, there is no definitive management consensus, though the Sistrunk procedure is widely regarded as sufficient for low-risk patients. More aggressive interventions may be warranted in high-risk scenarios. In our case, only a simple cyst excision was performed, underscoring the need for close follow-up. Additional case reports and series are crucial for refining diagnostic and therapeutic strategies for this uncommon malignancy.

E-PS-13-047
Middle Ear Neuroendocrine Tumour with extensive glandular pattern in a young woman
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Background & Objectives: Middle ear neuroendocrine tumours (MeNETs) are rare epithelial neoplasms with neuroendocrine differentiation. Formerly labeled as adenomas or carcinoid tumours, they are now classified as well-differentiated neuroendocrine tumours (NETs) according to the 2022 WHO classification. These tumours may exhibit variable architecture and unpredictable biological behaviour.

Methods: A 22-year-old woman presented with progressive unilateral conductive hearing loss and tinnitus. Imaging studies raised suspicion for a glomus tumour, leading to an exploratory tympanotomy and surgical excision of the mass.
Results: Histopathological examination revealed an epithelial neoplasm with a striking glandular architecture and tubules lined by a uniform single layer of cuboidal to columnar cells with eosinophilic cytoplasm and round to oval nuclei. The neoplastic cells appeared cytologically bland, with no evidence of mitosis or necrosis. Mucin production was noted in some of the glandular structures. The Ki-67 proliferation index was focally elevated (5–6%). Immunohistochemical analysis demonstrated positivity for INSM1, synaptophysin, chromogranin A, and CK7, while S100, SOX10, and CD117 were negative.
Conclusion: This case highlights a morphological spectrum of MeNET with extensive glandular architecture and focal proliferation. The absence of cytologic atypia and diffuse neuroendocrine marker expression supports a diagnosis of well-differentiated NET, despite elevated Ki-67. Accurate classification and long-term follow-up are critical, as recurrence may occur even in histologically low-grade lesions.

E-PS-13-048
Infection mimicking malignancy in the head and neck area. Report of three cases
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Background & Objectives: Infectious disease with serious or significant consequence to the patient arising in the Head and Neck area are not so common with mucosal candidosis, dental infection and herpes simplex related ulceration regularly encountered. Destructive invasive fungal infections are easily recognised, albeit as a rare event and typically in immunosuppressed individuals. Occasionally, head and neck lesions might be the first or even the only manifestation of rarer and more significant infectious disease and can present with a more confusing clinical and radiological picture that is suspicious for neoplastic disease processes. The purpose of this study is to present cases of rarely encountered infectious diseases with respect to our local population that arise in the Head and Neck area, and in which the clinical presentation was alarming for malignancy.
Methods: Historical search in the authors' archives to identify cases with clinical and/or radiological suspicion for malignancy but with infectious aetiology as the final diagnosis.
Results: Three cases were retrieved. One 59-year old male patient and two female patients aged 33 and 61 years old without relevant medical history known to the pathologists at the time they received the cases. The histopathological findings in combination with the results of special stains and further testing as well as an algorithmic approach to approach these cases is presented. The diagnoses include syphilis, a rhinoscleroma-like reaction to bacteria and leishmaniasis.
Conclusion: Although extremely rare, uncommonly encountered infectious diseases can be mimickers of malignancy in the Head and Neck area causing difficulty in diagnosis even amongst experienced specialist pathologists.

E-PS-13-049
Breast metastasis from nasopharyngeal carcinoma: a case report with literature review
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Background & Objectives: Metastases to the breast are rare, accounting for only 0.4-2% of all mammary malignant tumours. Melanoma and lymphoma are the most common two malignancies metastasizing to the breast. Non-keratinizing undifferentiated nasopharyngeal carcinoma (NPC) rarely metastasizes to the breast.
Methods: We report a case of breast metastasis from a non-keratinizing undifferentiated NPC in a male patient with literature review.
Results: We report the case of a 38-year-old man previously treated for NPC who consulted for breast swelling. Imaging survey revealed multiple breast masses. An ultrasound-guided biopsy was performed. Microscopic examination showed a tumour with solid and trabecular growth patterns. Tumour cells were medium to large sized with irregular nuclei. Immunohistochemical staining showed positivity for cytokeratin and p63 antibodies and negativity for GATA3 and hormone receptors antibodies. Based on patient's history and pathologic examination findings the diagnosis of NPC metastasizing to the breast was established.
Conclusion: The breast is an extremely rare site of metastasis for NPC and represents a diagnostic challenge due to the radiographic similarities with primary breast cancer. According to literature review, only 15 cases of NPC metastasizing to the breast have been reported until this date. Breast metastases may be revealed as palpable masses or as incidental findings on imaging. They can often be misdiagnosed as a mammary primary tumour, due to their morphological similarities. In such cases immunohistochemistry is of a great help.

E-PS-13-050
Fibroblastic and myofibroblastic benign tumours of head and neck location
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Background & Objectives: Head and neck fibroblastic/myofibroblastic tumours (HNFMT) are rare and often overlooked benign tumours. They can be of osseous origin, often resulting in craniofacial deformity such as fibrous dysplasia, or of a vascular origin such as angiofibromas.
Methods: Our study is retrospective, involving 31 cases of HNFMT collected at the Pathology Department of the Salah Azaiez Institute over a 20-year period from 2004 to 2024.
Results: Our series consisted of 17 men and 14 women. Nine tumours were of bone origin and represented fibrous dysplasia lesions. Histological examination revealed a proliferation consisting of anastomosing bone trabeculae without osteoblastic margins, on a densely cellular fibrous background composed of spindle cells.Fourteen cases represented nasopharyngeal angio-fibromas. Histological examination demonstrated benign mesenchymal proliferation rich in vessels and capillaries with a thick, hyalinized wall. All around, there was an abundant fibrous component associated with a mononuclear inflammatory infiltrate. One case was a juvenile fibroma occurring in 16-year-old boy whose biopsy revealed a well-circumscribed mass with a regular respiratory-type coating, sometimes with squamous cell metaplasia. One case was an ossifying fibroma in a 26-year-old man. Five cases corresponded to fibromatosis. Histological examination revealed a spindle cell proliferation made up of cells with eosinophilic cytoplasm and unclear boundaries. The nuclei were monomorphic, finely nucleolated, wavy and without mitotic figures. The tumour cells expressed Beta cathenin.
Conclusion: Fibroblastic tumours often arise diagnostic difficulties, which mainly come from the "head and neck" location leading to an uncertain recognition of the benign or malignant nature of the lesion, especially on biopsies (e.g. desmoid tumour versus fibromyxoid sarcoma of low degree of malignancy). The diagnostic approach must be

based first on the clinical presentation (age and clinical history of the patient, gender, location of the lesion) and then on the morphological study. Immunohistochemistry is only a complement to diagnosis, however it can be sometimes decisive.

E-PS-13-051

Histopathological diagnostic markers of otitis media with ANCA associated vasculitis

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Background & Objectives: Among refractory otitis media in adults, there exhibit otitis media with ANCA associated vasculitis (OMAAV), which develops by the same mechanism, and its difference from GPA has been debated. OMAAV is difficult to diagnose early and can cause serious complications . However, the histological characteristics and diagnostic criteria for OMAAV have not yet been established. Therefore, we extracted the histological parameters of OMAAV and validated them to formulate diagnostic criteria.
Methods: A total 81 cases were analysed including 34 cases of OMAAV, 32 cases of chronic sinusitis, 5 cases of non-specific chronic otitis media and 10 cases of laryngeal granuloma . As a preliminary analysis, histological parameters were qualitatively or semi-quantitatively evaluated in a double-blind manner. Histological parameters including erosion, oedema, fibrosis, type of nflammatory cells, inflammatory cell infiltration in small vessel walls, cell anchoring to vascular endothelium, occlusion of muscular arteries/veins, qualitative evaluation of vasculitis, irregular vascular thickening, etc. Next, to verify the validity of candidate parameters revealed in the preliminary study, we divide the above cases into a Training Set and a Testing Set, then share the whole slide images with the research collaborators.
Results: In the preliminary analyses, significant differences were found in: 1) manifestation of arteritis/phlebitis; 2) arterial/venous occlusion as positive findings in OMAAV, on the other hand, 3) oedema; 4) eosinophil infiltration and 5) plasma cell infiltration were found to be negatively correlated candidate histological parameters. In order to verify the validity of each of these parameters, the cases were divided into a training set and a testing set. The male to female ratio was almost the same, and the average age was within ±2 years. Using this set, we conducted the validity of extracted parameters.
Conclusion: We successfully obtained effective histological biomarker of OMAAV with statistical validity. We expected those parameters will be established as the diagnostic criterion.

Funding: This work was funded by Japan Research Committee of the Ministry of Health, Labor and Welfare for intractable vasculitis (JPVAS)

E-PS-13-052

Clinicopathological spectrum of intestinal-type sinonasal adenocarcinoma: a retrospective study

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Background & Objectives: Sinonasal adenocarcinomas (SNAC) are categorised into two subtypes: Intestinal-type (ITAC) and Non-intestinal-type (non-ITAC). ITACs are rare and exhibit a morphology and immunoprofile similar to primary intestinal adenocarcinoma. We present findings from a retrospective analysis of the clinicopathological characteristics of ITAC.
Methods: We identified and reviewed all cases of ITAC diagnosed at our institute between January 2012 and April 2024 from the pathology archives. Clinical details were obtained from electronic medical records.
Results: A total of 48 cases of ITAC were included in this study. The mean age was 47 years (Range, 19-81 years), with a male-to-female ratio of 3:1. The most common symptoms were epistaxis, followed by nasal obstruction, with the nasal cavity being the most affected site. Most patients presented at advanced stages of the disease, with T4 being the most prevalent stage (27/39, 56.3%). Histologically, the majority of tumours showed a mixed architectural pattern, with the papillary pattern being the most common component, followed by tubular and solid patterns. Mucin (intracellular and/or extracellular) was observed in 39.58% of the cases. The majority of tumours were classified as high grade (60.4%). Nodal and distant metastases were noted in 13.3% (2/15) and 33.3% (6/18) cases, respectively. Immunohistochemistry for p53 was done in 33 cases; 15 (45.5%) of them showed strong diffuse mutational type staining, 3 cases (9.0%) cases showed null-type mutation staining pattern, while the rest of the 15 cases (41.5%) showed a wild-type staining for p53. Most patients (40.7% of cases) were treated with surgery, followed by adjuvant therapy (radiotherapy, chemotherapy, or chemoradiation). Immunohistochemistry results were available for 43/48 cases.
Conclusion: We present one of the largest series of ITAC cases, including 48 cases. In our cohort, we observed a male predominance with a majority of cases presenting at advanced stage, exhibiting higher grade tumours, necessitating multimodality treatment.

E-PS-13-053

Papillary carcinoma arising in thyroglossal duct cyst. A case report

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Background & Objectives: Papillary carcinoma originating in a thyroglossal duct cyst (PCTDC) is a very rare entity, with a frequency less than 1% of all cases in that location, usually presenting within an otherwise benign developmental cyst of the neck. The thyroglossal duct cysts usually arise as cystic expansion of the remnants of the thyroglossal duct tract, and are mainly incidental findings.
Methods: A 44-year-old female patient presented to our hospital with a slow growing, soft, cervical mass, in the vicinity of the hyoid bone, measuring 3,6 cm on U/S showing suspicious sonographic features. The FNA cytologic findings, revealed a papillary carcinoma of the thyroglossal cyst, with papillary and solid components. Serological laboratory findings were compatible with an autoimmune Hashimoto thyroiditis.
Results: Histologically the lesion was well circumscribed, with a thin fibrous capsule, was composed of papillary structures as well as a centrally placed solid component with mainly a follicular growth pattern. The neoplastic cells were highly atypical, with nuclear features compatible with papillary carcinoma, and more specifically the neoplastic cells presented with overlapping, clearing of the nuclei and nuclear grooves. The tumour presented with a highly desmoplastic stroma and with mild inflammatory infiltrate. Part of the hyoid bone was also included in the specimen, which was decalcified and didn't reveal any signs of infiltration
Immunohistochemistry revealed positivity in HMBE1, CK19, TTF1 and Galectin.
Conclusion: PCTDCs are infrequent incidental findings, with higher prevalence rate in women (2.5:1). Main presenting symptoms include dysphagia, hoarseness and a slow growing mass. PCTDCs are either direct metastases of a papillary thyroid carcinoma or more often (up

to 65%) are generated de novo from ectopic thyroid tissue in the thyroglossal cyst.

E-PS-13-054

Tumours metastasizing to the jawbones, oral cavity and salivary glands: a retrospective study

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Background & Objectives: Distant metastasis to the oral cavity is rare, comprising approximately 1–1.5% of all oral malignancies. The most frequent primary sites are the breast and lung, with a jawbone-to-soft tissue ratio of 2:1. The study aims to evaluate the clinicopathological features of tumours metastasizing to the jaw bones, salivary glands and soft tissues of the oral cavity in the Central Anatolia region.
Methods: This study is a retrospective analysis spanning 25 years, covering the period from January 2000 to January 2025. Clinicopathological data were obtained from electronic medical records.
Results: A total of 43 cases (28 males, 15 females; M:F ratio 1.75:1) with a mean age of 60 years (range 25–85) were analysed. Metastases were located in the oral soft tissue (67%), salivary glands (28%), and jawbone (5%). Adenocarcinomas were the most common metastatic tumours (44%), primarily from the lung, gastrointestinal tract, colon, oesophagus, and prostate. Other tumour types included lymphomas (11%), squamous cell carcinoma/malignant epithelial tumour (9%), renal cell carcinoma, malignant melanoma, sebaceous carcinoma, and myeloid sarcoma (each 5%), and various others (16%). Adenocarcinoma and sebaceous carcinoma metastases were more frequent in males, while all malignant melanoma cases occurred in females. Survival data were available for 30 patients: 12 were alive, and 18 had died at the time of analysis.
Conclusion: Metastasis to the oral cavity is a rare occurrence and is characterized by a poor prognosis. Any lesion found in the oral cavity should undergo biopsy and thorough evaluation, as metastatic tumours can mimic benign conditions clinically. The challenging diagnosis requires a multidisciplinary approach. Oral and maxillofacial pathologists play a vital role in the early detection of oral cancers and in recognizing metastatic lesions affecting the maxillofacial region.

E-PS-13-055

Calcifying odontogenic cyst: a case series and literature review

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Background & Objectives: The calcifying odontogenic cyst (COC) is an uncommon, benign developmental cyst derived from odontogenic epithelium, characterized by its potential to undergo calcification and accounting for approximately 0.3–0.8% of all odontogenic cysts. The Aim of the study was evaluating clinical and pathologic characteristics of a case series of COC.
Methods: This study reports an 11-year (2014–2025) case series from our oral pathology department, comprising a total of 15 cases of COCs. Demographic data and histopathological diagnoses were evaluated descriptively. Additionally, a literature review of case series was conducted using PubMed.
Results: The average patient age was 36 years (range: 13–70), with 8 males and 7 females. The cysts were most frequently located in the posterior mandible, followed by the anterior maxilla, anterior mandible, and posterior maxilla. Clinically, most cases were asymptomatic, while a few presented with swelling or tooth mobility. Radiologically, all lesions appeared as well-defined, unilocular radiolucencies with an average size of 1.5 cm. Histologically, ghost cells, dystrophic calcifications, reverse polarization, and remnants of odontogenic epithelium were commonly observed. In two cases, palisaded, hyperchromatic ameloblast-like cells were noted. Notably, one case was a hybrid lesion exhibiting features of both a calcifying odontogenic cyst and an adenomatoid odontogenic tumour, with epithelial cells forming rosette- and duct-like structures within a hyalinized matrix.
Conclusion: COC is a rare developmental odontogenic cyst with a historically debated nature. It can present with a variety of clinical features and outcomes, appearing as a solid tumour, a unilocular cystic lesion, or, in rare cases, as a carcinoma. The distinguishing feature is the odontogenic cystic epithelium, which may include calcifications and ghost cells. In the differential diagnosis, it is important to distinguish it from dentinogenic ghost cell tumour and ghost cell odontogenic carcinoma.

E-PS-13-056

Morphologic diversity and clinicopathologic features of HPV-associated sinonasal carcinomas

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Background & Objectives: To explore the morphologic spectrum and clinicopathologic characteristics of HPV-associated sinonasal carcinomas, with an emphasis on histologic diversity, HPV subtypes, and their potential diagnostic significance.
Methods: We reviewed 102 cases of sinonasal carcinoma from the pathology archive with corresponding in-situ hybridization (ISH) for low-risk and/or high-risk HPV. Nineteen cases (18.6%) tested positive for HPV, and clinicopathologic data were collected.
Results: Among the 19 HPV-associated sinonasal carcinomas, 6 (31.6%) were squamous cell carcinomas and variants, 10 (52.6%) were HPV-related multiphenotypic sinonasal carcinomas, 2 (10.5%) were high-grade carcinomas, and 1 (5.3%) was an adenocarcinoma. The median age of affected patients was 66 years (range: 37–89), with 8 (42.1%) women and 11 (57.9%) men. These tumours were predominantly located in the nasal cavity. The adenocarcinoma displayed heterogeneous morphology, with invasive growth forming two distinct architectural patterns: papillary structures and nests with a cribriform-like configuration. High-risk HPV positivity was observed by ISH, showing strong, diffuse nuclear staining in the papillary component and a dot-like expression pattern in the cribriform nests. Two cases (10.5%) of HPV-related multiphenotypic sinonasal carcinoma were positive for low-risk HPV but negative for high-risk HPV by ISH. One case presented as a high-grade small round blue cell tumour with immunophenotypic evidence of myoepithelial differentiation, exhibiting adenoid cystic-like features. Focally, the surface epithelium showed severe dysplasia/carcinoma in situ. Worse overall survival and progression-free survival were observed in HPV-associated carcinoma patients with high-grade morphology, although this difference was not statistically significant [p=0.06].
Conclusion: Our study highlights an unusual association between low-risk HPV and multiphenotypic sinonasal carcinoma, which has not been previously reported. Additionally, we describe a novel heterogeneous morphology in HPV-associated sinonasal adenocarcinoma, with distinct HPV expression patterns by ISH. Further research is needed to evaluate the clinical and prognostic significance of these findings and their implications in distinguishing HPV-associated sinonasal carcinomas.

E-PS-13-057

Salivary duct carcinoma: analysis of the clinicopathologic spectrum of a rare aggressive malignancy from a tertiary cancer centre of North India

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Background & Objectives: Salivary Duct Carcinoma (SDC) is a rare and aggressive high-grade salivary gland malignancy, accounting for <1.8% of all major salivary gland tumours and about 10% of all salivary gland malignancies.
Objective: To comprehensively evaluate the entire clinicopathologic spectrum of SDCs treated at our centre.
Methods: A retrospective analysis of SDC patients treated at a tertiary cancer centre over a period of 5 years was undertaken.
Results: A total of 46 histologically confirmed cases of SDCs were identified. Mean age of the patients was 59.02 years (30-83 yrs) with a male predominance. Most common site involved was the parotid gland (74%), and the histology evinced was that of high-grade mammary ductal carcinoma with Androgen receptor (AR) positivity in 85% cases and HER2/neu expression in 41% cases. Perineural invasion was detected in 26%, lymphovascular invasion in 24%, regional lymph node involvement in 74% and distant metastases in 41% cases, with the most common metastatic site being lung followed by bones, non-regional nodes, brain and soft tissue. Majority of the patients presented at a higher stage (stage IV 69.5%). The chief modality of treatment was surgery (n=23) followed by adjuvant radiation, adjuvant chemo-radiation and adjuvant chemotherapy. On a median follow-up period of 11 months (1-43 months), the mean overall survival duration was 41 months, median time for distant metastasis 15 months and the 3-year progression-free survival rate 60.2±12%. Overall survival was perceived to be better for AR positive (42 months vs 9 months) and HER2/neu negative (39 months vs 10 months) patients, compared to their counterparts.
Conclusion: Distinction of SDC from other salivary neoplasms is of prognostic and therapeutic significance since it has a dismal prognosis. Analysis for AR and HER2/neu expression should be mandated on all SDC patients, as the benefits of androgen deprivation therapy and targeted HER2/neu therapy are becoming more evident.

E-PS-13-060

Spindle cell/Sclerosing and intra-osseous Rhabdomyosarcoma of the head & neck in adults: a tertiary care cancer centre case series

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Background & Objectives: Spindle cell/Sclerosing Rhabdomyosarcoma (SSRMS) is a rare subtype reclassified by the WHO as distinct from Embryonal RMS. Intraosseous (TFCP2 rearranged) RMS (IRMS) is a recently described entity with a unique histology and molecular profile. Rarity and the limited understanding of the clinical and pathological features, especially in adults, require further evaluation.
Methods: Retrospective observational clinicopathological study of 11 years duration (Jan 2014-March2025) of adult RMS patients (>/=18 years) with SSRMS and IPRMS histology and available material for review.
Results: 22 patients; 16 SSRMS and 6 IRMS, with a M:F ratio of 2.1:1 and mean age of 28.4 years were evaluated. SSRMS was characterised by upper alveolus as the most common site (31.2%), pure spindle morphology in 60% of cases, with sclerosis in 35%, mitoses >5/per mm² in 60%. MyoD1 (Diffuse/strong), desmin and myogenin expression was seen in 68%, 55% and 35% respectively. IRMS were characterised by M:F ratio of 2:1, mandibular involvement in 83.3%, unique morphology of round nuclei but spindle abundant eosinophilic cytoplasm (epithelioid leiomyosarcoma-like) in all, short fascicles in 80%, myxoid stroma in 70%, variable AE1/AE3 expression in all, ALK IHC positivity in all (n=5), myogenin in none, desmin in 20%, and EWSR1 gene rearrangement in 2 of 3 tested. 7 of 22 patients underwent resection. With a median follow up of 18.5 months, one patient is alive with no evidence of disease (disease-free survival: 74 months), three are alive with the disease, and two have died (one from recurrence, one from metastasis).
Conclusion: Adult SSRMS and IRMS share a male predilection, and MyoD1 positivity. They differ in spindle vs epithelioid histology, maxilla vs mandibular involvement, very focal vs diffuse keratin positivity, and none vs majority with ALK IHC positive. EWSR1 gene rearrangement is frequent in IRMS. Dismal outcomes in both necessitate accurate distinction and further research to improve treatment strategies.

E-PS-13-061

Glomangiopericytoma of the nasal cavity: a case report

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Background & Objectives: Glomangiopericytoma is a rare vascular neoplasm of the sinonasal tract, accounting for <0.5% of neoplasms in this region. It typically affects patients aged 40–70 years, with a slight female predominance. Classified by the World Health Organization as a borderline/low-malignant-potential tumour, it is distinguished by its indolent behaviour and unique histopathological features. This case report aims to describe the clinical presentation, diagnostic approach, and management of glomangiopericytoma in a 74-year-old patient.
Methods: A 74-year-old woman presented with recurrent epistaxis and unilateral nasal obstruction. Endoscopic examination revealed a polypoid, friable mass in the nasal cavity. The lesion was excised via endoscopic surgery, yielding soft, elastic tissue fragments measuring 0.5–1.5 cm. Histopathological analysis was performed to evaluate the tumour's morphology, while immunohistochemical studies assessed its molecular profile.
Results: Histopathological examination revealed respiratory epithelium overlying a submucosal mesenchymal neoplasm composed of monomorphic spindle-shaped cells arranged in a perivascular growth pattern with a prominent branching ("staghorn") vascular network. No nuclear atypia, mitotic activity, or necrosis was observed. Immunohistochemistry demonstrated diffuse positivity for smooth muscle actin (SMA), vimentin, β-catenin, and cyclin-D1, confirming myoid perivascular differentiation. CD31 and CD34 highlighted endothelial cells within vascular channels. The Ki-67 proliferation index was <1%.
Conclusion: Glomangiopericytoma is characterized by somatic β-catenin mutations and lacks NAB2-STAT6 gene fusions seen in conventional hemangiopericytomas. Key diagnostic features include SMA positivity, absence of pleomorphism or necrosis, and low Ki-67 index. Endoscopic resection with clear margins remains the gold standard treatment. Long-term follow-up is essential due to recurrence risks (17%–50% after incomplete resection), though metastases

are exceptionally rare.Accurate diagnosis of glomangiopericytoma is crucial for appropriate management and requires integration of clinical, histopathological, and immunohistochemical findings. Complete surgical excision remains the gold standard and ensures optimal outcomes.

E-PS-13-062

Laryngeal liposarcoma: a challenging diagnosis

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Background & Objectives: Laryngeal and hypopharyngeal liposarcomas are exceedenly rare entities. They represent approximately 10% of all head and neck liposarcomas. Dyspnea and dysphagia often are the only symptoms present at diagnosis. The main differential diagnoses are lipoma and spindle cell/pleomorphic lipoma (SCL/PL). We present the case of an 81-year-old man who consulted for dyspnea and dysphagia. Two tumours were identified, one in the hypopharynx and another in the right piriform sinus.
Methods: The hypopharyngeal mass was biopsied and diagnosed as a lipoma. Then the pyriform sinus lesion was removed and diagnosed as a spindle cell lipoma. Following a recurrence, the pyriform sinus lesion was removed once again. After macroscopic, microscopic, immunohistochemical and molecular studies the diagnosis of low-grade liposarcoma/atypical lipomatous tumour (LGLS/ALT) was achieved.
We reviewed all laryngeal and hypopharyngeal biopsies diagnosed as lipoma, SCL/PL and LGLS/ALT at our hospital from January 2013 to February 2025. Clinical and epidemiological data were collected from the medical records.
Results: A total of two cases were identified, male 81 years and male 85 years, both presented with dyspnea and dysphagia at the time of diagnosis. One of them was diagnosed as a SCL . The second one was a diagnostic challenge being first diagnosed as lipoma, then as a SCL before reaching the diagnosis of LGLS/ALT. Inmunohistochemical studies with CD34, MDM2 and CDK4 were positive. Nuclear expression Rb protein was preserved. Amplification of MDM2 and CDK4 was evidenced using fluorescence in situ hybridization (FISH).
Conclusion: Laryngeal and hypopharyngeal LGLS/ALT are a diagnostic challenge. Atypical cells or other indicators of malignancy may not be observed in a biopsy. To date there have been no specific recommendations for molecular testing in lipomatous tumours in the head and neck region, but based on our experience it may be advisable to perform molecular studies in all lipomatous tumours in this location.

E-PS-13-063

Paediatric adenoid cystic carcinoma of the submandibular gland: a rare case report

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Background & Objectives: Adenoid cystic carcinoma (ACC) is a rare malignant salivary gland tumour of epithelial and myoepithelial origin, typically occurring between the ages of 40 and 60, with a median of 57 years. ACC is often characterized by perineural invasion and a high risk of local recurrence. This case report presents a paediatric patient diagnosed with ACC of the left submandibular gland at an unusually early age, emphasizing its pathological features and treatment approach.
Methods: A 7-year-old patient with a six-month history of a palpable mass in the left level 2 cervical region underwent imaging, revealing a 13×11 mm lesion in the left submandibular gland. An incisional biopsy confirmed ACC. Surgical management included left level 1B neck dissection and tumour excision. Histopathological evaluation assessed tumour size, perineural invasion, lymphovascular invasion, and lymph node involvement. Immunohistochemical staining for c-MYB expression was performed.
Results: Histopathology confirmed a 1.5 cm ACC confined to the salivary gland capsule (pT1), with perineural invasion and absence of lymphovascular invasion. Four reactive submandibular and 13 cervical lymph nodes were identified. Lymphoepithelial lesions were observed in non-neoplastic salivary gland tissue, particularly in periductal regions. Immunohistochemistry demonstrated strong nuclear c-MYB positivity in tumour cells. Surgical margins were clear. Postoperatively, the patient received adjuvant radiotherapy. Regular clinical and radiological follow-up was recommended due to the high risk of local recurrence. Given the paediatric age, molecular and genetic evaluation may be warranted to assess potential predisposition or hereditary association.
Conclusion: This case highlights the sporadic nature of ACC, with no known hereditary or other predisposing factors. The presence of perineural invasion underscores the need for close follow-up to monitor for recurrence. Additionally, lymphoepithelial lesions raise the possibility of an associated immunological condition. Further molecular studies may provide insights into the pathogenesis and contribute to the development of targeted therapies for paediatric ACC.

E-PS-13-064

Sinonasal mucosal melanoma: a case report highlighting diagnostic and therapeutic challenges

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Background & Objectives: Sinonasal mucosal melanoma (SNMM) is an extremely rare malignancy, accounting for 0.5–2% of all melanomas and approximately 4% of sinonasal malignancies. Its pathogenesis involves mucosal melanocytes derived from neural crest cells during embryogenesis. SNMM predominantly affects males over 60 years of age and is often diagnosed at advanced stages due to nonspecific symptoms, leading to a poor prognosis (median survival: 18 months). The molecular profile of SNMM is distinct from that of cutaneous melanomas, presenting challenging therapeutic considerations. This study presents a rare case of SNMM in a young patient, highlighting diagnostic challenges and therapeutic considerations.
Methods: A 34-year-old Asian male with a history of smoking and drug use presented with nasal congestion, recurrent epistaxis, and nasal swelling. Imaging revealed a 5.5 cm soft-tissue mass involving the nasal cavity, paranasal sinuses, and intracranial extension. Biopsies measuring 0.7–1 cm were obtained for histopathological examination. Immunohistochemical (IHC) analysis for melanoma markers (S100, HMB45, Melan-A, SOX10), proliferation index (Ki-67), and vimentin was performed.
Results: Histology revealed a malignant epithelioid neoplasm beneath the respiratory-type mucosal epithelium, characterized by marked nuclear atypia, high mitotic activity, and abundant melanin production. IHC confirmed positivity for melanoma markers with a high Ki-67 index (50%). The presence of intraepithelial atypical melanocytes supported the primary mucosal origin. The patient underwent combined modality therapy (CMT) with immunotherapy and showed a partial clinical response at follow-up.
Conclusion: SNMM is a rare and aggressive malignancy requiring early recognition and multidisciplinary management to improve outcomes. This case highlights the importance of biopsy in patients with

atypical nasal symptoms and underscores the need for further research into effective treatment strategies for this challenging disease.

E-PS-13-066

Pseudoendocrine sarcoma: a case report of a newly described soft tissue tumour

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Background & Objectives: Pseudoendocrine sarcoma (PES) is a recently reported tumour that usually arises in paravertebral deep soft tissues and shares histological similarities with well-differentiated neuroendocrine tumours, but it lacks epithelial and neuroendocrine marker expression. Most of the reported PES exhibited aberrant nuclear β-catenin expression with confirmed mutations in the CTNNB1 gene. We here describe the clinicopathological, immune histochemical, and molecular findings of one case.
Methods: **Case presentation:** A 70-year-old man presented with left posterior neck mass that was discovered on surveillance imaging for a previously diagnosed colorectal carcinoma. Imaging revealed an enhanced left paraspinal soft tissue mass measuring 5x6.2x7 cm. The mass is separate from the adjacent bone and nerve roots.
Results: Histologically, a relatively circumscribed neoplasm with lobular invasion into the adjacent tissue. The tumour is made up of epithelioid cells with uniform, central round nuclei with speckled chromatin and pale cytoplasm with focal clear cell change. The cells are arranged in sheet-like, trabecular, organoid, and/or nested patterns. Occasional pseudo-glycular architecture, eosinophilic hyaline globules and psammomatous calcifications are noted. Immune histochemical staining showed negative expression of Pan-cytokeratin, CK7, CK8/18, CK20, EMA, p63, synaptophysin,chromogranin A, GFAP, and SOX10 with weak S100 positivity. Strong nuclear β-catenin expression was observed throughout the tumour. The Ki-67 labelling index was 10–15% in areas with increased mitotic activity. DNA-based targeted next-generation sequencing (NGS) confirmed the presence of a CTNNB1 (p.S37F) mutation.
Conclusion: The prominent epithelioid morphology and predilection for deep soft tissues in the paravertebral region of PES may raise the possibility of other tumour types such as paraganglioma, ependymoma, glomus tumour and some round cell sarcomas such as Ewing sarcoma and so it may represent a diagnostic pitfall. Accurate diagnosis is challenging on morphology alone, and it mandates immune histochemical and molecular evaluation. This is very important because of the varied biological behaviours and clinical outcomes.

E-PS-14 E-Posters History of Pathology

E-PS-14-001

The fall of the old guard - evolving perceptions on the origin of disease in the Early Modern period

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Background & Objectives: To explore the evolution of medical philosophy and perspectives on the origins of disease in the Early Modern period, its resulting controversies, and its influence on modern pathology.
Methods: Robert Hooke first described the cell as seen under his microscope in 1665, but it would not be for nearly another two hundred years before Virchow's 'Cellular Pathology' would be published. For much of the Early Modern period, medical theory and practice was predominately shaped by the works of Galen and Hippocrates. Any challenge to these ancient authorities was considered a direct attack on the medical, and even religious, orthodoxy of the day.
Results: However, new schools of thought did begin to emerge. Empiricists such as Lord Francis Bacon condemned the unquestioning adherence to Galen's teaching, and instead promoted direct observation and experimentation. William Harvey's description of circulation typified a new mechanical philosophy of the human body, and while his main focus was on physiology, he did explore how disturbances in the circulation could lead to disease. Others, such as the iatrochemists, believed that disease arose from disturbances in chemical reactions in the body, and that specific chemical remedies were required to treat them – though unfortunately making frequent use of mercury and arsenic. These deviations from the medical establishment were not without their critics however – Lord Bacon and his "Baconical" followers were denounced as "pretender[s] to Physick", whose ignorance made them "unfit to be entrusted with the life of any man".
Conclusion: While many of the theories developed in this period would be ultimately superseded in the following centuries, the willingness to question entrenched tradition and embrace experimentation laid the groundwork for modern medicine. As we enter into this new epoch of precision medicine, we too must not fall into the trap of clinging to the familiar at the expense of progress.

E-PS-14-002

Pathology through the legacy of the sanctuary of asclepius in epidaurus: integrating ancient wisdom into modern medicine

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Background & Objectives: This historical case presents the Sanctuary of Asclepius in Epidaurus as a significant centre for healing in the ancient Mediterranean world, blending mystical and systematic medical practices. Dedicated to Asclepius, the divine healer, it promoted a holistic approach to health, considering physical, psychological, and spiritual well-being. The sanctuary's natural environment, purification rituals, physical activities, and artistic engagement contributed to the healing process.
The aim is to highlight the sanctuary's role in early medical practices and its influence on modern healthcare. It emphasises the importance of holistic healing, the integration of psychological and physical treatments, and the lasting impact of Epidaurus on medical ethics, preventive medicine, and integrative healthcare approaches.
Methods: Treatment methods started at the natural setting of Epidaurus, with its serene landscape and fresh water sources, contributed significantly to the healing process. Patients engaged in purification rituals, physical exercise, dietary regulations, and artistic activities, such as attending performances at the renowned Epidaurus theatre, reinforcing the link between emotional and physical health. A key element of the healing practice was 'incubation' or 'enkoimesis,' where patients slept in a sacred space, seeking divine guidance in dreams. This method, blending psychological suggestion with religious belief, prefigures modern psychosomatic and placebo-based healing techniques.
Results: The sanctuary's emphasis on treating the whole person, rather than just symptoms, aligns with contemporary medical principles. The World Health Organization's definition of health as complete physical, mental, and social well-being echoes these ancient practices. Furthermore, modern integrative medicine, which combines conventional treatments with alternative therapies, reflects the holistic approach of Epidaurus.
Conclusion: Beyond its religious function, the sanctuary served as a foundation for medical science, influencing ethics, preventive medicine, and the integration of psychological and social aspects in healthcare. Its enduring legacy affirms the relevance of ancient medical wisdom in shaping contemporary healthcare practices.

E-PS-14-003

Prevalence of *concha bullosa* in the natural mummies of a monastic community in central Italy (17th-18th century)

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Background & Objectives: *Concha bullosa* (CB) is the pneumatization of the middle turbinate and the most common anatomical variant of the sinonasal complex. The prevalence of CB in the modern population ranges from 13 to 72%, and this condition is frequently associated with nasal septal deviation (NSD). CB can be classified as unilateral, bilateral symmetric, and bilateral asymmetric. CB may be easily identified in skulls by inspection, but is under-reported in archaeological collections due to the poor preservation of nasal bones. CB has only been demonstrated in mummified heads by endoscopy.

Methods: The aim of this study was to investigate the prevalence of CB in 17 mummified bodies and 1 mummified head from the monastic community of the Poor Clares Hermits of Fara in Sabina, who followed the First Rule of Saint Clare combined with strict seclusion and absolute loyalty to ecclesiastical hierarchies. After a careful external examination, the mummies were investigated by computed tomography (CT) scanning with multiplanar reconstruction and 3D rendering. The nasal cavities, turbinates, and septum were examined to detect their significant morphological variations.

Results: Due to the presence of mummified nasal pyramids, no alteration of the structures could be visualized by external examination. CT scans revealed pneumatization of the middle turbinates in 5 out of 18 individuals (27.78%). Age at death of the subjects ranged from 40 to >60 years. Unilateral CB with contralateral NSD was observed in 2 cases (1 left, 1 right), bilateral asymmetric CB with NSD contralateral to the larger CB was observed in 2 cases, and bilateral symmetric CB with right NSD was observed in 1 case.

Conclusion: Our study represents the first investigation of CB in a series of natural mummies. CT scanning represents an essential tool to disclose this condition in mummified bodies. Our data confirm the close relationship between CB and NSD.

E-PS-14-004

Reviving autopsy reports from Baroque era

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Background & Objectives: Post mortem was already settling in European medicine and autopsy reports were giving more and more information concerning pathologies found. The objective was to set the proces of transformation of ancient medical language (Latin) and terms into contemporary.

Methods: We analysed two chosen post mortem reports from beginnning of 17th and 18th centuries. After transliteration from original texts, Latin was translated to Polish and English. Anatomical and pathological terminology was correlated with contemporary knowledge and nomencalture. We also analysed the style of those professional medical documents, noting nevertheless distinct differences between two reports almost 100 years apart.

Results: Analysed reports differed in style though not in the anatomical and pathological approach. First from 1613 was devoid of linguistic embellishments, referred strictly to description of external view with detailed, and divided into separate chapters description of internal organs noting every pathology found. Information included was similar to present autopsy reports. The second performed in 1724 described thorough analysis of conjoined twins, though we see no information concerning mother who died before the foetuses were extracted. The language of the report printed afterwards in a form of a little book was more baroque, rich in embellishments, with introduction addressed to City Hall members and nobility present during the public autopsy.

Conclusion: The analysis let us compare two reports published after procedures performed in the same facility 100 years apart. Translation from Baroque Latin showed us different approach to the body with full profesionalism in performance maintained. Vocabulary like „arteria aspera" was new to us. But description of the foetus malformation let us state that it was the first presentation of Limb Body Wall Complex in literature, quoted shortly afterwards by Caspar Bauhin in his „*De hermaphroditorum et monstrosorum partuum natura"*

E-PS-14-005

The enigma of death of Barbara Radziwill – wife of the last king of Jagiellonian dynasty

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Background & Objectives: Barbara was king's second wife. Sources negate any maladies until 1547. She died less than six months after her coronation... Before her death, she suffered with high fever, cachexia and growing growth/tumour in her abdominal area present.

Methods: We analysed available historical sources including family letters and published articles. The data show progressive weakness, specific and nonspecific symptoms. We can hypothesize the possible course of disease of King's wife leading to her demise. Additional information include her previous life, helath conditions and other possible threats of the court enviroment inlcluding her mother-in-law, Bona Sforza.

Results: We had to deal with several hypotheses, sometimes contradicting each other, including the risk of poisoning, puerperal fever, concequences of treatment of possible syphylis with mercurium, SIRS (systemic inflammatory response syndrome) and last but not least malignancy of the uterus. Differential diagnosis is rather difficult as no autopsy was performed, only the report after analysis of remains of her body, mainly skeleton, centuries later. On the other hand we have quite detailed medical history and course of disease basing on the rich correspondence, where continuous deterioration and appearing new symptoms are reported. Some of them let us narrow the possible final diagnosis.

Conclusion: The analysis of body remains proved no trace of mercurium which could exclude syphilis, as Barbara Radziwill came from nobility and would be treated with best possible methods of the time. There is no evidence of any malformation of skeleton, nor trace of metastases. The reports stating increasing foul odour, deterioration, progressive weakness, foul smelling discharge from vagina indicate malignancy of the uterus. In this case squamous cel carcinoma seems to be most probable, nevertheless other types cannot be excluded.

E-PS-15 E-Posters Infectious Diseases Pathology

E-PS-15-001
Pathological features of lung tissue as a major finding in COVID-19 deaths

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Background & Objectives: Understanding the characteristics of fatal COVID-19 cases is crucial for comprehending the pathogenesis of severe complications and identifying effective treatment methods.
This study aims to investigate the morphological features of fatal COVID-19 cases.
Methods: A retrospective analysis was conducted on the results of 3,744 postmortem examinations of patients who died from COVID-19 at the Lviv Regional Pathology Bureau between 2020 and 2021. Histological examination of lung tissue samples utilized the standard haematoxylin-eosin method, the modified Zerbino—Lukasevich MSB method, Masson's trichrome, and immunohistochemical studies using inflammatory and proliferative antibodies.
Results: A significant predominance was observed in young and middle-aged men compared to women, who showed a higher prevalence among the elderly ($p < 0.001$). The highest mortality rates were noted from 1 to 14 days ($72.92 \pm 0.73\%$) and from the 15th to the 21st day ($68.71 \pm 1.45\%$).
Among patients, the highest mortality (72.89%) occurred in the first 14 days, with 16.05% dying on days 15-21, and 11.06% passed on day 22 and later.
During the exudative phase, signs of haemorrhagic interstitial pneumonia were observed, characterized by a predominance of CD3, CD31, and CD34-positive T-lymphocytes, CD20-positive B-lymphocytes, and CD163-positive macrophages. Additional findings included intraalveolar oedema, hyaline membranes, pronounced plethora, and multiple thrombi. The proliferation phase was characterized by inflammation, marked by clusters of CD68- and CD163-positive cells and CD8-positive cytotoxic T cells. There was a thickening of the interalveolar septa due to the proliferation of fibroblasts and the hyperplasia of pneumocytes II (TTF1-positive). During the organization phase, a predominance of CD68- and CD163-positive macrophages was observed, accompanied by a small number of T-lymphocytes and solitary B-lymphocytes. Additionally, pneumofibrosis with arteriosclerosis also progressed.
Conclusion: The described lung histology indicates the progression of diffuse alveolar damage from an exudative to a fibrotic phase, leading to severe disease with potentially fatal consequences.

E-PS-15-003
Ecthyma gangrenosum in an immunosuppressed patient post-liver transplant: a diagnostic challenge

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Background & Objectives: Ecthyma gangrenosum is a rare and severe cutaneous infection, most often associated with Pseudomonas aeruginosa and typically observed in immunocompromised patients. Early recognition and targeted therapy are critical due to its potential for rapid progression and high mortality. This report highlights the diagnostic and therapeutic approach in a 67-year-old post-liver transplant patient with ecthyma gangrenosum, emphasizing the importance of timely intervention.
Methods: The patient presented with a chronic necrotic lesion on the left foot, initially suspected to be of vascular origin. Clinical and histopathological findings revealed extensive ulceration with lymphohistiocytic and neutrophilic inflammation, capillary proliferation, interstitial haemorrhage, and fibrosis extending into the subcutis. Vessel walls showed marked thickening without occlusion, and PAS staining identified gram-positive bacterial colonies. These findings confirmed the diagnosis of ecthyma gangrenosum. Multidisciplinary management included targeted antibiotics, wound care, and adjustment of immunosuppressive therapy.
Results: The patient responded well to treatment, with significant ulcer healing and no systemic complications. The early histopathological diagnosis was pivotal in guiding therapy. This case underscores the challenges of managing infections in immunosuppressed patients, particularly with concerns of antibiotic resistance in Pseudomonas aeruginosa.
Conclusion: Ecthyma gangrenosum is a critical diagnosis to consider in necrotic ulcers, especially in high-risk patients. Early detection is essential to prevent severe complications and improve outcomes. Antibiotic resistance and the potential involvement of other pathogens demand a broader understanding of the disease. Reporting cases like this emphasizes the need for precise diagnostic tools, multidisciplinary collaboration, and careful antibiotic stewardship to address this life-threatening condition.

E-PS-15-004
Cerebral sparganosis: intracranial parasitic infection with diagnostic challenges and histopathological insights

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Background & Objectives: Sparganosis is a parasitic infection caused by migration of the plerocercoid larvae of *Spirometra*. It is among the understudied entities in pathology, especially due to its rarity and occurrence at unexpected locations. We hereby depict a case of cerebral sparganosis to increase awareness and emphasize diagnostic clues.
Methods: An 11-year-old female without relevant previous medical history presented with recurrent seizures. Magnetic resonance imaging revealed a mass in the right parietal lobe, measuring 13x7 millimeters. Together with multiple calcifications and peripheral contrast enhancement, the preliminary radiological differential diagnoses were glioneuronal tumours and paediatric diffuse gliomas. The parietal mass is resected for pathological evaluation.
Results: Entire specimen was submitted for evaluation. Histology revealed reactive gliosis, perivascular and parenchymal lymphoplasmacytic cells along with scattered eosinophils as well as multiple foci of microcalcification. Only on one of the sections a parasite, morphologically compatible with helminth was detected. Measuring 12 millimeters in the greatest piece, the parasite was characterized by an eosinophilic tegument and underlying pale myxoid matrix with characteristic longitudinal smooth muscle fibres, suggestive of sparganosis. No scolex was observed. Systemic imaging showed no signs of involvement in any other site.
Conclusion: Sparganosis is a parasitic zoonosis transmitted by contaminated water or consumption of raw snakes/frogs. With larvae characterized by outer tegument, inner calcareous corpuscles and longitudinal muscle fibres, sparganosis differs from cysticercosis. It is seen more commonly in superficial soft tissue but also rarely in internal organs, including the brain. Complete surgical removal, accurate diagnosis and antihelminth treatment remain crucial in management.

E-PS-15-005
Kaposi Sarcoma a case series of unusual locations

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Background & Objectives: Kaposi sarcoma (KS) is an angioproliferative malignancy associated with Human Herpesvirus 8(HHV8), predominantly affecting immunocompromised individuals. Its incidence is highest in HIV/AIDS patients, but also occurs in transplant recipients and endemic populations. KS can manifest in various anatomical regions, typically affecting the skin but occasionally extending to the gastrointestinal tract and lungs.
We present a case series of KS with atypical anatomical locations diagnosed in our department.
The aim of the study was to investigate the clinical and pathological characteristics of KS cases particularly focusing on atypical presentation.
Methods: We present a retrospective study of five cases of KS diagnosed at LaRabta department of pathology between 2021 and 2025. Clinical, radiological, and endoscopic findings led to gastric, hypopharynx biopsies, lymphadenectomy and parotidectomy. All of the specimens underwent examination using Haematoxylin and Eosin staining and Immunohistochemistry using CD34 and HHV8 antibodies.
Results: There were 5 males aged between 47 and 81 years with a mean age of 57. Four out of five patients were HIV-positive, One patient was HIV-negative and non-immunocompromised. Three patients had multiple locations of KS. The affected sites were lymph nodes both cervical and inguinal (n=2), gastric antrum (n=2), gastric fundus (n=1), oesophagus (n=1), parotid gland (n=1), and hypopharynx (n=1) with n referring to the number of affected locations. Histopathological evaluation of all the specimens showed typical features of KS revealing nodular and diffuse spindle cell proliferation with elongated cells, hyperchromatic nuclei, eosinophilic cytoplasm, cytonuclear atypia, and mitoses. Hemorrhage was noted between tumour cell bundles (n=6).
Immunohistochemistry showed intense and diffuse nuclear positivity using HHV8 antibody (n=8) and CD34 antibody (n=1).
Conclusion: This case series is one of the few that highlights the atypical locations of Kaposi sarcoma and also reports a sporadic, HIV-negative case in an immunocompetent patient, underscoring the importance of considering KS in any difficult-to-classify spindle cell lesions.

E-PS-15-006

A case of pulmonary echinococcosis mimicking neoplasm in a patient from the Amazon Region, Brazil

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Background & Objectives: Echinococcosis, a parasitic zoonosis caused by the larval stage of Echinococcus tapeworms, is a global health concern, particularly in regions with close contact between humans and infected canids. The disease can manifest as cystic lesions in various organs, most commonly the liver and lungs, often mimicking neoplastic processes in clinical and radiological assessments. This report presents a case of pulmonary echinococcosis in a patient from the Amazon region of Brazil, highlighting the diagnostic challenges and the importance of considering this parasitic infection in the differential diagnosis of lung nodules.
Methods: A 55-year-old male indigenous patient from the Amazon region presented with cough and pulmonary nodules. Initial investigations led to a referral to an oncology centre. Following a lung segmentectomy, a definitive diagnosis of echinococcosis was confirmed through histopathological examination of the resected tissue.
Results: The patient underwent surgical resection of a pulmonary lesion initially suspected to be a neoplasm. The histopathological analysis revealed the characteristic features of a hydatid cyst, confirming the diagnosis of pulmonary echinococcosis. This finding underscores the potential for this parasitic disease to mimic malignancy, necessitating careful consideration in endemic areas.
Conclusion: Pulmonary echinococcosis should be included in the differential diagnosis of lung nodules, especially in patients from endemic regions like the Amazon. This case highlights the challenges in distinguishing parasitic infections from neoplastic processes based on clinical and radiological findings alone. Accurate diagnosis through histopathological examination is crucial for appropriate patient management and to avoid misdiagnosis that could lead to inadequate or delayed treatment. The awareness of pathologists regarding this disease is paramount for accurate diagnosis and appropriate clinical approach.

E-PS-15-007

Herpetic hepatitis in a young, immunocompetent patient

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Background & Objectives: Herpes simplex virus (HSV) is a double-stranded deoxyribonucleic acid (DNA) virus that is rarely implicated in the pathogenesis of hepatitis, especially in immunocompetent patients. Herpetic hepatitis accounts for less than 1% of fulminant hepatic failure and, due to its rarity, is often underrecognised in clinical practice. Of the approximately 1% of patients who develop herpetic hepatitis, around 25% are immunocompetent. Unfortunately, herpetic hepatitis is fatal in up to 74% of cases, with the majority of cases diagnosed on postmortem examination.
Methods: In this report, an interesting case of herpetic hepatitis in a previously healthy male of 19-years-old is described. The patient presented to a tertiary hospital in Bloemfontein, South Africa, with a 1-week history of intermittent fever, vomiting, nausea and epigastric pain. No travel history was noted and the patient did not present with mucocutaneous lesions. He was anicteric and haematological and chemical investigations revealed that he was in fulminant hepatic failure, of unknown aetiology, complicated by hepatorenal syndrome and hepatic encephalopathy. His transaminases were markedly elevated with an aspartate transaminase of 20 437 U/L and ammonia of 393 umol/L was recorded. Whilst awaiting admission, he demised. A post-mortem was requested to ascertain the cause of death.
Results: On gross examination, the patient had a markedly enlarged, yellow liver and haemorrhagic mucous membranes in the gastrointestinal tract. Microscopic examination showed features of herpetic hepatitis that were confirmed by immunohistochemical stains. Despite the absence of HSV IgM and IgG positivity, virologic investigations verified the presence of HSV-1 associated hepatitis. Electron microscopy showed HSV within the hepatocytes, even though the tissue was formalin-fixed.

Conclusion: This case serves as an important reminder to consider the possibility of herpetic hepatitis in young, previously healthy patients who present with acute hepatic failure, severely deranged liver functions and features of disseminated intravascular coagulopathy.

E-PS-15-008

Hyperinfestation syndrome of Strongyloides Stercolaris: when the biopsy leads to diagnosis

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Background & Objectives: Strongyloidiasis is caused by the penetration of infective mature filiform larvae through the skin and/or the ingestion of immature forms (eggs and rhabditiform larvae) of the nematode Strongyloides Stercolaris, endemic to tropical and warm regions. Clinically, the disease progresses from an acute cutaneous phase, during which the host's unprotected skin is penetrated, to a chronic systemic phase which ends with the migration of the parasite from the organs of the gastrointestinal tract, via the host's bloodstream, to the respiratory and lymphatic systems. Asymptomatic cases which remain undiagnosed until reaching advanced stages, carry a high mortality rate.
Methods: We present the case of a 59-year-old apparently immunocompetent woman from Colombia with no relevant medical history. She was admitted to our hospital due to persistent vomiting, diarrhoea, and weight loss, associated with unexplained eosinophilia and hyponatremia. Stool cultures were negative. CT scan showed ascites, pleural effusion and consolidations in addition to diffuse gastroenterocolitis. Gastroscopy from oesophagus to duodenum was non-specific with oedema, thickening and friable mucosa suggesting an inflammatory origin.
Results: Biopsies were performed from the oesophagus, stomach, and duodenum, showing acute inflammatory response associated with parasitic forms of Strongyloides Stercolaris at different stages of development. Only the duodenum was ulcerated. Following the pathology report, a bronchial aspirate sample was obtained with evidence of mature filiform larvae confirming the diagnosis. Although the patient was immediately started on antiparasitic treatment, she died in less than 24 hours. Post-mortem serology for HTLV-1 virus turned out positive, justifying the clinical picture.
Conclusion: Although culture or serology are the usual diagnostic methods, the importance of an adequate histopathological diagnosis remains crucial, as it can directly identify the parasite. Just as in our case, hyperinfestation syndrome should be taken into consideration as a differential diagnosis in apparently immunocompetent patients from endemic areas with severe chronic gastrointestinal symptomatology.

E-PS-15-009

Leprosy does not disappear: remembering its reality beyond Europe

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Background & Objectives: Leprosy although it is very rare in our continent, it continues to be endemic in Africa. Diagnosis requires clinical assessment,Acid-resistant bacilli are not always identified. Leprosy was classified by Ridley-Jopling into tuberculoid leprosy (with epithelioid cell aggregates), lepromatous leprosy (with Virchow cells), and a borderline spectrum. The New Indian classification introduced indeterminate leprosy, which shows only lymphohistiocytic infiltrates localized around nerves and appendages, without the presence of bacilli.
Methods: We received 42 cases for diagnosis at the end of 2024 from various regions of Malawi through the NGO "DERMALAWI". Clinical histories, histological preparations, and immunohistochemical/histochemical techniques were reviewed for suspected infectious dermatoses. A bibliographical review of leprosy was conducted.
Results: 4 cases of tuberculoid leprosy: These showed a well-defined granulomatous inflammatory infiltrate with epithelioid cells, giant cells, and macrophages without necrosis, and a lymphocytic crown. The distribution was perineural and perianexial in both superficial and deep dermis.
2 cases of lepromatous leprosy: These showed a perineural accumulation of foamy macrophages in an "onion skin" pattern in the dermis, with a visible Grenz zone and atrophic epidermis.
1 case of borderline tuberculoid leprosy: This case showed poorly defined granulomas with fewer lymphocytes and macrophages. The epidermis was atrophic, and the nerves did not show complete destruction.
5 cases of indeterminate leprosy: These showed a lymphocytic inflammatory infiltrate, both superficial and deep in the dermis, surrounding blood vessels, appendages, and nerves, with few macrophages.
Conclusion: Despite not being in an endemic zone, it is important to understand its histology, as cases may be referred to us at any time, and proper identification is crucial. We emphasize the importance of international collaboration and monitoring in endemic areas for proper diagnosis and timely intervention in vulnerable populations. There are two histological forms that may overlap with other conditions, making it essential to rely on diagnostic clues.

E-PS-15-010

Hydatidosis infection in an unusual sites: an ongoing diagnostic problem in the 21st Century

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Background & Objectives: Hydatidosis is a zoonotic disease caused by the larval form of *Echinococcus granulosus*. Tunisia is an endemic country, with an incidence of 15.1 per 100,000 inhabitants. The disease typically affects the liver and/or lungs. However, in exceptional cases, hydatid cysts can develop in atypical locations, posing diagnostic challenges.
The aim of this study was to report the epidemiological, clinical, and histological features of hydatid cysts of uncommon hydatid cyst localizations.
Methods: This is a retrospective study conducted in our department of pathology between 2004 and 2024, including cases of hydatid cysts diagnosed in rare anatomical sites.
Results: Twenty-six patients were included (female/male=1) aged between 18 and 76 years with a mean of 44. The most frequently involved organ werechest wall (n=18) and spleen (n=4) followed by pancreas (n=2). The other localizations female genital and peritoneum were noted in one cases each. For chest wall, the most common site was costal (n=13), followed by vertebral (n=2), clavicular (n=1), and sternal (n=1) involvement. The most frequently affected ribs were the 7th (n=6) and 8th (n=6), followed by the 3rd, 5th, 6th, and 9th ribs (each in 2 cases). Clinical presentations varied based on cyst location. Bone cysts typically presented with chest pain. While splenic cysts presented with mild abdominal discomfort and pancreatic cysts were associated with episodes of acute pancreatitis. Radiological investigations revealed cysts appearing as multiple opacities. All patients underwent surgical treatment. Histopathological examination confirmed hydatidosis infection of by identifying the

hydatid membrane and its multivesicular nature. The postoperative course was favourable in all patients, with no reported recurrences.
Conclusion: This case series emphasizes the importance of considering hydatid cysts in the differential diagnosis of cystic lesions in unusual locations. Imaging aids in preoperative evaluation, but histopathology remains the key diagnostic tool for confirmation. Surgery remains the preferred curative treatment for this condition.

E-PS-15-011

Mycobacterium tuberculosis complex: an unexpected cause of necrotizing granulomatous epididymo-orchitis mimicking malignancy

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Background & Objectives: We present a case of a 67-year-old immunocompetent man, born in Austria, who was referred to the urology outpatient clinic, because of an enlarged right testicle for the last 9 months. The patient did not report any tenderness of the testis, fever, weight loss or night sweats. Because of suspected malignancy, a radical orchiectomy was scheduled. Blood analysis showed no signs of lymphoma and no elevated tumour biomarkers. Performed thoracic and abdominal computational tomography (CT) revealed unspecific retroperitoneal lymphadenopathy and no metastatic lesions.
Methods: Right radical orchiectomy was performed and the tissue was analysed at the institute of pathology.
Results: The histology revealed extensive necrotizing granulomatous infection of the epididymis and testis with interspersed Langhans giant cells and no evidence of malignancy. A Ziehl-Neelsen staining was performed, in which no acid-fast bacilli were detected. PCR from the tissue was positive for *Mycobacterium tuberculosis* complex (MTBC). No culture was obtained as repeated sputum and urine samples were negative for MTBC. Chest X-ray did not show any abnormalities. After surgery, the patient developed active lesions in his left testicle, which were observed by ultrasound. The patient was started on standard treatment. After 4 months, follow-up ultrasound showed a significant improvement.
Conclusion: Necrotizing granulomatous epididymo-orchitis can mimic malignancy and is caused by a myriad of pathogens such as *Brucella* spp., *Salmonella typhimurium*, *Histoplasma capsulatum* and MTBC. Some cases have been reported after Bacillus Calmette-Guérin (BCG) instillation. Literature suggests that the majority of cases are caused by MTBC or *Brucella* spp. and should be tested in order to provide adequate treatment.

E-PS-15-012

Chronic cutaneous infection by dematiaceous fungi: a case report of chromoblastomycosis with leprosy-like features

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Background & Objectives: Chromoblastomycosis is a chronic fungal infection that affects the skin and subcutaneous tissue, caused by dematiaceous fungi. This disease is predominantly found in tropical and subtropical regions, particularly in areas with warm and humid climates. Infection is typically acquired through traumatic inoculation of fungal spores present in the environment. Cutaneous lesions can be easily mistaken for other infectious and non-infectious conditions, making early diagnosis challenging. In this report, we present the case of a 50-year-old male farmer with a chronic leg lesion following an injury, who was initially treated under the clinical suspicion of leprosy. Through this case, we aim to highlight the diagnostic and clinical features of chromoblastomycosis, a rare and under-recognized disease.
Methods: A skin biopsy obtained from the patient was evaluated through histopathological analysis. The specimen was subjected to several special stains, including Haematoxylin and Eosin (H&E), Periodic Acid-Schiff (PAS), silver stain, and Ziehl-Neelsen (ZN), in order to identify characteristic fungal structures and to rule out other potential infections.
Results: Microscopic examination revealed pseudoepitheliomatous hyperplasia with intraepidermal abscesses and pigmented fungal sclerotic bodies (Medlar bodies) located in both the superficial and reticular dermis. Fungal elements were clearly visualized with PAS and silver stains, confirming the presence of dematiaceous fungi. Ziehl-Neelsen staining was negative, effectively ruling out the presence of mycobacteria.
Conclusion: The histopathological findings, in conjunction with the patient's clinical history, are consistent with a diagnosis of chromoblastomycosis. Consideration of epidemiological factors and the clinical presentation is critical in reaching an accurate diagnosis. In tropical countries, a wide range of microorganisms must be included in the differential diagnosis. Therefore, early and accurate recognition of this disease is essential for initiating timely treatment and preventing complications.

E-PS-15-013

Non-tuberculous mycobacterial nasal cavity infection caused by mycobacterium simiae in an immunocompetent 86-year-old female patient

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Background & Objectives: *Mycobacterium simiae* is a non-tuberculous mycobacterium (NTM) primarily associated with pulmonary disease and rarely presents as localized lesions. We report a case of *M. simiae* infection manifesting as a nasal cavity mass in an immunocompetent 86-year-old woman with a history of hypertension and a prior left pontine infarct. She experienced recurrent right-sided epistaxis for 20 days in February 2022. Laryngoscopic examination revealed a soft, non-tender, pea-sized mass originating from the right nasal septum. Paranasal sinus computed tomography identified a 1 cm-sized nodular lesion in the right anterior nasal cavity. The mass was excised via laryngoscopic examination. Routine laboratory tests were unremarkable, and a nasal swab for COVID-19 was negative.
Methods: The excised tissue underwent haematoxylin-eosin staining for histopathological evaluation and acid-fast bacilli staining for mycobacterial detection. Real-time polymerase chain reaction (PCR) and sequencing analysis were performed to identify NTM species.
Results: Histopathologic examination revealed poorly defined, irregularly shaped, chronic granulomatous inflammation with extensive foamy macrophages and suppurative inflammation. Acid-fast bacilli staining and PCR for NTM yielded positive results. An atypical mycobacterial infection was diagnosed. Real-time PCR, followed by sequencing, identified *Mycobacterium simiae* strain MH4 based on 16S-23S ribosomal RNA analysis. The patient remained asymptomatic following mass excision and did not require additional antimicrobial therapy. She continues routine follow-up for preexisting condition.
Conclusion: *Mycobacterium simiae* infections can closely mimic tuberculosis and other granulomatous diseases. As NTM infections are increasingly recognized worldwide, heightened awareness and the

use of molecular diagnostic tools are essential for accurate diagnosis and management. This case underscores the importance of considering *M. simiae* as a differential diagnosis in localized granulomatous nasal lesions, even in immunocompetent patients.

E-PS-15-014

Hydatid cyst in an unusual sites: a challenging diagnosis

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Background & Objectives: Hydatid disease, caused by Echinococcus granulosus, typically affects the liver and lungs, but rare atypical localizations pose diagnostic challenges. This study presents cases of uncommon hydatid cyst sites, highlighting their clinical and pathological features.
Methods: We retrospectively reviewed cases of hydatid cysts diagnosed in rare anatomical sites over 15 years in our pathology department. Diagnosis was confirmed by histopathology following surgical excision. Clinical, imaging, and histopathological characteristics were analysed.
Results: Eight cases were included (age range: 24–65 years, F/M ratio: 3:1). Uncommon localizations included the spleen (4 cases), pancreas (2), uterus (1), and peritoneum (1). Clinical presentations varied: splenic cysts were mostly incidental or caused mild discomfort, while pancreatic cysts were associated with acute pancreatitis. The uterine cyst appeared as a solid-cystic pelvic mass with pain, and the peritoneal cyst was incidentally discovered. Imaging findings showed well-defined, hypoechoic splenic cysts (4 cases), with a "water lily" sign on CT (2 cases). Pancreatic cysts exhibited ductal dilatation and multiple cystic lesions, while the uterine cyst appeared solid-cystic on ultrasound and CT. Cyst sizes ranged from 7 to 18 cm. Macroscopic examination revealed fibrous and calcified cyst walls with hydatid membranes in most cases. Histologically, all cases showed fibrous cyst walls with granulomatous inflammation. One splenic case lacked hydatid membranes, suggesting degeneration.
Conclusion: Hydatid cysts should be considered in the differential diagnosis of cystic lesions in unusual locations. Imaging is valuable for preoperative assessment, but histopathology remains essential for definitive diagnosis.

E-PS-15-015

Unusual hydatid cysts: 5 cases report with heart, brain, kidney, muscle and bone localization

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Background & Objectives: Cyst Hydatid, the causative agent of which is Ecinococcus Granulosus, is a zoonotic disease that causes significant public health problems and serious economic losses, especially in developing Mediterranean countries. The parasite lives in the small intestines of dogs. Humans ingest the eggs, which are spread to the environment through dog feces; the ingested eggs hatch in the human intestine and first reach the liver via blood, where they most frequently form cysts. Those that manage to pass through the liver sinusoids cause disease by forming cysts in other organs, especially the lungs.
Methods: In this report, cases of hydatid cysts localized in the tibia in a 70-year-old male patient, intramuscular localization in the cruris in a 37-year-old female patient, cardiac localization in a 45-year-old male patient, renal localization in a 44-year-old female patient, and brain parenchymal localization in a 30-year-old male patient will be presented.
Results: Almost any anatomic location can be the host site of the parasitic cysts. Hydatid cysts in the liver and lung constitute 90-95% of all hydatid cyst cases. Hydatid cysts with unusual localization are extremely rare, even in endemic areas.
Conclusion: The disease may have many different clinical presentations. The widespread use and development of imaging methods such as CT and MRI make our job easier in diagnosis. Although it is a benign disease, sometimes it can cause serious morbidity and even mortality. It is for this reason that it should definitely be kept in mind in differential diagnosis. Surgery is the mainstay of treatment. Albendazole is used in drug therapy.

E-PS-15-017

Morphological changes in lung vessels in Covid-19

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Background & Objectives: Covid-19 infection has caused a large number of complications and deaths. Studying the causes of the disease is a very urgent task.
Methods: The study examined histological lung sections from 68 deceased COVID-19 patients, autopsied in August-September 2021. Samples were processed, embedded in paraffin, and stained with haematoxylin and eosin for microscopic analysis. Significant pathomorphological changes in pulmonary vessels were documented.
Results: COVID-19 induces severe endothelial damage due to high ACE2 expression. This results in endotheliosis, endotheliitis, coagulopathy, and vasculitis. Vessels of varying calibers show fibrinoid necrosis, thrombus formation, and haemorrhagic-fibrinous inflammation. Microscopic examination reveals dilated capillaries, perivascular haemorrhage, and thickened alveolar walls. The proliferative phase shows lymphohistiocytic infiltration, vessel wall oedema, and sclerosis. Some vessels display fibrin thrombi and destroyed endothelial layers. During the proliferative phase, vessel walls thicken, showing mucoid and fibrinoid degeneration with perivascular lymphohistiocytic infiltration. Severe infiltration by histiocytes extends into alveolar tissue. The alveolar walls become airless and indistinguishable due to deventilation and haemorrhagic inflammation. Fibrin thrombi are commonly found in small pulmonary vessels.
Conclusion: SARS-CoV2-induced endothelial damage and ACE2 receptor abundance result in severe discirculatory changes, including endotheliosis, coagulopathy, vasculitis, and thrombus formation. The proliferative phase is marked by lymphohistiocytic infiltration, vessel wall destruction, and subsequent sclerosis.

E-PS-15-018

Unveiling granulomatous skin lesions story

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Background & Objectives: Granulomatous skin lesions present a diagnostic challenge, displaying varied clinical forms with overlapping histopathology. Accurate diagnosis requires clinical correlation and tests. India, endemic to TB and Leprosy, sees many infectious skin diseases like these presenting as granulomatous lesions. A systematic approach helps distinguish infectious, inflammatory, and immune causes. This case series aims to study the diagnosis and incidence of such lesions reported to our department.
Methods: This case series of 20 granulomatous skin lesions at Bharati Vidyapeeth Deemed University, a tertiary centre in Western Maharashtra, analyzes age, gender, histopathology, and final diagnosis after special staining.

Results: The mean age of 20 cases was 38.3 years (range: 14–70). There were 7 females (35%) and 13 males (65%). Swelling was the most common feature (9 cases, 45%). Lesions were on the upper limb in 13 cases (65%) and head-neck in 7 (35%). Histopathology showed 15 granulomatous lesion (75%) —3 suggestive of TB (20%). 5 of foreign body granuloma (25%)- 02 infected epidermoid cyst with foreign body granuloma(10%), 03 only showing foreign body granuloma(60%). Special staining confirmed 10 cases (50%), including 5 tuberculoid (25%) and 4 borderline tuberculoid leprosy (20%).
Conclusion: Our case series highlights the diagnostic complexity of granulomatous skin lesions, emphasizing the need for a systematic approach incorporating histopathology and ancillary tests for accurate identification. While most cases were correctly diagnosed histopathologically, special staining played a crucial role in confirming infections such as tuberculoid leprosy and fungal granulomas. A multidisciplinary correlation remains essential to differentiate between infectious and non-infectious causes, ensuring appropriate patient management.

E-PS-15-019
Histopathological diagnosis of rhinosinusitis-mucormycosis during the COVID-19 Pandemic. A cases serie from Venezuela
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Background & Objectives: Mucormycosis is a potentially fatal infection.
Methods: Cases of rhinosinusitis-mucormycosis during 2021 are studied. Pathological diagnosis was done by means H&E, Grocott´s methenamine silver, and PAS stains in rhinosinusal biopsies.
Results: Four patients were male (51-71 years old), two were female (38-59 years old). Three cases develop a mucormycosis-actinomycosis co-infection. All cases exhibited a necrotizing process. Radical surgical debridement was performed in all cases.
Conclusion: Pathological diagnosis was fundamental for specific antifungal-antibacterial treatment. Favorable clinical outcome was observed.

E-PS-15-021
Unmasking the unseen enemy: a retrospective study of the clinicopathological spectrum of histoid leprosy at a tertiary care hospital in South India
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Background & Objectives: Leprosy is one of the oldest chronic infectious diseases known to man caused by Mycobacterium leprae. Leprosy has been declared eliminated (<1 case/ 10,000 population) in our country on December 31st, 2005. However, cases continue to be reported with varying prevalence all over India. Histopathological study in clinically suspicious cases plays a critical role in confirming the diagnosis, subtyping, prognostication and assessment of disease in patients. Histoid leprosy is a highly bacilliferrous type of lepromatous leprosy. It was previously believed to manifest after failure of long-term dapsone monotherapy or due to irregular and/or inadequate therapy. However, we now know that it sometimes arises de novo.
To study the incidence and clinicopathological characteristics of histoid leprosy.
Methods: All histopathologically confirmed cases of Hansen's disease received over a period of 5 years (January 2020-December 2024) were examined. Haematoxylin and Eosin and Fite-Faraco stained sections of all the cases were examined. Clinical details and corresponding slit-skin smears, wherever available, were also reviewed.
Results: 590 new cases of leprosy were registered in the Department during the study period. Histoid Leprosy was seen in 16 patients (0.027%). The mean age of 42.25 years along with male preponderance (68.7%) was observed. Skin nodules were seen in half the cases, but only one patient had deformity during their first visit. One patient developed type II lepra reaction (erythema nodosum leprosum). None of these patients had received any anti-Hansen's disease treatment prior to presentation and the lesions all appeared de novo.
Conclusion: Histoid leprosy is a rare subtype of Hansen's disease. Mimics, lack of knowledge of this variant with high bacillary load among pathologists and medical officers may lead to misdiagnosis. Histological awareness of this entity and use of special stain is warranted to differentiate it from its mimics for early treatment and prevention of deformities.

E-PS-15-022
Secondary syphilis – condyloma lata: an unusual clinical manifestation of secondary syphilis. Case report
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Background & Objectives: Syphilis, caused by Treponema pallidum, is resurging globally, particularly in developing regions. Secondary syphilis presents with varied mucocutaneous manifestations. Condyloma lata—broad-based, moist, gray-white papules in the anogenital region—is rare but highly contagious. In endemic areas like Colombia, underreporting and clinical misdiagnosis remain common due to atypical presentations.
Methods: A 77-year-old illiterate, widowed male from rural Colombia presented with weeks-long hematochezia and progressive, painless perianal verrucous lesions. He denied pruritus, systemic symptoms, or high-risk sexual behaviour. Colonoscopy revealed grade II internal hemorrhoids. Differential diagnoses included condyloma acuminata, squamous cell carcinoma, and rectal carcinoma.
Results: Skin biopsy showed psoriasiform epidermal hyperplasia, plasma cell-rich infiltrates, endothelial proliferation, and spirochetes highlighted by IHC using anti-Treponema pallidum antibody. Serologic tests (VDRL, FTA-ABS) were positive; HIV was negative, confirming secondary syphilis.
Conclusion: Though uncommon, condyloma lata is highly infectious and clinically relevant. Its resemblance to viral or fungal lesions can mislead clinicians and delay appropriate treatment. Histopathology and serology are essential for definitive diagnosis. In endemic, underserved areas, awareness of such atypical syphilitic manifestations is critical for early intervention and public health efforts.
This case underscores the importance of considering condyloma lata in the differential diagnosis of perianal lesions, even in immunocompetent patients without classic risk factors. Timely recognition through histopathology and serologic confirmation is vital to ensure treatment and reduce transmission, especially in resource-limited settings.

E-PS-15-023
Differential expression of TLRs in HPV-related oral benign lesions with and without concomitant *Candida* infection
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Background & Objectives: Human Papillomavirus (HPV) is a DNA virus with over 200 genotypes, transmitted through skin or mucosal contact. It can cause both low-risk and high-risk lesions, with low-risk types leading to benign epithelial lesions such as squamous papillomas, condyloma acuminatum, verruca vulgaris, and focal epithelial

hyperplasia. HPV can disrupt the innate immune system, particularly by impairing cytokine production and Toll-like Receptor (TLR) signalling, which has made TLRs a target for immunotherapy research. HPV infects basal keratinocytes, and these cells express TLRs, which act as the body's first line of defense against pathogens. In our Oral Pathology Service, we observed that some of these HPV-related lesions are also infected by Candida. This study aimed to examine the relationship between HPV-induced benign oral lesions, Candida infection, and TLRs 1, 2, and 3 expressions.
Methods: We reviewed 129 HPV-related cases from our archives, including 107 papillomas, 21 cases of condyloma acuminatum, and 2 cases of papillary hyperplasia. We used PAS staining for Candida detection and immunohistochemistry to assess TLR expression.
Results: Out of 129 cases, 13 (12 papillomas and 1 condyloma) showed Candida infection. The tongue was the most commonly affected site. Histologically, all cases showed papillomatosis, koilocytes, exocytosis, and elongated rete ridges. Immunohistochemistry revealed that in Candida-infected lesions, TLRs 1 and 2 expression was completely lost, while TLR3 expression remained unchanged.
Conclusion: Our study suggests that HPV-related benign oral lesions, when associated with Candida infections, alters the expression of TLRs 1 and 2, but not TLR3.

E-PS-15-024
Cutaneous Leishmaniasis in an immunocompetent patient: a clinical and pathological case report
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Background & Objectives: Cutaneous leishmaniasis (CL) is a parasitic infection caused by protozoa of the Leishmania genus, transmitted by sandflies. It is endemic in tropical and subtropical areas, including Latin America, the Middle East, North Africa, and South Asia. In the Americas, Colombia, Brazil, Peru, and Bolivia report the highest cases. While immunosuppression increases susceptibility, CL can also occur in immunocompetent individuals, where it may present diagnostic challenges, particularly in urban or non-endemic settings.
We report the case of a 66-year-old retired woman living in a Colombian city at an elevation of 959 meters above sea level, with no history of immunosuppression. She presented with a 2-week history of a non-healing, painless, ulcerated lesion measuring 5 cm on the left cheek. Physical examination revealed a well-demarcated ulcer with raised, indurated borders and a granulating base.
Methods: A skin biopsy was performed for histopathological analysis. Haematoxylin and eosin staining revealed a dermal infiltrate of lymphocytes, plasma cells, and histiocytes containing intracellular amastigotes. In these cases, re-cuts of thin paraffin sections (3 microns) with H&E are considered to be enough and highlight the presence of Leishmania spp. within macrophages; Giemsa staining was not used. The patient was treated accordingly and showed significant clinical improvement within two weeks. PCR confirmation was not available due to resource limitations.
Results: This case illustrates the typical presentation of CL in an immunocompetent host in an endemic region. CL can mimic other infectious or neoplastic conditions, emphasizing the importance of clinical suspicion and histopathological confirmation, particularly in settings with limited access to molecular diagnostics.
Conclusion: CL remains a public health concern in endemic regions. Early recognition and biopsy-based diagnosis in immunocompetent patients are crucial for timely treatment and improved outcomes.

E-PS-15-025
Molecular diagnosis of parasites in formalin-fixed paraffin-embedded tissue: lessons from a national parasitology reference laboratory in South Africa
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Background & Objectives: A wide variety of parasites is encountered in human tissue, including arthropods, protozoa and helminths. Many parasites cannot be cultured in vitro and often, a formalin-fixed paraffin-embedded (FFPE) tissue specimen is the only sample submitted for assessment. In general, the microscopic anatomic morphology of each of the major groups of parasites is sufficiently different to enable discrimination with the aid of a few key features; however, further genus and species-level identification may be required to guide appropriate treatment. Here we describe a few clinical cases referred to a national and regional parasitology reference laboratory in South Africa that warranted molecular testing.
Methods: Tissue specimens with suspected parasitic infections referred over a three-year period (2022 to 2025) were investigated at the reference laboratory following clinical consultation and referral by histopathologists from across the private and public healthcare sectors. Slides were reviewed by the pathologists and directed towards specific molecular testing, depending on the morphology observed in tissue.
Results: Three cases of *Leishmania tropica*, one case of *Leishmania infantum*, two cases of *Balamuthia mandrillaris* (and a third in which the diagnosis was made on archived DNA) and the first reported human case of *Cephalobus cubaensis*, a free-living nematode, were confirmed using PCR and sequencing on DNA extracted from FFPE. These cases, along with relevant images, are described.
Conclusion: Molecular diagnostics to identify parasites from FFPE tissue is becoming more important in the setting of global travel, climate change, emerging and re-emerging infections. Definitive diagnosis and directed management are not possible in many cases based on histomorphology alone. Histopathologists are critical to the detection of infectious diseases in many instances and a multidisciplinary approach, together with clinical microbiologists and clinicians, is key in improved diagnosis and patient outcomes. Molecular diagnostics in medical parasitology has an increasingly important role to play in infectious diseases pathology and surveillance.

E-PS-15-026
Mucosal leishmaniasis masking as squamous cell carcinoma of the tongue - a case report
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Background & Objectives: With the potential to cause disabling sequelae, mucosal leishmaniasis is a rare clinical variant most commonly caused by *Leishmania brasiliensis* in northeast Brazil and *Leishmania infantum* and *Leishmania donovani* in Africa and the Mediterranean Europe. Albeit its severity, this condition is still

overlooked in endemic areas. Here we present a case report of fatal case of mucosal leishmaniasis.
Methods: The patient was a 76-year-old woman that presented a tumour at the base of the tongue with 3cm at its widest measure with a 1.5cm ulceration in the right glossopharyngeal pillar, which retracted and distorted the epiglottis. The vallecula was not ulcerated but superficialized by the tumour, with the laryngeal surface of the epiglottis and the glottis free. A synchronous tumour of 1.5cm was found in the right tonsillar fossa. Patient also presented with enlarged lymph node of 2cm width on the right side of the neck. The initial and clinical differential diagnosis was squamous cell carcinoma (SCC).
Results: Biopsy of the tumour at the base of the tongue was done and histological sections showed fragments of tissue lined by squamous epithelium with ulceration and neutrophil exocytosis. The lamina propria exhibited a prominent mixed granulomatous inflammatory infiltrate containing numerous histiocytes. These histiocytes displayed numerous small, round and oval basophilic structures within their cytoplasm, consistent with amastigotes, which confirmed the diagnosis of mucosal leishmaniasis. Unfortunately, the patient passed away shortly after the biopsy due to respiratory insufficiency and an autopsy was not performed.
Conclusion: Even though its severity is known, mucosal leishmaniasis is still overlooked even in endemic areas, highlighting the need to lower the threshold for suspicion when inflammatory and granulomatous mucosal lesions are present in patients from endemic regions. Biopsy should not be delayed in such cases due to their high potential of destructive and disabling outcomes.

E-PS-15-027
Review and discussion of alveolar hydatid cyst cases
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Background & Objectives: Alveolar hydatid cyst is a chronic, complicated, and sometimes fatal parasitic infection caused by Echinococcus multilocularis (EM). It is seen mainly in Eastern and Southeastern Anatolia, Trakya, and Central Anatolia regions in our country. Since EM leads to exogenous proliferation, invasion, and tissue destruction, it can be difficult to differentiate it from malignant tumours. Diagnosis is often challenging, leading to late detection and poor prognosis. Given the often non-specific clinical presentation, diagnosis relies on radiologic imaging, serologic tests, and pathologic findings. We aimed to contribute to the literature by reviewing the clinicopathologic features of patients diagnosed with alveolar hydatid cyst in our clinic.
Methods: We retrospectively evaluated the demographic characteristics, histopathologic, and radiologic findings of cases diagnosed with alveolar hydatid cyst between 2010 and 2024 using archival data.
Results: The study included 10 cases. The mean age of the patients was 43.3 years, with 6 females and 4 males. Nine cases were located in the liver, and one in the brain (left frontal and left parietal regions). Radiologically, the possibility of malignancy could not be excluded in 6 cases due to heterogeneous contrast enhancement and irregular contours. In one case, suspicion of cholangiocarcinoma was indicated. In the resection specimen, large and small cysts surrounded by a cuticular membrane on a necrotic background, along with histiocytic giant cells and chronic inflammatory cells, were observed, and the cases were reported as alveolar hydatid cysts.
Conclusion: The mean age, gender distribution, and localization of our cases are consistent with the existing literature. The radiologic suspicion of malignancy in most cases suggests that alveolar hydatid cyst should be considered in the differential diagnosis of lesions that are clinically and radiologically suggestive of malignancy, especially in the liver.

E-PS-15-028
Tularemia orchitis following pneumonic tularemia: a histopathologically confirmed case in a patient under TNF(tumour necrosis factor)-α inhibition
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Background & Objectives: Tularemia is a rare zoonotic infection caused by Francisella tularensis, with highly variable clinical presentations. Orchitis is an extremely uncommon manifestation, particularly in immunosuppressed patients. This case report highlights a rare recurrence of tularemia presenting as orchitis, emphasizing the pathological findings and diagnostic challenges in a patient under TNF-α inhibitor therapy.
Methods: A 71-year-old male with psoriatic arthritis on adalimumab was diagnosed with pneumonic tularemia, confirmed by blood cultures. Following initial remission under doxycycline, the patient presented three months later with unilateral orchitis. After orchiectomy, the testicular specimen underwent histological examination. Routine haematoxylin and eosin (H&E), PAS/alcian blue, Gram stains, and immunohistochemistry (OCT4, SALL4, CD3, CD20, CD45, CD68, CD163) were performed. PCR for F. tularensis was conducted on native tissue.
Results: Gross examination revealed an irregular, enlarged testis with an inhomogeneous mass. Histologically, a pronounced orchitis with only minimal epididymal involvement was observed. The seminiferous tubules were filled with predominantly histiocytes (partly epithelioid), neutrophilic granulocytes, and CD3-positive T-lymphocytes. In less affected areas, interstitial oedema and Sertoli-cell-only-like changes were noted, with focal spermatogenesis. Spermatogonia were detected focally using the SALL4 stain. The testicular stroma exhibited mild inflammatory infiltration, composed primarily of histiocytes, neutrophils, and CD3-positive T-cells. Scattered small purulent foci were present. No granulomatous reaction or caseous necrosis was identified at this stage. Focal lymphadenitis was also observed. Notably, no bacteria were seen microscopically, and germ cell neoplasia in situ was excluded via OCT4 staining. This represents a relapse likely due to the blood-testis barrier and limited doxycycline penetration.
Conclusion: This is the second histopathologically confirmed case of tularemia orchitis worldwide. In immunosuppressed patients, especially those under TNF-α inhibition, F. tularensis should be considered in atypical inflammatory presentations. Orchiectomy combined with extended antibiotic treatment (doxycycline and ciprofloxacin) resulted in remission. Pathologists should be sensitized to the possibility of rare relapse forms of tularemia.

E-PS-15-029
Spatial profiling of the intratumoral microbiome with RNAscope and QuPath
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Background & Objectives: The intratumoral microbiome recently gained significant attention, offering a new perspective on cancer research. The spatial distribution of microbes within tumours could provide more details regarding the interaction with tumour cells (TC). We sought to define the spatial representation of tumour microbes in tissues by utilizing RNAscope and QuPath.
Methods: We selected 7 primary colorectal carcinomas (CRC), 11 lung metastases originating from CRC (mCRC), and 6 primary lung adenocarcinomas (PLA). For each case, one section of formalin-fixed paraffin-embedded tissue was analysed with RNAscope assay (16S rRNA Eubacteria; Advanced Cell Diagnostics). Slides were scanned using the Pannoramic 1000 Scanner (3DHISTECH) at 40x resolution, and image analysis was performed with QuPath.
Results: Out of 24 slides, 10 were successfully evaluated. The remaining slides were excluded due to artifacts or scanning issues. The 10 cases were represented by 6 CRC, 3 mCRC, and 1 PLA.
For CRC, the mean tumour bed area (TBA) was 202 mm², containing an average of 435,434 TC. In mCRC, the mean TBA measured 92 mm², with an average of 43,005 TC, and the single case of PLA had a TBA of 113 mm², with an average of 334,410 TC.
Comparing the number of detected signals, CRC showed the highest mean with 7,401 signals, followed by the case of PLA with 2,145 signals, and mCRC with a mean of 139 signals, further supporting the idea of increased microbial load in CRC compared with other tumours. Regarding subcellular distribution, the majority of signals in all tumour types were localized in the cytoplasm; specifically, CRC showed 65% of signals in the cytoplasm, PLA 85%, and mCRC 69%.
Conclusion: QuPath proved to be a valuable tool for analysing large amounts of data from histological slides; however, it requires high-quality slides. Future studies should aim to include larger cohorts and a more standardized approach to analysis.

E-PS-16 E-Posters Molecular Pathology

E-PS-16-001

Pitfalls in the interpretation of DNA mismatch repair protein expression by immunohistochemistry: experience with unusual expression patterns from the University Hospitals Birmingham

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Background & Objectives: Testing for mismatch repair (MMR) defects is routine care for patients with advanced cancer across a broad spectrum of tumour types. Commonly, the first step is immuno-histochemistry for MLH1, PMS2, MSH2 and MSH6. The interpretation of MMR protein immunohistochemistry is usually straightforward, but a minority of cases is challenging. Our objective was to aid histopathologists in the interpretation of these rare patterns and further testing based on our experience.
Methods: We collected all cases with unusual MMR protein expression patterns on immunohistochemistry performed between the 1st of July 2018 and the 1st of March 2025 at the Molecular Pathology Diagnostic Service in Birmingham. An unusual staining pattern was defined as different from a classical pattern (no loss of expression, loss of MLH1/PMS2 expression, isolated loss of PMS2 expression, loss of MSH2/MSH6 expression or isolated loss of MSH6 expression). Further testing was performed by immunohistochemistry for BRAF V600E or PCR for BRAF codon 600 and/or MLH1 methylation profiling by Pyrosequencing.
Results: We found 70 cases with unusual patterns out of a total number of 21561 specimens (0.3%) for which MMR immunohistochemistry was performed. The most frequently observed unusual pattern was the additional (complete or clonal) loss or reduced expression of MSH6 in the presence of loss of MLH1 and PMS2 expression (45/70 patients). In the majority of these cases (42/45 patients) we found a BRAF V600E mutation or methylation of the MLH1 promoter, strongly favouring sporadic nature.
Conclusion: Rare cases with unusual MMR protein expression patterns showed clonal loss of expression, reduced loss of expression or rare combinations of loss of expression, in particular concurrent loss of MSH6 and/or MSH2 in the presence of MLH1 loss. By testing for BRAF mutations and MLH1 methylation profiling we were able to prevent unnecessary referral to a clinical genetics service in most of these patients.

E-PS-16-002

Impact of oxidative stress and hypoxia status on glioblastoma development

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Background & Objectives: Gliomas represent 30% of all brain tumours and 80% of malignant tumours. Glioblastoma is the extremely aggressive type of these tumours and accounts for half of them, as it expresses the worst prognosis, limited to 14 months. The WHO 2021 classification of brain tumours identified certain classification criteria based on molecular confirmation involving several signalling pathways adding to histological features such as necrosis, endothelial-capillary proliferation, multiple mitoses. Furthermore, the resistance against radiotherapy and chemotherapy has been related to oxidative stress and hypoxia a predominant feature in gliomas and their microenvironment and is associated with tumour growth, progression, and resistance to conventional therapy.
This study aims to highlight the main biomarkers identified in glioblastomas and establish a correlation based on the overall survival of patients. It is a retrospective study conducted over a period of 3 years, involving 90 cases of GBM collected at the Ibn Rochd University Medical Centre in Casablanca.
Methods: Our study cohort included 35 women and 55 men, with a median age of 54 and ages ranging from 13 to 79. An immunohistochemical study was conducted using anti-IDH R132H, anti-NOX4, and anti-HIF-1α antibodies.
Results: Immunostaining with the anti-IDH R132H antibody yielded negative results in 7% of the cases (3 cases), consistent with findings reported in the literature. Additionally, immunostaining with the anti-NOX4 antibody was positive in 4% of cases, while the anti-HIF-1α antibody was expressed in 32% of cases.
Conclusion: Glioblastomas are rare and highly heterogeneous tumours. Their prognosis is closely linked to the molecular profile, making it essential to tailor therapeutic strategies to the individual characteristics of each case.

E-PS-16-003

Screening of Lynch syndrome in CRC: a monocentric consecutive case series

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Background & Objectives: Lynch syndrome (LS) accounts for 1-3% of all colorectal cancers (CRC). LS screening starts evaluating mismatch-repair (MMR) proteins expression. In case of MSH2, MSH6 and PMS2 isolated deficiency (d) a genetic counselling is mandatory. Whereas, in presence of MLH1 loss, often due to somatic alterations, the analysis of *BRAF*-V600E mutation and *MLH1* promoter methylation is recommended to identify likely sporadic cases.
This study assessed LS screening efficacy in a CRC monocentric and consecutive series.
Methods: From 2022 to 2024, 1,368 CRC were evaluated for MMR proteins expression by immunohistochemistry (IHC). In dMLH1 cases *BRAF*-V600E was analysed by IHC, then only negative *BRAF*-V600E cases underwent *MLH1* methylation test by pyrosequencing. Cases negative or indeterminate for both *BRAF*-V600E and *MLH1* promoter methylation were considered LS high-risk, requiring genetic counselling.
Here, we evaluated the prevalence of LS high-risk dMLH1 cases and their clinical-pathological characteristics.
Results: Overall, 162 CRC (12%) were dMMR, 121 (73%) were dMLH1. Forty-nine dMLH1 cases were *BRAF*-V600E negative: 24 showed *MLH1* methylation, 16 were non-methylated and 9 were indeterminate. Twenty-five (non-methylated/indeterminate) dMLH1 cases were LS high-risk (diagnosis median age: 61 years *versus* 76 for low-risk group). Genetic test was performed in 22 high-risk cases: 2 were LS positive and 20 negative. Seventy-one dMLH1 cases had a special histological subtype (42 with mucinous features, 17 mucinous, 5 medullary, 4 poorly differentiated and 3 signet-ring cells), with a higher prevalence in *BRAF-V600E* positive group.
Conclusion: In CRC, the dMMR phenotype can be sporadic (75%) or constitutively present within LS (25%). LS screening, mainly based on clinical criteria, can be improved by molecular tests. Our results supported the cost-effectiveness of the sequential analysis of MMR proteins, *BRAF*-V600E mutation and *MLH1* promoter methylation in the definition of high-risk patients, reducing unnecessary genetic counselling. Indeed, here only a small proportion of dMLH1 cases (25/121) was identified as high-risk.

E-PS-16-004

Combined positive score to evaluate PD-L1 expression in gastric and gastroesophageal junction adenocarcinomas

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Background & Objectives: PD-L1 expression has been investigated as a predictive biomarker of response to immunotherapy in several tumours, and is reported to be elevated in up to 40% to 65% of gastric or gastroesophageal junction adenocarcinoma (G/GEJ). There is a need to provide reliable, standardised training for pathologists to improve their accuracy of interpretation and scoring, as the results are used directly to inform clinical decisions. We present findings regarding reproducibility and improvement for scoring PD-L1 expression for GC using online training tool.
Methods: This study included 102 cases of G/GEJ adenocarcinoma. PD-L1 expression is scored using the combined positive score (CPS), which is calculated as the number of PD-L1–stained cells (tumour cells, lymphocytes, and macrophages) divided by the total number of viable tumour cells multiplied by 100.
The CPS was categorized into a four-step score (0–3) based on clinical relevant thresholds: 0 (CPS < 1), 1 (CPS 1–4), 2 (CPS 5–9), 3 (CPS ≥ 10). Online training was led by qualified and trained pathologists from Targos Molecular Pathology.
Results: The positive rates of CPS with a cutoff value of 1 and 5 were 38,2% (39/102) and 20,5% (21/102), respectively. More than half of the cases was PD-L1 negative (CPS < 1; 61,8%), 17,6% showed low PD-L1 expression (CPS ≥ 1, < 5), 2,9% moderate (CPS ≥ 5 to < 10) and 17,6% strong expression (CPS ≥ 10). Positivity rate after online training according to 1> and 5> cutoff value were 53,3% (24/45) and 35.6% (16/45), increased in line with the literature.
Conclusion: Consistent, accurate, and reproducible scoring of PD-L1 expression, regardless of scoring method, remains a concern.The online training tool offers a means of standardised training for practising pathologists in a clinical setting and can help pathologists successfully learn techniques to confidently score PD-L1 CPS across histologic subtypes and cutoffs.

E-PS-16-005

Assessment of morphological quality and nucleic acid yield and purity from FFPE tissue samples across various clinical tissue processors

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Background & Objectives: The ability to successfully isolate adequate and pure DNA for Next-Generation Sequencing (NGS) from Formalin-Fixed Paraffin-Embedded (FFPE) tissue is critical to molecular diagnostic tests known as NGS, which are gaining popularity. These diagnostic methods empower clinicians to provide personalized treatment and care to patients. The study's objective was to demonstrate that FFPE tissue processed on the Revos tissue processor yields sufficient amounts of nucleic acids required for downstream NGS testing and is of better quality for NGS than other tissue processors.
Methods: Fresh specimens from normal (n=15) and tumour (n=8) tissues were harvested via surgical resection and immediately fixed according to standard clinical laboratory practices using 10% Neutral Buffered Formalin (NBF). Each tissue was divided into three equal parts and processed according to each manufacturer's indicated routine program; three separate tissue processors were used to assess morphological integrity across each system, and isolated DNA was evaluated for quantity and quality to be used for NGS.
Results: The Epredia Revos tissue processor resulted in excellent tissue processing with no unprocessed tissues or tissue damage from all tissues (normal and tumour) observed macroscopically and microscopically. Using the routine surgical protocol setting, we obtained excellent morphology on all tissues (normal and tumour), as observed microscopically by H&E stained slides processed on the Epredia Revos tissue processor. Importantly, we could isolate DNA and RNA from the FFPE samples with enough material (> 0.5 micrograms of total DNA) for Next-Gen sequencing or molecular testing. The 260/280 ratio of the purified DNA was greater than two units, suggesting excellent purity
Conclusion: We observed that tissue processed on the Epredia Revos Tissue Processor demonstrated the isolated DNA samples should have enough starting material to perform next-generation sequencing; sample data suggests high purity and shows excellent overall morphological features compared to the other tissue processors in the study.

E-PS-16-007

AXL: an emerging biomarker and putative tyrosine kinase inhibitor target

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Background & Objectives: AXL, a receptor tyrosine kinase (RTK), has gained significant attention in cancer therapy due to its role in mediating resistance to Tyrosine Kinase Inhibitors (TKIs). AXL is involved in key signalling pathways that regulate cell survival, migration, and immune evasion, contributing to resistance in cancers such as non-small cell lung cancer (NSCLC), glioblastoma, and others. While AXL's role as a driver of TKI resistance is well-documented, the underlying mechanisms remain an area of ongoing research. Several AXL inhibitors, including BGB324 and R428, are currently undergoing clinical trials to evaluate their efficacy in overcoming TKI resistance or as potential novel stand-alone therapies across various malignancies. As new inhibitors targeting AXL approach clinical application, it is crucial to better understand the mechanisms through which AXL facilitates escape from TKI therapy. Furthermore, identifying potential escape mechanisms, particularly mutations, that may arise when AXL is directly inhibited is critical for improving therapeutic strategies.
Methods: In this study, we investigated AXL's mutational potential at both the DNA and RNA levels, focusing on known DNA mutations, methylation patterns, and RNA fusions. This is done by a comprehensive in silico analysis of clinical data repositores and samples analysed with our clinical partners. A key hypothesis in AXL-mediated TKI resistance is its ability to form heterodimers with other RTKs. To examine this, we employed AlphaFold 3 and subsequent PyMOL analysis to predict potential protein interactions, identifying the specific amino acids and corresponding DNA sequences relevant to successful heterodimerization
Results: Our findings aim to enhance the understanding of AXL-mediated resistance mechanisms and provide critical insights into optimizing AXL inhibition in clinical settings, with the potential to improve the effectiveness of both established and emerging TKI therapies.
Conclusion: Our primary findings highlight the importance of closely examining the molecular mechanisms underlying AXL signalling and AXL-mediated therapy resistance.

Funding: FWF doc.funds.connect PhD Program TOPICO: „Transformation of Pre-Clinics into Clinics by Organoids"

E-PS-16-008

Studying on EBER in situ hybridization with automated high-frequency ultrasonic cavitation-assisted rapid tissue processing method: an institutional experience

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Background & Objectives: Detection of EBER by in situ hybridization (ISH) has been established as the most sensitive and practical method for detecting EBV infection. However,tissue processing is still time consuming in most of pathology department. Finding a quick method of tissue processing can help reduce the detection time of EBER.
Methods: A total of 132 cases of nasopharyngeal carcinoma biopsy were collected. They were randomly divided into two groups. The control group used the traditional method which needs overnight, the experimental group used automated high-frequency ultrasonic cavitation-assisted rapid tissue processing method which needs only several hours. Compare the result of EBER ISH with two different dehydration procedures.
Results: There's no statistically significant difference between two methods, but there's statistically significant difference between the treatment time.
Conclusion: Rapid tissue processing with an ultrasonic cavitation-assisted device has no negative effect on EBER in situ hybridization in nasopharyngeal carcinoma(NPC) biopsies. It reduces the turnaround time for histopathology reports. Staining was with diaminobenzidine(DAB) may diminish heavy background compared to NBT.

E-PS-16-009

Real-world circulating tumour DNA (ctDNA) burden and androgen receptor ligand binding domain mutations (AR LBDm) in US prostate cancer patients

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Background & Objectives: ctDNA from blood-based liquid biopsies has emerged as a potential prognostic biomarker for managing prostate cancer (PC) and identifying actionable gene mutations for therapeutic targets. Recent evidence suggests that AR LBDm may play an important role in treatment resistance in PC, resulting in poor outcomes. This study utilized a large real-world database to better understand ctDNA burden and AR LBDm in US PC patients.
Methods: PC patients were identified between 06/2014 and 06/2023 from the Guardant Health INFORM™ clinical-genomic database, which links ctDNA results from the Guardant360® next-generation sequencing assay (G360) to de-identified medical claims. ctDNA burden was defined as the maximum variant allele frequency (MVAF) of all detected somatic variants. The prevalence of 12 AR LBDm detected by G360 and its association with real world overall survival (rwOS) was assessed.
Results: Among 16,757 PC patients, 87% had detectable ctDNA (median MVAF=1.9%; range: 0.01%-96.4% among ctDNA positive patients). Patients with metastatic PC had higher ctDNA positivity and burden: metastatic castration-resistant PC (mCRPC): N=6,712, ctDNA positivity 89%, median MVAF=2.4%; metastatic hormone-sensitive PC (mHSPC): N=1,348, ctDNA positivity 87%, median MVAF=1.7%; non-metastatic CRPC (nmCRPC): N=220, ctDNA positivity 81%, median MVAF=0.9%; nmHSPC: N=262, ctDNA positivity 84%, median MVAF=1.0%; p-value<0.0001). The overall prevalence of 12 AR LBDm was 15% in all patients and was higher in patients with mCRPC, with bone only metastasis, or who had received multiple lines of treatment (19% in each subgroup). PC patients with AR LBDm (N=2,482) had significantly higher median MVAF (8.7% vs. 1.3 %) and shorter median rwOS (16.2 vs. 27.4 months) than patients without AR LBDm (N=12,064).
Conclusion: Higher ctDNA burden and AR LBDm detection were observed in patients with advanced PC and associated with worse rwOS. The study suggests that ctDNA detection and presence of AR LBDm may be prognostic biomarkers that identify high-risk PC patients in clinical care.

Funding: This study was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

E-PS-16-012

Relationships between genetic changes, tumour location, morphological patterns, and protein expression in pancreatic ductal adenocarcinoma

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Background & Objectives: Pancreatic ductal adenocarcinoma (PDA) shows different morphological profiles and genetic alterations between the head (hPDA) and body/tail (btPDA). Differences in histological type and protein expression, rather than tumour location, can influence the frequency of lymph node metastasis and prognosis. Therefore, in this study, we investigated genetic alterations in 30 hPDA and 30 btPDA mutants. We also analysed the results, along with the findings from a previous study on characteristic morphological features and protein expression.
Methods: We evaluated the histological patterns based on haematoxylin and eosin stains. Histological patterns were evaluated using PDA-L and PDA-S. Regarding immunohistochemistry (IHC), reactivity was scored as three grades of colorimetric intensity (0, 1+, and 2+) and four grades of positive cell populations (0, 1+, 2+, and 3+). For the genetic analysis, sequencing libraries for iSeq100 were constructed using AmpliSeq PLUS for Illumina and AmpliSeq for Illumina Cancer Hotspot Panel V2 to search for 50 genes.
Results: *ERBB4*, *KDR*, and *NPM1* were frequently identified in the hPDA among the detected mutations. No significant association was observed between the investigated genetic alterations and PDA-L/PDA-S classification. IHC showed significant associations between HNF1β and *KDR*. Lymph node metastasis was significantly associated with *PIK3CA* expression. Regarding overall survival (OS), significant mutations were observed in *ERBB4* and *FLT3*. In addition, a positive correlation was observed between *ERBB4* and *FLT3*. Although *ATM* and C11ORF65 levels were not significantly correlated with OS, a positive correlation was observed.
Conclusion: Tumour prognosis may depend more on genetic alterations than on tumour location, morphological changes, or protein expression. However, treatment of PDA cases with *FLT3* mutations may be especially effective when using FLT inhibitors.

E-PS-16-013
Consensus molecular subtypes of colorectal cancer in various regions of Oman
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Background & Objectives: Colorectal cancer (CRC) is a major health concern and a leading cause of cancer-related deaths. Recent data indicate that CRC is among the most prevalent cancers in Oman, particularly in adult males. Advances in molecular biology have identified four consensus molecular subtypes (CMS) of CRC: CMS1, CMS2, CMS3, and CMS4, classified by the Colorectal Cancer Subtyping Consortium. To assess the prevalence of molecular characteristics/genetic pathways of CRC in various regions of Oman.
Methods: One hundred fifty colorectal cancer patients were recruited from Sultan Qaboos University Hospital and Royal Hospital, Muscat, Oman, from January 2023 to December 2024. These patients underwent colonoscopic biopsy or resection. Histological examination confirmed colorectal adenocarcinoma. Paraffin-embedded tissue samples were analysed at the pathology department for mismatch repair (MMR) proteins, including PMS2, MLH1, MSH2, and MSH6. Later, they underwent further testing to categorise them into four CMS subtypes. Also, region codes were allotted to patients from all geographical regions of Oman.
Results: MMR testing via immunohistochemistry (IHC) categorised cases into two groups: MMR deficient (19 cases) and MMR proficient (131 cases). All MMR-deficient cases tested negative for BRAF mutation. MMR-proficient cases underwent further testing for p53, KRAS, beta-catenin, and TGF-beta. The findings were CMS1: 19 cases (12.6%), CMS2: 62 cases (41.3%), CMS3: 16 cases (10.6%), and the remaining 53 cases were categorised as CMS4 (35.3%).
Conclusion: CMS2 is the most common molecular subtype of CRC in Oman, followed by the CMS4 subtype. Regionally, Muscat, the largest city, bears the most significant burden of cancer cases. Understanding CRC subtypes and their regional distribution will help clinicians tailor therapy, modify healthcare policies, and enhance targeted therapeutic strategies for the Omani population. Introducing molecular testing for CMS subtyping as part of routine diagnostic protocols will help guide personalised treatment.

E-PS-16-014
Comparative analysis of molecular testing and immunohistochemistry for KRAS mutation detection in colorectal carcinoma
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Background & Objectives: KRAS testing is crucial for diagnosing, prognosticating, and selecting targeted therapies in various cancers, particularly colorectal carcinoma (CRC). Two primary methods for detecting KRAS mutations are molecular testing, such as PCR or NGS, and immunohistochemistry (IHC). Molecular testing provides high sensitivity and specificity by directly identifying genetic mutations at the DNA level, such as wild-type or mutant KRAS. In contrast, IHC is a cost-effective and rapid screening tool that detects mutant KRAS protein expression but may sometimes lack precision.
Objective: This study compares the diagnostic accuracy, sensitivity, specificity, and clinical utility of molecular testing for KRAS mutations with immunohistochemistry (IHC) in detecting KRAS alterations in colonic adenocarcinoma, assessing their advantages and limitations in guiding targeted therapy decisions.
Methods: The cases were selected from January 2023 to December 2024. We performed simultaneous Molecular testing for KRAS and IHC on the same paraffin-embedded tissue from 100 CRC patients. IHC was scored as 0 = negative, 1+ = weakly positive, 2+ = moderately positive, and 3+ = strongly positive. KRAS mutation was noted as positive or negative.
Results: In the molecular lab, Molecular testing was done using PCR after DNA extraction from the paraffin-embedded tissue, whereas IHC was done using routine tissue sections in the immunohistochemistry lab. Fifty-nine cases were scored as 2+ or 3+ by IHC , whereas KRAS mutation was detected in 54 cases of the 100 cases. The numbers corresponded to those detected on molecular testing; however, false positivity was seen in 5 cases, mostly 2+.
Conclusion: There is a fair concordance of KRAS detection by PCR-based molecular tests and IHC tests in routine pathology labs. However, the false negatives can be minimised by reviewing the criteria for scoring 2 + cases. While IHC can be an initial screening method, molecular testing remains the gold standard for confirming mutations and guiding targeted therapies.

E-PS-16-015
Rapid simultaneous detection of 15 pathogenic *BRAF* mutations in advanced colorectal cancer specimens
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Background & Objectives: *BRAF* mutations are associated with poor prognosis and high therapeutic resistance, particularly in colorectal cancer (CRC). Thus, accurate and rapid detection of *BRAF* mutations is essential for guiding further treatment decisions. The present study aimed at demonstrating the concordance between NGS-based tumour characterization and multiplex PCR-based characterization on the MODAPLEX platform. The MODAPLEX BRAF Mutation Kit was designed to detect 15 key mutations covering *BRAF* class 1 (including V600E/K), class 2 (including K601E & G469R/A/E) and class 3 (including D594G/N & N581S) alterations.
Methods: A total of 100 characterized CRC samples (EK59032007), selected and provided by the TNTB Dresden, were analysed using the MODAPLEX BRAF Mutation Kit and subsequently evaluated for concordance to NGS. NGS was conducted as part of a routine molecular diagnostic workflow via panel sequencing at the UKD Dresden. A subset of samples was analysed via whole-exome sequencing by a commercial provider.
Results: The MODAPLEX BRAF Mutation Kit accurately detected *BRAF* mutations in FFPE-derived CRC samples using 10 ng DNA input demonstrating high level of concordance to NGS. Amending preliminary analyses showed the assay's limit of detection of at least 5 % tumour content and the assay's capability to assess the *BRAF* mutation status in other entities such as melanoma and endometrial cancer. Up to 46 DNA samples were successfully analysed within 4 h underlining the rapid workflow of the MODAPLEX BRAF Mutation Kit.
Conclusion: Our study highlights the potential of a PCR-based assay on the MODAPLEX platform as a robust and time efficient alternative for the *BRAF* mutation screening in clinical settings, particularly for CRC. Its ability to rapidly and accurately identify class 1–3 *BRAF* mutations demonstrates its potential, providing tools to shape the future of personalized medicine.

E-PS-16-018

Detecting progression with liquid biopsy in a patient with three synchronous primary tumours

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Background & Objectives: Liquid biopsy is transforming molecular pathology, yet its full integration into routine diagnostics remains under investigation. In our case, liquid biopsy was the only feasible method to detect tumour progression in a 63-year-old man with three synchronous primary tumours. He underwent left pneumonectomy after neoadjuvant chemotherapy for lung adenocarcinoma in 2021. In 2022, malignant melanoma was excised from his left arm, and at the same time, colorectal adenocarcinoma was diagnosed during a staging PET-CT examination for which he received adjuvant chemotherapy. Two years later, follow up imaging revealed multiple pulmonary metastases. Surgical or core biopsy was not feasible due to the location of the lesions and previous interventions.
Methods: Circulating free nucleic acid (cfNA (cfDNA and RNA)) were extracted from the patient's plasma via liquid biopsy, and the Oncomine Precision Assay NGS panel test was performed. Molecular analysis was also conducted on all primary tumours. Tumour DNA was extracted from formalin-fixed paraffin-embedded tissue blocks. KRAS, NRAS, and BRAF mutations were assessed using the COBAS test, while EGFR mutations were analysed with AmoyDx test.
Results: Liquid biopsy detected a BRAF V600K mutation in the cfDNA, indicating that the mutation originated from the metastasis, confirming the presence of circulating tumour DNA (ctDNA). The clonal hematopoietic origin of the mutation was excluded by examining lymphocytes from the blood sample. No actionable mutations were identified in the lung adenocarcinoma, whereas the driver mutation in the colorectal adenocarcinoma was KRAS G12X. The malignant melanoma harboured the same BRAF V600K mutation found in the cfDNA.
Conclusion: The identical mutation in both ctDNA and the primary melanoma highly suggested that the pulmonary nodules were metastatic lesions from the melanoma. Liquid biopsy not only provided a minimally invasive solution to the sampling challenge but also revealed a potential therapeutic target, highlighting its clinical utility.

E-PS-16-019

Molecular cancer profiling in microsatellite instability context: study of current pathology practice trends

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Background & Objectives: Molecular cancer profiling, including widely applied immunohistochemical and genetic testing on microsatellite instability (MSI), progresses in optimizing early detection, monitoring, and treatment of cancer by integrating more methods of advanced molecular technologies into clinical pathology practice. Study objective is to determine current trends of molecular cancer profiling testing in MSI context.
Methods: 502 cases of various neoplasia tested for MSI in local pathology centre in 2018-2025 (February) were selected for the study. Considering molecular profiling guidelines for a particular cancer group, application of additional molecular testing of RAS, BRAF (V600E), POLE, PD-L1, p53, HER2, and receptors of oestrogens, progesteron was also monitored. Descriptive statistics, Mann-Whitney U, $\chi 2$ tests were applied ($p<0.05$).
Results: 46.6% (n=234; 66 (15) years old (y.o)) male and 53.4% (n=268; 67.5 (18) y.o.; p=0.619) female cases were tested for MSI which was detected in 20.3% (n=102) cases. KRAS and NRAS mutation testing was performed in 4% (n=20) and 2.4% (n=12) cases, correspondingly. BRAF (V600E) testing was performed in 14.8% (n=72) cases, while p53 and POLE was checked in 6% (n=30) and 3.4% (n=17) cases, correspondingly. Molecular testing of PD-L1, receptors of oestrogens and progesteron (1.2% (n=6) of each marker), HER2 (1%, (n=5)) was rare among selected cases. 2 markers for molecular cancer profiling was performed in 21.9% (n=110), whereas ≥4 of molecular cancer profiling was performed in 1% (n=5) of cases. Molecular cancer profiling of at least 3 markers, including MSI, became a trend starting from 2023 ($p<0.001$). Female cancer patients were more likely to receive molecular profiling of 3 markers ($p<0.001$).
Conclusion: Trends of current pathology practice of molecular cancer profiling in MSI context were characterised. Accurate data on increasing count of markers in molecular profiling can serve as an ancillary tool for more complex molecular information on oncogenesis, also optimizing guidelines of molecular cancer testing in clinical practice.

E-PS-16-020

Germline structural variants in Russian patients with solid tumours: whole genome sequence results

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Background & Objectives: To analyse the significant (pathogenic/likely pathogenic – PV/LP) structural variants (SVs/CNV) in cancer patients with suspected hereditary cancer syndromes (HCS).

Methods: During the period from January 2023 to March 2025 2788 patients >18 y.o. with solid tumours and suspected HCS whole genome sequencing (WGS) were performed.

WGS: 30x, DNBseq-T7, EVOGEN LLC; bioinformatics analysis accelerators: EVA Pro, EVOGEN, Russia; MegaBOLT, MGI, China.

Results: 563 significant variants (PV/LP) in cancer-associated genes were identified (20,2%) including 40 SVs. We show some previously undescribed structural variants identified:

Male, 59 y.o., colorectal cancer, polyposis - *SMAD4,* chr18:51047298-51054779; deletion; 7481 b.p., exons 3-4, introns 2-4;

Male, 25 y.o., colorectal cancer, polyposis - *SMAD4,* chr18:50778738-53834227; deletion; ~3Mb;

Male, 38 y.o., colorectal cancer - *MSH6,* chr2:47796532-47803196; deletion; 6664 b.p., exons 4, introns 3-4;

Female, 39 y.o., breast cancer - *BRCA2,* chr13:32370570-32380320; deletion; 9750 b.p., exons 20-24, introns 19-23;

Female, 42 y.o., breast cancer - *BRCA1,* chr17:43068355-43070981; deletion; 627 b.p., exon, intron 15;

Female, 58 y.o., breast cancer - *BRCA1,* chr17:43138933-43140891; deletion; 1958 b.p.;

Female, 45 y.o., endometrial cancer - *MSH2,* chr2:47439298-47450442; deletion; 11 145 b.p., exon 8, introns 7-8;

Female, 58 y.o., breast cancer - *RAD51D,* chr17:35100447-35101208; deletion; 762 b.p.,
exons 9-10, intron 9;

Male, 48 y.o., colorectal cancer - *MLH1,* chr3:g.36600000-38800000; deletion; 2Mb, 49 genes;

Male, 27 y.o., colorectal cancer, polyposis – *APC,* chr5:112392108-112716492; inversion; 324 385 b.p., intron 1;

Female, 42 y.o., breast cancer - *NF1,* chr17:31222988-31244937; deletion; 21 950 b.p.,
exons 16-29, introns 15-29.

Conclusion: The prevalence of germline SVs in cancer patients cohorts is poorly understood due to technical limitations of NGS panels and exome sequencing. WGS makes it possible to identify SVs, including large gene deletions and copy number variations, which is a significant contribution to understanding the HCS aetiology.

Funding: Moscow City Health Department financial support

E-PS-16-021

Results of a pilot external quality assessment of ESR1 testing in cfDNA for breast cancer

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Background & Objectives: In ER+/HER2- metastatic breast cancer, *ESR1* variants drive acquired resistance to endocrine therapy and have demonstrated response to targeted therapy. Therefore, there is clinical need for testing circulating tumour DNA (ctDNA) in cell free DNA (cfDNA) for *ESR1* actionable variants at recurrence. However, testing of cfDNA is challenging due to the low fraction of ctDNA, so analytical methods require high sensitivity. This external quality assessment (EQA) was designed to assess the genotyping accuracy and reporting of *ESR1* variants in cfDNA.

Methods: GenQA delivered a pilot international EQA to thirty laboratories. Three samples were supplied to participating laboratories containing commercially available artificial plasma to mimic patient samples. Two samples contained actionable *ESR1* hotspot variants and one sample contained no actionable *ESR1* variants. Participants performed testing according to their local protocols and submitted results in the form of clinical reports. Laboratories were assessed on their genotyping accuracy and interpretation of the result.

Results: The genotyping accuracy of *ESR1* testing by participating laboratories was of a high standard. There was one false positive and one incorrect variant reported, classed as critical errors. Several laboratories did not discuss known resistance to therapies and potential therapeutic strategies associated with the *ESR1* variants reported. There was a lack of consideration for the reduced sensitivity for detecting variants in a plasma sample containing no actionable variants.

Conclusion: This EQA has demonstrated an overall high genotyping accuracy in the challenging sample type. Improvements could be made in the interpretation of the result, both in terms of therapeutics and consideration of the sample type tested. This assessment has highlighted the need for EQA participation to educate and promote standardisation of reporting.

E-PS-16-023

ESR1 hotspot mutations in metastatic breast cancer: a Tunisian series

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Background & Objectives: Breast cancer (BC) is a major public health issue, with over 70% of cases being oestrogen receptor-positive (ER+), making hormone therapy the primary treatment. However, resistance to hormone therapy is a critical challenge. Often associated with mutations in the ESR1 gene, which encodes the oestrogen receptor alpha (ERα). This study aims to analyse the ESR1 hotspot mutations in metastatic breast cancer, assess their frequency in a Tunisian patient cohort and compare the sensitivity of real-time PCR to Sanger sequencing in detecting the D538G mutation.

Methods: A total of 43 formalin-fixed, paraffin-embedded (FFPE) tissue samples from metastatic BC patients diagnosed at Charles Nicolle Hospital, Tunisia, were analysed. DNA was extracted and ESR1 hot spot region (exon 8) was screened using Sanger sequencing and real-time PCR for the D538G mutation.

Results: The median patient age was 54 years (range: 31–82). The most common metastatic sites were pleura (86%, n=37 /43), followed by bone (9%, n=4/43) and mediastinum (5%, n=2/43). Six samples

were excluded due to insufficient quality, leading to PCR amplification failure. ESR1 mutations were detected in 10/37 cases (27%) . Sanger sequencing identified 12 genetic variations, including 11 mutations and one polymorphism. Eight mutations (D538G, Y537S, R548H, V533M, A546T, R548R, S578Y, and M528V) have been previously described, with Y537S and D538G being the most common. Four variations (A546S, G572D, S578T, S518S) were novel and unreported in databases. Real-time PCR targeting D538G showed superior sensitivity (37% vs. 5% for Sanger sequencing) in detecting rare mutations, underlining the importance of selecting appropriate and optimized molecular testing techniques.
Conclusion: This study highlights the clinical significance of ESR1 mutations in hormone therapy resistance and emphasizes the need for high-sensitive molecular diagnostic techniques. Further investigations in a larger patient cohort will provide deeper insights into the clinical relevance of these mutations.

E-PS-16-024
Molecular differences between atypical Spitz tumour and Spitz melanoma: an in-silico analysis
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Background & Objectives: Atypical Spitz tumour and Spitz melanoma are melanocytic lesions that pose histopathologic diagnostic challenges. The lack of clear distinguishing features and the high rate of interobserver discordance are the main reasons for this difficulty. In this study, we aimed to identify molecular alterations that may aid in the differential diagnosis of these two groups.
Methods: The search for Spitzoid melanoma was performed on the GEO Datasets website (https://www.ncbi.nlm.nih.gov/gds/) and, the datasets GSE142441 and GSE139314 were selected for evaluation. The determination of differentially expressed genes (DEGs) between Spitz tumour and Spitz melanoma in the first dataset, and between Atypical Spitz tumour and Malignant Spitzoid tumour groups in the second dataset, was performed using the GEO2R program. Subsequently, gene set enrichment analysis (GSEA) was conducted with the WebGestalt bioinformatics service (www.webgestalt.org) for the common genes in both comparisons. $P<0.05$ and $FDR<0.05$ were considered statistically significant.
Results: In the analysis performed for both data sets, 94 DEGs were identified. The genes with the highest level of significance included COL6A6, FGF19, DNMT3A, IRAK3, and PIK3CD ($p<0.05$). Subsequent Gene Set Enrichment Analysis (GSEA) revealed that these genes were implicated in integrin-related signalling pathways, as well as pathways associated with cell adhesion, extracellular matrix binding, extracellular receptor interaction, and protein digestion and absorption ($FDR<0.05$).
Conclusion: In the present in-silico analysis, the aim was to ascertain the distinguishing molecular features of atypical Spitz tumours and Spitz melanomas, two lesion groups that pose a challenge in the context of histopathological differential diagnosis in dermatopathology practice. Through a comprehensive gene expression profile analysis, statistically significant differences were identified. Subsequent pathway analysis revealed that DEGs were associated with cell adhesion, extracellular matrix proteins, and interactions. This finding suggests that these pathways play an important role in the progression of these lesion groups.

E-PS-16-025
Tissue acidity as a preanalytical factor affecting molecular testing: a case of lung adenocarcinoma with *EML4::ALK* fusion
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Background & Objectives: Molecular profiling by next generation sequencing (NGS) performed on tissue sections from formalin fixed paraffin embedded (FFPE) tissues has been incorporated into the routine management of patients with non-small cell lung cancer. Approximately 5% of lung adenocarcinomas harbour a targetable *ALK* rearrangement, detectable even on the limited tissue of biopsy specimens. Since testing failure can lead to detrimental delays in clinical decision making, herein we aim to highlight the importance of tissue acidity as a preanalytical factor affecting the feasibility of molecular testing.
Methods: A 56-year-old woman diagnosed with a right upper lobe lung mass underwent bronchoscopic biopsy. Haematoxylin-eosin stained FFPE tissue sections were examined, followed by histochemistry, automated immunohistochemistry and targeted NGS, the latter employing the Oncomine Precision Assay in a Genexus Integrated Sequencer (CE-IVD).
Results: Microscopy showed an invasive, poorly differentiated, mucinous adenocarcinoma, with signet ring cells. Alcian blue-PAS confirmed the presence of acidic nature of neoplastic mucin. Immunostaining showed expression of keratin 7 and TTF1, notably without ALK (clone ALK1) expression by tumour cells. The first NGS attempt failed, because of inadequate performance of the molecular template. Nucleic acid extraction was performed anew by alkalinizing the lysis buffer. This template was successfully analysed in the repeated NGS run. An *EML4::ALK* fusion was detected between *EML4* exon 13 and *ALK* exon 20. Subsequently, the patient was treated with crizotinib and achieved a complete clinical, radiological and pathological response, as confirmed after examination of the lung lobectomy surgical specimen. The patient remained free of disease during a 15-month follow-up interval from the initial diagnosis.
Conclusion: This case highlights the importance of tissue acidity as a modifiable preanalytical factor that may lead to NGS failure. Validation in further studies may allow for the development of a standard operating procedure for optimal handling of inherently acidic FFPE tissues.

E-PS-16-026
ESR1 testing in circulating tumour DNA in patients with endocrine-resistant metastatic breast cancer
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Background & Objectives: The introduction of selective oestrogen receptor degraders (SERDs) for patients with ESR1-mutated metastatic breast cancer requires ESR1 mutation testing. ESR1 encodes for the ER alpha protein and ESR1 mutations are the main mechanism of acquired resistance to endocrine therapy, occurring in 20-40% of patients who receive aromatase inhibition. In patients with ESR1 mutations, treatment with SERDs improves progression-free survival. Our objective was to establish whether we could test for ESR1 mutations in circulating tumour DNA (ctDNA) in routine clinical practice.
Methods: 42 patients with hormone-positive HER2-negative metastatic breast cancer who received first line endocrine therapy with an aromatase inhibitor and had early recurrence were included in January 2025 prior to decision for treatment with Elacestrant. Per patient 20ml of blood was collected in Streck or Paxgene tubes. The APIS ESR1 Mutations Kit was used on a QuantStudio Real-Time PCR (RT PCR) system to detect 11 common ESR1 mutations.
Results: For 38/42 patients we were able to test for ESR1 mutations, as for 4 patients we received less than 20ml of blood. In the ctDNA of

12/38 cases (32%) we detected a mutation in ESR1. The average turn-around-time for all 38 cases tested was 7 calendar days.
Conclusion: We share our experience with implementing ESR1 ctDNA mutation testing in our routine practice using a validated RT PCR assay. Our department receives 5 new samples every week; we will therefore show data on a larger cohort of patients at the time of the meeting; we also recently implemented a NGS panel and will share preliminary comparative data between NGS and RT PCR.

E-PS-16-028
Pole mutations using modaplex technology (Biotype) in high-grade endometrial carcinomas
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Background & Objectives: The TCGA study clearly differentiated four molecular types of endometrial carcinoma: POLE-mutated, P53-mutated, microsatellite instability, and no specific alterations. The implementation of this classification in clinical guidelines and the recent FIGO 2023 classification emphasizes the prognostic value of POLE-mutated tumours, which have a better prognosis compared to the other groups. The technical approach to detecting POLE mutations can be performed using Sanger sequencing of pathogenic exons (exons 9, 11, 13, and 14) or through massive sequencing. In this study, we used a technology that combines PCR and fragment analysis by capillary electrophoresis (Modaplex TM, BIOTYPE GmbH, Dresden, Germany).
Methods: Samples from 120 patients with high-grade endometrial carcinoma, aged between 43 and 86 years, were studied. The tumour types included 33 serous, 32 mixed with a high-grade component, 23 endometrioid G3, 19 carcinosarcomas, 8 clear cells, 4 dedifferentiated, and 1 undifferentiated, all collected between 2015 and 2025. Paraffin-embedded tumour samples were used, and after DNA extraction, the Modaplex POLE/POLD1 Mutation Analysis Kit (BIOTYPE GmbH, Dresden, Germany) was employed. This kit identifies nine (P286R, V411L, S297A, S459F, A456P, F367S, L424V, P436R, M444K) of the eleven pathogenic POLE mutations. As a confirmatory test, Sanger sequencing was performed targeting the identified mutation using the same extracted DNA.
Results: Seven samples with POLE mutations were detected, representing 5.83% of the cases. Four of these were positive for P286R in exon 9 (two endometrioid G3, one dedifferentiated, and one mixed high-grade) and three were positive for V411L in exon 13 (two serous and one mixed high-grade). The two serous cases positive for V411L were also p53-positive, classifying them as "multiple-classifiers." No mutations were detected in exons 11 and 14. All identified mutations were confirmed by Sanger sequencing.
Conclusion: These findings reinforce the role of *POLE* as a biomarker and highlight the importance of molecular profiling for accurate classification.

E-PS-16-029
Learnings from a pilot External Quality Assessment (EQA) for cfDNA extraction from plasma
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Background & Objectives: Efficient extraction is critical to enable sensitive and accurate detection of variants in cfDNA. EMQN has established a global pre-analytical EQA for extraction of artificial cfDNA from plasma. The objective was to evaluate the quantity and quality of eluted cfDNA and provide an external benchmark of participants' extraction processes.
Methods: Each laboratory was provided with three 4mL plasma samples containing a defined amount of cfDNA, shipped at room temperature. Participants were instructed to extract the cfDNA using their routine methodology, return all eluted cfDNA and complete a form with details of the method used. The volume of each returned sample was recorded and the cfDNA was analysed using a custom qPCR assay, the Agilent TapeStation Cell-free DNA ScreenTape assay and the Qubit™ High-Sensitivity (HS) assay.
Results: A range of different extraction methodologies were used by the participants, and a broad range of cfDNA yields were obtained for each sample.
Sample concentrations were notably higher when measured with the Qubit HS Assay compared to qPCR and the TapeStation cfDNA Screentape assay, especially for the lower-concentration sample.
The peak cfDNA fragment sizes were highly consistent across all participants and across the samples. The average size for the nucleosomal peak was 148bp (SD = 7). Only one laboratory provided samples outside the mean ± 2 standard deviation, with peaks falling below 130bp across all three samples.
Conclusion: The majority of laboratories extracted sufficient cfDNA for downstream applications such as Next Generation Sequencing (NGS) and cfDNA was mostly of a high quality. However, the broad range of cfDNA yields achieved for these standarised reference materials indicates that it may be possible for some laboratories to increase the efficiency of their cfDNA extraction. Many laboratories indicated that Qubit was used for cfDNA quantification which may not be suitable for extraction methods using carrier RNA.

E-PS-16-030
Streamlined analysis of DNA methylation and its functional consequences from FFPE tumour samples
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Background & Objectives: Methylation of DNA sequences is an important mechanism for regulating gene expression, in normal cell physiology and in diseases. To detect and analyse the effects of methylation, multiple assays must be performed; however, in clinical research sample amounts are often limiting. The multifactorial analysis of consequences of methylation depends on efficient utilization of precious samples. We show efficient methods for characterizing links between methylation, mismatch repair gene expression, and microsatellite instability from small amounts of colon tumour samples.
Methods: DNA and RNA were isolated from ten 5µm FFPE preserved colon tumour samples using an automated sequential DNA/RNA extraction method. Microsatellite instability was analysed using fragment analysis by capillary electrophoresis. Mismatch repair enzyme gene expression was measured using a 5-plex panel of qPCR assays that queried *MLH1, MSH2, MSH6 and PSM2*, with *PPIA* as an internal control, and confirmed by droplet-free dPCR. Twelve potentially methylated CpGs in *MLH1* promoter were analysed by Sanger sequencing, and the fraction methylated was determined by droplet-free dPCR.
Results: From the extracted genomic DNA, two samples (CT11 and CT15) were found to have high microsatellite instability. Using the extracted RNA, *MLH1* was found to be significantly decreased in the two samples that demonstrated MSI instability. This was confirmed using dPCR with the same MMR multiplex panel. Samples with MSI had significant methylation in all CpGs in the *MLH1* promoter region. The fraction of genomic DNA methylated was determined by droplet-free PCR; both samples with high MSI had greater than 50% of the *MLH1* promoter DNA methylated.

Conclusion: Together, these results show how DNA methylation and its impact on the MMR pathway can be analysed from precious samples using fast, simple, and cost-effective laboratory assays.

E-PS-16-031

Assessment of ALK, ROS1, RET and MET exon 14 alterations using the Biocartis Idylla GeneFusion Assay and Platform; single laboratory experience on over 11000 lung cancer samples

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Background & Objectives: At the University Hospitals Birmingham NHS Foundation Trust, as in most of the English trusts, any newly diagnosed lung non small cell carcinoma is submitted to reflex testing for the following alterations, prior to first line treatment: EGFR, KRAS, BRAF, ALK, ROS1, RET, MET E14, HER2 amplification and PD-L1 expression. We report on our experience of testing ALK, ROS1, RET and MET exon 14 alterations for rapid assessment of FFPE samples using the Idylla GeneFusion assay on the Biocartis Idylla real time PCR platform.
Methods: One to three paraffin sections (5 micrometer thick) were loaded in Genefusion cartridges; testing incorporates RNA extraction and analysis, which is completed within 3 hours following 3 minutes handling. Testing offers flexibility for urgent cases. The analysis of raw data in equivocal cases, including the use of expression imbalance for the detection of novel fusions, was supported by Idylla Explore.
Results: 11473 FFPE lung cancer samples, referred from over 100 NHST trusts, were tested between January 2021 and January 2025. 845 cases (7%) were invalid due to insufficient material or poorly preserved tissue; by repeating the testing with more tissue, the rate of failure went down to less than 5%. 10648 samples were successfully tested and showed the following results: ALK fusions: 1.3%; ROS1 fusions: 0.4%; RET fusions: 0.5%; MET exon 14 skipping: 2.3%.
Conclusion: We report on a cost-effective method for rapid gene fusion assessment of 4 targetable alterations in lung tumour specimens. The detected rate of the respective alterations was as expected from widely published data on comparative platforms and gene fusion data correlated well with ALK and ROS1 immunohistochemistry data.

E-PS-16-033

BRCA mutations in ovarian and prostate cancer

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Background & Objectives: High-grade serous carcinoma of the ovary (HGSC) has defects in the DNA damage response (DDR) pathways. Mutations in the DDR genes, such as BRCA1 and BRCA2, are also common in prostate cancer. A better understanding of DDR pathways is essential to optimizing therapeutic options.
Methods: At the request of our hospital's Oncology Department, we analysed paraffin-fixed ovarian and prostate tissue samples from 58 patients diagnosed with HGSC or metastatic acinar adenocarcinoma of the prostate using Next-Generation Sequencing (NGS) (NextSeq/Panel HRR-IMEGEN or MiSeq).
Results: Of the 58 cases analysed, 56 (96.5%) were completed, although 5 cases (8.9%) were not evaluable. Alterations in DDR pathways were detected in 11 cases (19.6%) of HGSC and in 5 cases (8.9%) of metastatic acinar adenocarcinoma of the prostate. Among the HGSC, 6 cases (54.5%) exhibited homologous DNA recombination deficiency, 3 cases (27.2%) had a pathogenic BRCA1 variant, and 2 cases (18.1%) had a BRCA1 variant of undetermined significance. Regarding metastatic acinar adenocarcinoma of the prostate, 2 cases (40%) harboured pathogenic variants in CDK12 and ATM. Additionally, variants of undetermined significance were detected in ATM (40%) and in CHEK2 (20%).
Conclusion: Unlike literature, the most frequent alteration observed in our study in HGSC was homologous recombination deficiency with somatic BRCA mutations. However, it has been reported that germline BRCA1 and BRCA2 mutations are more common, occurring in approximately 15% of cases. Regarding metastatic acinar adenocarcinoma of the prostate, no BRCA2 alterations were identified, despite it being the most frequently mutated gene. However, according to the literature, mutations in CDK12 and ATM were detected. Currently, detecting these alterations is crucial, as treatment with PARP inhibitors is indicated for patients with HGSC and those with metastatic adenocarcinoma of the prostate.

E-PS-16-034

Assessing ChatGPT's capability against oncologists in molecular pathology report analysis

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Background & Objectives: Molecular pathology test reports play a vital role in guiding personalized oncology care, but their quality and interpretative consistency can vary significantly. As part of the Canadian Pathology Quality Assurance (CPQA) External Quality Assessment (EQA) molecular scheme (Run M1), seven laboratories conducted colorectal cancer biomarker testing and submitted molecular pathology reports for quality assessment. This study explores the potential of ChatGPT, an artificial intelligence (AI) tool, to analyse these reports.
Methods: Reports generated during CPQA Run M1 EQA scheme for colorectal cancer biomarkers were analysed by ChatGPT and a panel of oncologists and pathologists. Evaluations covered eight key domains: patient/specimen information, diagnostic findings, molecular analysis, result interpretation, therapeutic recommendations, technical details, report formatting, and authentication. Reports were graded on their completeness and clinical relevance, with the panel's assessments serving as the gold standard.
Results: ChatGPT excelled in identifying structural deficiencies and accurately evaluated technical details and patient/specimen information. AI effectively highlighted actionable findings such as mismatch repair deficiency (dMMR) and *KRAS* mutations, however, its ability to evaluate clinical interpretations and therapeutic recommendations in the reports was less comprehensive than the expert panel. , particularly when integrating molecular findings within patient context was required. The AI tool's ability to standardize the evaluation of a report was recognized, but areas requiring nuanced clinical judgment were identified for improvement.
Conclusion: ChatGPT demonstrates promise as an adjunct for analysing molecular pathology reports in quality assurance settings, excelling in standardization and technical critique. While it effectively supports quality assurance initiatives, human oversight remains essential for clinical correlation and therapeutic planning. The integration of AI tools into quality assurance workflows could enhance report consistency and educational value for participating laboratories. This study highlights the potential for AI in pathology quality assurance programs and its role in improving report analysis across laboratories.

E-PS-16-035

Modulation of the immune microenvironment during chemoimmunotherapy in gastric cancer patients

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Background & Objectives: Gastric cancer (GC) ranks as the fifth most common malignancy globally. Neoadjuvant chemoimmunotherapy not only reduces tumour size preoperatively but also improves long-term outcomes. However, treatment efficacy depends on tumour molecular profiling, underscoring the need for predictive biomarkers and patient stratification. Given that immunotherapy modulates local immune responses, analysing changes in the tumour microenvironment (TME) under PD-1 blockade is critical. Study aim was to compare the immune cell composition of the TME in primary gastric tumours before and after anti-PD-1-based chemoimmunotherapy.
Methods: The study included 9 patients with gastric cancer who received neoadjuvant chemotherapy in combination with pembrolizumab. Biopsy material was collected from each of them before therapy, and tumour material (surgical) was obtained after therapy. Formalin-fixed tumour sections were stained with multiplex immunofluorescence (TSA) using CD8, CD20, CD163, PD-1, and FoxP3 antibodies and Opal 7-colour Fluorophore Kit. All staining steps were performed using the automated immunohistochemistry stainer BOND RXm. Visualization of the stained samples was carried out using the automated scanning system Vectra 3.0.
Results: Immunotherapy led to a significant two-fold increase in the number of CD8+ T-lymphocytes ($p=0.038$). The observed changes in CD8+ cytotoxic lymphocyte counts during anti-PD-1 immunotherapy were most pronounced in the PD-1-expressing subpopulation. A 10-fold increase in CD8+PD-1+ cytotoxic T-lymphocytes was detected ($p=0.0156$). The numbers of CD20+ B-lymphocytes, CD163+ macrophages, and FoxP3+ lymphocytes remained unchanged ($p>0.05$). Additionally, a significant five-fold increase in the CD8+ cytotoxic lymphocytes to FoxP3+ lymphocytes ratio was observed during anti-PD-1 immunotherapy ($p=0.0039$).
Conclusion: Combined chemoimmunotherapy for gastric cancer induces remodelling of the tumour microenvironment in patients. The obtained results may play a significant role in further research aimed at identifying predictive factors for the efficacy of immunotherapy in gastric cancer. The study was supported by the Russian Science Foundation (grant # 20-75-10033-P).

Funding: Russian Science Foundation (grant # 20-75-10033-P)

E-PS-16-036

A molecular classification to supplement the World Health Organisation classification of tumours

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Background & Objectives: The current WHO classification of tumours (WCT) is a differentiation-rooted hierarchical classification, based on anatomical site, histopathology, and well-established relevant molecular information. Advances in personalised treatment have resulted in an increasing need for a molecular classification of tumours, based on the established and potential therapeutic targets present within tumours, irrespective of tumour type. Our objective was to provide a molecular classification tool for oncological and research use based on the WCT.
Methods: The framework used in the WCT - Genetic Tumour syndromes 5th edition (GTS-5) was expanded to map molecular targets. Each target (affected gene) was categorised according to the molecular pathway to which it belongs. Information on the type of molecular abnormality (e.g. mutation, amplification, fusion etc), associated with individual tumour types and therapeutic class of drugs available for each target were included in the map. The information was cross referenced to the relevant sections in the WCT books.
Results: Mapping molecular targets based on the molecular pathways identified in GTS-5 provides an effective structure to classify the molecular information available in the WCT. Its pathway-based approach could help personalise treatment for patients and provide cancer researchers with a framework to identify potential targets for treatment. At present over 40 molecular targets (genes) have been mapped according to this framework alongside the relevant tumours and therapeutic drug class.
Conclusion: The final version of this molecular classification of tumours will be made available on the WCT website as an online molecular classification tool with links to the relevant WCT volumes online. Having the molecular classification as an online live tool will allow it to evolve as new evidence is incorporated into the WCT.

E-PS-16-037

The impact of bile acids on the antiinvasive potential of a selective COX-2 inhibitor in malignant cells

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Background & Objectives: Chronic inflammatory response and increased expression of isoenzyme cyclooxygenase-2 (COX-2) are recognized as important factors in the etiopathogenesis of colorectal cancer. Therefore, selective COX-2 inhibitors represent potential agents in the prevention and therapy of this malignant disease.
The aim of this study was *in vitro* investigation of the cytotoxic effect of celecoxib, a selective COX-2 inhibitor, and bile acids on human colorectal adenocarcinoma cells (HT-29 cell line), and to analyse the expression of genes involved in the inflammatory response, invasion and metastasis of cells.
Methods: The cytotoxic effect of celecoxib and bile acids against the HT-29 cell line was determined using the dye exclusion test (DET) and the MTT assay. Gene expression experiments were performed using the real-time reverse transcription polymerase chain reaction (qRT-PCR). The expression i.e. the amount of mRNA of the following genes was investigated: *PTGS2* (encodes the inducible isoenzyme COX-2), *CDH1* (encodes E-cadherin), *MMP2* and *MMP9* (encode matrix metalloproteinases-2 and -9).
Results: After treating the HT-29 cell line with increasing concentrations of celecoxib (10-200 μM) for 48 hours, a concentration-dependent cytotoxic effect of celecoxib was demonstrated. Compared to the untreated control group of cells, celecoxib caused a decrease in *PTGS2* and *MMP2* ($p<0.01$) and *MMP9* gene expression ($p<0.05$), and increased *CDH1* gene expression ($p<0.01$). The addition of chenodeoxycholic acid (CDCA) completely antagonized the aforementioned effects of celecoxib. Ursodeoxycholic acid (UDCA) showed a synergistic effect with celecoxib in reducing *PTGS2* and *MMP2* gene expression (without statistical significance) and *MMP9* gene ($p<0.01$ *vs.* C), while contributing to a further increase in *CDH1* expression levels ($p<0.05$ *vs.* C).
Conclusion: The results of cytotoxicity tests indicate the importance of COX-2 isoenzyme in the proliferation and survival of malignant cells. UDCA in combination with celecoxib shows favourable antiinflammatory, antiinvasive and antimetastatic potential in colorectal cancer cells.

E-PS-16-038

Mutations that matter: a case series on molecular insights into lung adenocarcinoma

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Background & Objectives: Lung adenocarcinoma, most frequently diagnosed non-small cell lung cancer, exhibits notable histological heterogeneity. While immunohistochemistry (IHC) aids in identification of poorly differentiated carcinomas, conservation of tissue for subsequent molecular analyses is paramount. Detection of specific molecular aberrations is crucial for determining patient eligibility for targeted and immune-based therapies, which often present superior outcomes compared to traditional chemotherapeutic regimens. This case series aims to elucidate critical role of accurate molecular profiling in optimizing treatment strategies and prognostic outcomes for patients with lung adenocarcinoma.
Methods: A retrospective and observational study performed at a tertiary care centre and teaching institute, Bharati Vidyapeeth (Deemed to be University) Medical College, Pune, Western Maharashtra, India. Twenty cases of histologically confirmed lung adenocarcinoma were analysed. Patient demographic data and comprehensive histopathological assessments, performed by two independent pathologists, were collected. IHC was performed, followed by detailed molecular testing. Cases exhibiting pure adenocarcinoma histology were included, while other carcinoma subtypes were excluded to maintain focus.
Results: Mean age of our study was 62.8 years. Molecular profiling revealed EGFR exon 21 mutations in 50% (n=10) of cases, while 40% (n=8) demonstrated PD-L1 expression. Less frequent alterations were observed in ERBB2 and KRAS. Targeted therapies were administered to patients based on their specific molecular profiles, aligning with personalized medicine principles.
Conclusion: This case series emphasizes the significant impact of thorough molecular profiling in guiding therapeutic decisions for lung adenocarcinoma. Identifying key genetic alterations, such as EGFR mutations and PD-L1 expression, enables the implementation of tailored treatment regimens, potentially leading to improved patient outcomes. Integration of molecular profiling into routine clinical practice is essential for optimizing patient care in lung adenocarcinoma.

E-PS-16-039

Overlapping evaluation of TNFa expression in fresh and paraffin embedded Inflammatory Bowel Disease (IBD) mucosal biopsies

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Background & Objectives: The anti-TNFa drugs represent one of the most important efficacious biological drugs available for IBD patients. These drugs reduce symptoms, hospitalizations, surgeries, heal mucosal ulcers and limit the use of corticosteroid but, 30-40% of patients with IBD do not respond to these drugs, and 30-50% of patients who initially benefit from the drug, no longer respond over time. For this reason, there is the need to identify specific biomarkers to predict treatment response and monitor IBD patients. The aim of this study is to compare TNF-α levels obtained from fresh biopsies with TNF-α expression levels obtained through real-time PCR using paraffin-embedded tissues in patients with IBD, to show which of the two approaches is more accurate and cost-effective.
Methods: Tissue samples from IBD patients treated with biological or conventional treatment were included. RNA was extracted both from fresh biopsies that paraffine-embedded tissue and subsequently it was evaluated the relative expression of TNF-α/β-actin through Real-Time PCR. We used healthy colon biopsies as a control. We compared results with those previous obtained from fresh biopsies.
Results: We included 30 UC patients (25 on biological treatment and 5 on conventional treatment) who were previously tested with fresh biopsies, along with 15 normal controls. We found a very strong correlation between TNF-α expression levels evaluated with the two different methods ($r=0.89$; $p<0.0001$) confirming the higher levels in patients with active disease and the overlapping of the two different analysis.
Conclusion: We showed the potential utility of real-time PCR for quantifying TNF-α levels in paraffin-embedded tissues. This approach is more cost-effective than that involving fresh samples and offers the advantage of utilizing biopsy samples already collected for diagnostic purposes, removing the need for other samples.

E-PS-16-040

Uncommon EGFR compound mutations in NSCLC: case insights

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Background & Objectives: *EGFR* mutations occur in approximately 14% of non-small cell lung cancer (NSCLC) cases and are crucial for identifying patients who may benefit from tyrosine kinase inhibitors (TKIs). Exon 19 deletions and exon 21 p.L858R point mutations are the most frequent, accounting for 80-90% of all *EGFR* mutations. The remaining 10-20%, known as uncommon mutations, include p.G719X, p.L861Q, and p.S768I. Compound mutations, defined as the presence of more than one *EGFR* mutation within the same tumour, are reported with a heterogeneous incidence (4-26%).
Methods: A 76-year-old female patient underwent lobectomy for NSCLC after diagnostic bronchoscopy. Histology revealed a papillary-acinar adenocarcinoma without lymph node involvement. The patient was staged as stage I and therefore did not receive adjuvant chemotherapy. Molecular analyses were performed on DNA extracted from FFPE tissue using real-time PCR. Subsequent NGS analysis was performed to further validate the real-time PCR results.
Results: Real-time PCR analysis detected two uncommon *EGFR* mutations: exon 18 p.G719X and exon 21 p.L861Q. To confirm these findings, a new DNA extraction was performed, and the same compound mutations were identified by real-time PCR. Subsequent NGS analysis confirmed the presence of the *EGFR* pathogenic variants c.2156G>C p.G719A and c.2582T>A p.L861Q, with allelic frequencies of 25.78% and 25.61%, respectively.
Conclusion: The equivalent allelic frequencies suggest that these compound mutations are likely in cis, indicating the presence of a molecularly homogeneous neoplastic cell population. The clinical efficacy of *EGFR*-TKIs in patients with uncommon *EGFR* compound mutations remains uncertain. While p.G719X + p.L861Q mutations respond well to first-generation TKIs, second-generation TKIs demonstrate a stronger inhibitory profile. Moreover, preclinical and clinical data have shown that osimertinib has activity against these complex mutations. Further research is needed to define the optimal therapeutic strategy for this patient group.

E-PS-16-041

Unusual *BRAF* mutations in melanoma patients: discordance between molecular testing methods

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Background & Objectives: *BRAF* mutations occur in 40-50% of cutaneous melanomas and the majority of the mutations results in codon 600. *BRAF* p.V600E is the most frequent mutation and is present in approximately 70-88% of cases. Less common mutations have been also described in the codon 600, including p.V600K (10-20%), p.V600R (2-5%), p.V600D (1-4%), p.V600M (<1%) or p.V600G (<1%); furthermore, others unusual mutations concern codons 599 and 601 (<5%). We report two cases of unusual *BRAF* mutations detected in melanoma patients that presented discordance between molecular testing methods utilized.
Methods: A 52-year-old male patient with ulcerated nodular melanoma and an 81-year-old male patient with acromic melanoma underwent to molecular characterization after surgical excision. For both patients, DNA was extracted from FFPE skin samples and the *BRAF* status was assessed by real-time PCR utilizing *BRAF* Codon 600 Mutation Analysis Kit II (EntroGen), intended for the detection of *BRAF* mutations p.V600E/E complex (GTG>GAG/GTG>GAA), p.V600K (GTG>AAG), p.V600R (GTG>AGG), p.V600D (GTG>GAT), p.V600M (GTG>ATG) and p.V600G (GTG>GGG).
Results: *BRAF* mutations were detected in both patients by real-time PCR: variant p.V600M (c.1798G>A) in 52-year-old patient and p.V600R (c.1798-1799GT>AG) in 81-year-old patient. The same unusual *BRAF* mutations were found in two patients repeating twice the analysis. Successively, an orthogonal test was performed utilizing next generation sequencing (NGS) approach with the Myriapod NGS Cancer panel DNA (Diatech Pharmacogenetics). *BRAF* mutations in codons 599 and 601 were respectively detected in two patients. In particular, variant p.T599dup (c.1795-1797dupACA) VAF 43.76% was found in 52-year-old patient, while the variant p.K601E (c.1801A>G) VAF 84,3% was found in 81-year-old patient.
Conclusion: The presence of gene variants different from reference genes of test utilized may determine not only a false negative result but also the detection of a mismatched variant. Therefore, in molecular testing NGS should be preferred to predefined target methodologies.

E-PS-16-042

Contribution of molecular profiling in melanomas diagnosed in cutaneous and extracutaneous sites

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Background & Objectives: Molecular genotyping has been incorporated into the routine clinical management of patients with melanoma. Cutaneous and uveal melanomas are characterized by *BRAF/RAS* and *GNAQ* mutations, respectively, while in some patients the primary site remains unknown. In the herein presented mini case series of cutaneous and non-cutaneous melanomas, we highlight the role of molecular profiling in patient management, including diagnostic workup and therapeutic decision making.
Methods: We present routinely diagnosed melanoma cases that were referred to our department for molecular profiling in 2022-2024. Tissue examination was performed on haematoxylin-eosin and immunohistochemical stained sections. Molecular profiling was assessed by targeted next generation sequencing (NGS) with the Oncomine™ Precision Assay GX.
Results: This series includes nine patients, five females and four males (median age: 78 years). Three patients (3/9, 33,3%) had cutaneous lesions, while the remaining six (6/9, 66,6%) had non-cutaneous tumours in the eye, nasal cavity, small intestine, axillary lymph nodes, lung and liver. In the latter group, no cutaneous primary was clinically identified, apart from the patient with the liver mass, who had a primary lesion in the eyelid conjunctiva. The following mutations were detected in lesions from respective sites: *BRAF* p.V600E (skin, nasal cavity), *BRAF* p.G469R (small intestine), *GNAQ* p.Q209P (eye, liver), *NRAS* p.Q61K (skin, lymph nodes), *HRAS* p.Q61L (skin) and *CDKN2A* loss (lung). Molecular analysis identified patients that could benefit from treatment with BRAF/MEK or tyrosine kinase inhibitors. Furthermore, in cases of unknown primary site, a cutaneous (*BRAF*, *RAS* mutations) or uveal (*GNAQ* mutations) origin might be suggested.
Conclusion: Molecular profiling by targeted NGS is feasible in the pathology laboratory and can be informative not only for identifying candidates for targeted treatment, but also for indicating a potential primary site in patients diagnosed with non-cutaneous melanoma.

E-PS-16-043

Multiplex digital PCR as a tool for detection of *BRAF* and *KRAS* mutations in liquid biopsy specimens

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Background & Objectives: Testing *KRAS* and *BRAF* mutations in liquid biopsy is crucial for detection of different cancers. While liquid biopsy samples can be sequenced for mutation detection, digital PCR can offer a quicker and cheaper alternative for detection of known pathogenic mutations. We designed and assessed the performance of 2 digital PCR multiplexes for detection of *BRAF* V600 mutations and *KRAS* G12 mutations for liquid biopsy testing.
Methods: Research use only assays were designed to detect and differentiate *BRAF* V600K/E/R mutations in a single reaction. A separate multiplex was designed to detect and differentiate *KRAS* G12C and G12D and undifferentiated G12A/R/S/V in one reaction. Performance of each multiplex was assessed for analytical specificity, analytical sensitivity, limit of blank and assay linearity. In addition, testing was performed on contrived liquid biopsy specimens using EDTA plasma with synthetic DNA targets. Cell free DNA was isolated using the MagMAX™ Cell-Free DNA Isolation Kit (Thermo Fisher Scientific). Digital PCR was performed on Absolute Q™ instrument (Thermo Fisher Scientific).
Results: Mutations in both genes could be accurately detected down to allelic frequency of 0.1% with 1000 copies/µl of wild type. Analytical specificity of the assays was determined to be >99.0% in reference material at 8000 copies/µl. Limit of blank was determined to be in the range of 0.0-0.05 copies/µl and linearity for all channels at $R^2 \approx 1$ across all multiplexes. *BRAF/KRAS* were detectable to 200-300 copies of wild type per ng of cfDNA from EDTA plasma.
Conclusion: *BRAF* V600 and *KRAS* G12 mutations can be detected with high accuracy down to the allelic frequency of 0.1% using the newly developed digital PCR multiplex assays on Absolute Q instrument. This rapid method for *BRAF* and *KRAS* mutation detection can be a valuable tool for analysing liquid biopsy specimens for cancer research.

E-PS-16-045

Detection of CD28 T-lymphocyte subpopulations in elderly patients with rheumatoid arthritis at the onset of the disease

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Background & Objectives: Studying CD28 and T-cells is essential for understanding age-related changes in T-cells and for developing potential intervention strategies to improve immune functions in the elderly. The aim of this study is to investigate the subpopulations of CD28 T-lymphocytes in the peripheral blood of patients with rheumatoid arthritis at the onset of the disease using flow cytometry.
Methods: The study included 100 patients with a confirmed diagnosis of rheumatoid arthritis (RA) according to the ACR/EULAR 2010 criteria. The mean age of the participants was 60 years (Me [25th; 75th percentile] = 60 [38.0; 68.0] years). The patients were divided into two groups: 50 patients with disease onset over the age of 60, with an average age of 68 years [64; 73], a disease duration of 2 years [1; 2], and a DAS28 score of 4.9 [4.3; 5.6] points; and 50 patients with disease onset before the age of 60, with an average age of 38 years [27; 45], a disease duration of 1.3 years [1; 2], and a DAS28 score of 4.8 [3.4; 5.4] points.
Results: The study comparing donors and patients with RA over 60 years old revealed significant differences in the percentage and absolute counts of CD8+CD28- cells. In donors, the percentage was 29.8% and the absolute count was 0.1 x 10^9/L, while in patients with RA, these values were 60.1% and 0.2 x 10^9/L, respectively ($p < 0.05$). Additionally, the percentage and absolute counts of CD8+CD28+ cells were higher in healthy donors compared to patients with RA over 60 years old, with values of 70.2% and 0.3 x 10^9/L in donors compared to 39.9% and 0.2 x 10^9/L in patients ($p < 0.05$).
Conclusion: A direct correlation was identified between patient age and the quantity of CD8+CD28- T lymphocytes, indicating that rheumatoid arthritis potentially leads to accelerated immune aging.

E-PS-16-046

Analytical validation of a highly multiplexed Droplet Digital PCR (ddPCR) assay for simultaneous detection of up to 37 variants in the EGFR, KRAS and BRAF genes

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Background & Objectives: Lung cancer is the second most common cancer globally, of which 80-85% are Non-Small Cell Lung Cancer (NSCLC). Even with advanced screening methods, about 53% of lung cancers are still diagnosed at an advanced stage with a 5-year survival rate of 9%. Biomarker testing for actionable oncogenic driver mutations is recommended in national and international guidelines based on the improved outcomes observed with use of targeted therapies in eligible patients with metastatic NSCLC. Here, we demonstrate the performance of the ddPLEX EGFR/KRAS/BRAF Mutation Detection Assay Kit, a research use only kit developed for the QX600™ ddPCR™ System.
Methods: This kit is designed for the detection, discrimination and quantification of 37 actionable variants in the *EGFR*, *KRAS*, and *BRAF* genes in a single ddPCR well. It also has a companion total quantification well that allows for variant allele frequency (VAF) calculation. It can provide same day results with a streamlined workflow, includes positive and internal controls and is compatible with plasma and formalin-fixed paraffin-embedded (FFPE) samples. We tested analytical sensitivity, specificity, reproducibility and linearity using contrived samples. Accuracy of the assays in the kit was further validated with cfDNA samples using an orthogonal NGS method.
Results: The results demonstrated an analytical sensitivity of 0.025%-0.1% in a background of 40,000 copies of human genomic DNA for all targeted variants and an analytical specificity of 100%. The assay was linear from 20% to 0.1% VAF with a $R2 > 0.95$. With previously extracted and archived cell-free DNA from plasma, the assay showed high concordance.
Conclusion: Results indicate that the ddPLEX EGFR/KRAS/BRAF Mutation Detection Assay Kit is sensitive, accurate, and time- and cost-efficient for detecting clinically relevant NSCLC variants. Multiplexing maximizes information and reduces sampling bias from specimens with low nucleic acid quantities such as FFPE and plasma.

E-PS-16-047

Usefulness of molecular characterization in diagnostic orientation: a case report

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Background & Objectives: In the era of precision oncology, molecular characterization of tumours has emerged as an important tool, primarily for predictive purposes. However, sometimes, molecular tests can also play a crucial role in diagnostic orientation.
Methods: In January 2024, an 81-year-old male patient was diagnosed with lung adenocarcinoma, and subsequently enrolled in a prospective study evaluating the impact of liquid biopsy in advanced tumours. Molecular characterization was performed on both a blood sample (FoundationOne®Liquid CDx) and FFPE lung tumour tissue (Myriapod NGS Cancer Panel DNA). In April 2024, after episodes of rectal bleeding, a colonoscopy revealed rectal carcinoma, later confirmed by histology. To determine whether the lung lesion represented secondary progression from the rectal carcinoma or a primary lung lesion, synchronous with the rectal carcinoma metastatic to the liver, molecular analyses were also performed on both the rectal biopsy and a re-biopsy of the lung tumour.
Results: The patient was initially staged as stage IVA, and first-line treatment with vinorelbine therapy was started. Molecular characterization revealed *KRAS* p.G12V mutation (VAF 12.5%) in liquid biopsy, while KRAS p.G12C variant was found in FFPE lung tumour tissue (VAF 59.85%). Subsequent molecular profiling of the rectal biopsy and the re-biopsy of the lung tumour showed *KRAS* p.G12V variant in the rectal tumour and *KRAS* p.G12C mutation in the lung tumour. Given the clinical, instrumental and biomolecular findings, a new diagnostic orientation was formulated: hepatic secondary

lesions from inoperable rectal adenocarcinoma, with an early-stage synchronous lung adenocarcinoma. Based on this revised differential diagnosis, therapy with capecitabine plus bevacizumab was initiated in July 2024, as recommended for patients with unresectable metastatic colorectal cancer.
Conclusion: In some pathological contexts, such as the one just described, formulating a correct diagnosis can be challenging. In these cases, molecular characterization should also be used to prevent inappropriate assessments and ensure correct patient management.

E-PS-16-048
Unusual signal patterns of FISH probes in synovial sarcoma: immunohistochemical and clinicopathological examination of 2 cases
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Background & Objectives: Fluorescence in situ hybridization (FISH) is one of the methods applied in daily clinical practice for the molecular pathological diagnosis of Synovial Sarcoma (SS). The most commonly used probe in FISH analysis is the SS18 break dual-colour signal probe designed to label sequences adjacent to SS18 on chromosome 18, and the recommended criterion for positive evaluation in FISH testing is the presence of unpaired (isolated) red and green signals. However, very few cases with an atypical pattern where the green signal is missing have been reported in the literature. We investigated the clinicopathological and immunohistochemical features of two cases with atypical patterns diagnosed with SS at our institution using the FISH method.
Methods: Two pathologists re-examined all Haematoxylin Eosin (H&E) and IHC stained slides. Cases using ZytoLight ® SPEC SS18 Dual Color Break Apart Probe in FISH testing were re-evaluated in Argenit Brand easyFISH Model software program. Clinicopathological data were analysed and followed up retrospectively.
Results: The cases were a 24-year-old male with a tumour located in the paraspinal region and a 28-year-old female with a tumour located in the lung, respectively. TLE-1 and VIMENTIN were stained diffusely and strongly positive in IHC studies. SS18 FISH tests showed an atypical pattern with isolated 5' signals in most cells. Clinically, the first case died approximately two years after diagnosis. The second case developed breast metastasis and still carries the disease.
Conclusion: SS is an aggressive tumour and SS18 rearrangement with FISH testing is important in the differential diagnosis of soft tissue tumours. Although one of these two cases with an atypical pattern showed unusual localization and high rates of poor differentiation, whether this variant is related to this pattern type can be understood with a larger case series.

E-PS-16-049
Prevalence of BRAF and RAS mutations and their association with clinicopathological factors in colorectal cancer: experience from our insitution
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Background & Objectives: Colorectal cancer (CRC) is a multifactorial disease caused by a combination of environmental and genetic factors, such as chromosomal abnormalities, epigenetic changes, and mutations. Epidermal growth factor receptor (EGFR)-signalling pathway is crucial to CRC development by activating RAS-RAF-MEK-ERK and PI3K-PTEN-AKT. RAS and BRAF are key genes in these pathways, present in 40–50% and 8–12% of CRCs, respectively. Both mutations are associated with poor prognosis in advanced disease.
We aim to determine BRAF and RAS mutation rates in CRC and their association with clinicopathological characteristics.
Methods: KRAS, NRAS, BRAF mutations was determined using PCR in total of 50patients with CCR over a period of 4years. Statistics were performed using SPSS software version20. Correlation between RAS and BRAF mutational profile and clinicopathological features were analysed by Chi-square or Fisher's exact test. *P*-value $\leq$0.05 considered statistically significant.
Results: Mean age was 54.49years, and sex-ratio was 1.9:1. Left/sigmoid localization (46.2%) and NOS subtype (84.6%) were the most frequent, with 82.7% being low-grade. Stage III/IV was reported in 86%. KRAS, NRAS, and BRAF were mutated in 27cases, 4cases (two with KRASmutated), and 2cases, respectively. KRAS and BRAF mutated were more frequent in men, unlike NRAS mutated. Left/sigmoid localization was most reported in KRAS/NRAS mutated. BRAF mutated cases exhibited balanced distribution between right and left colon. NOS subtype, low-grade and stage III/IV were most common in cases with all 3mutated genes. KRAS and NRAS mutations tended to be significantly associated with lymphatic emboli (p=0.055, p=0.075, respectively). KRAS mutated tended to be associated with perineural invasion (p=0.052) and budding (p=0.09). NRAS mutated tended to be associated with tumour grade (p=0.089) and tumour stage (p=0.089). No association was noted with BRAF mutated.
Conclusion: Our results are partly consistent with literature findings, though they are limited by sample size, lack of clinico-histological data, and by the retrospective methodology.

E-PS-16-050
Impact of TP53 and RB1 mutations on gene expression and biological pathways in extrapulmonary small cell neuroendocrine carcinomas
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Background & Objectives: Extrapulmonary small cell neuroendocrine carcinomas (EP-SCNCs) are rare, highly aggressive neuroendocrine malignancies that arise in various anatomical sites. These tumours share histopathological and molecular features with pulmonary small cell carcinoma, particularly frequent TP53 and RB1 alterations, which drive genomic instability and tumour progression. However, their impact on the transcriptomic landscape of EP-SCNCs remains insufficiently characterized. This study explores the molecular consequences of TP53 and RB1 alterations, providing insights into tumour biology and potential classification refinements.
Methods: We performed rRNA-depleted whole RNA sequencing (RNA-Seq) on 109 EP-SCNC samples, stratified into four groups based on mutational profiles: TP53+RB1 co-altered (n=43), RB1-only altered (n=11), TP53-only altered (n=29), and tumours without TP53 and/or RB1 alterations (n=26). Differentially expressed genes were analysed using the Gene set Ordinal Association Test (GOAT) to identify biological processes associated with each subgroup.
Results: Tumours without TP53 and RB1 alterations exhibited upregulation of translation-related pathways, including cytoplasmic translation, ribosome biogenesis, and RNA metabolism, suggesting enhanced biosynthetic activity. TP53+RB1 co-altered tumours showed a significant downregulation of immune-related processes, indicating potential

immune evasion. TP53-only altered tumours had fewer deregulated pathways, primarily involving downregulation of nervous system processes, possibly reflecting neural de-differentiation. RB1-only altered tumours exhibited downregulation of epithelial development, cell differentiation, and tissue development pathways, suggesting a role for RB1 loss in altering cell fate determination.
Conclusion: Our findings reveal distinct transcriptional signatures associated with different TP53 and RB1 mutational profiles in EP-SCNCs. The upregulation of ribosomal and translational processes in tumours without these mutations, the suppression of immune pathways in TP53+RB1 co-mutants, and the distinct de-differentiation processes in RB1-only and TP53-only subtypes underscore the complex molecular landscape of these tumours. These transcriptomic insights provide a foundation for further multi-omics characterization of EP-SCNCs. This work was supported by the Ministry of Health, Czech Republic (MH CZ AZV NU22-03-00130 and DRO-VFN 64165).

Funding: Ministry of Health, Czech Republic, AZV NU22-03-00130 and DRO-VFN 64165

E-PS-16-051
External Quality Assessment (EQA) for Homologous Recombination Deficiency (HRD) testing in ovarian cancer: findings of a new IQN Path pilot scheme
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Background & Objectives: HRD is a genomic signature where cells lose their ability to repair double-stranded DNA breaks via the homologous recombination repair (HRR) pathway. HRD has been reported in approximately 50% of ovarian cancers and is a predictive marker for PARP inhibitor treatment.
A range of assays with different HRD scoring systems are used to identify HRD, and new diagnostic tests can have a high error rate when introduced into clinical practice presents. Five EQA providers collaborated under the umbrella of IQN Path to establish an international model for provision of EQA, to help assure quality of HRD testing for patients.
Methods: Fifty laboratories from 15 countries were selected to participate and sent three FFPE samples for HRD testing using their routine methodology. Clinical reports were returned for assessment of genotyping accuracy, result interpretation and clerical accuracy.
Results: Forty-four laboratories submitted results. Accuracy was high with only four instances where incorrect HRD status was reported (3.0%, 4/132). Clinical interpretation was also generally of a high standard with 88% of reports interpreting the result in relation to PARP inhibitor therapy.
However, the EQA did identify areas where improvements could be made and harmonisation is required. The main observations were as follows;

- There was variability in the terminology used to describe HRD status and score.
- The cut-off for the genomic instability score (GIS) was not stated in many cases and may be relevant for results close to the threshold.
- Laboratories using a method that included HRR panel analysis did not consistently report variants in HRR genes other than *BRCA1/BRCA2*.

Conclusion: This pilot EQA identified need for improvement and harmonisation in HRD reporting. The ongoing provision of EQA based on the model developed by IQN Path will promote high quality HRD testing through harmonisation of practice and publication of EQA results.

E-PS-16-053
The unreliability of neoplastic cell percentage visual estimation for molecular testing
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Background & Objectives: Molecular testing plays a crucial role in routine diagnostic pathology. Accurate determination of the neoplastic cell percentage (NCP) is essential to assess sample adequacy and for the correct interpretation of the results. This is routinely done by pathologists by visual estimation on H&E-stained slides, a highly subjective method.
Methods: We aimed to assess interobserver agreement in NCP estimation among pathologists in our centre. NCP, defined as the proportion of tumour cells relative to the total number of nucleated cells, was estimated on previously delineated tumour areas of 36 H&E-stained slides, corresponding to all cases which underwent molecular analysis from January/2024 to February/2024. These included 19 colon adenocarcinomas, 7 endometrial carcinomas, 5 melanomas, 2 ovarian carcinomas, and 3 prostate adenocarcinomas. All cases were independently evaluated by 8 specialists and 5 residents.
Results: The median difference between the highest and lowest estimated NCP per sample for all 36 cases was 50 (range 35–80). Accounting only for specialists' evaluations, median difference was 40 (range 20–80). When categorizing NCP at a 20% threshold (frequently used as the recommended minimum for NGS studies) we found that in 19/36 samples at least one pathologist (range: 1-6) estimated the NCP below 20%.
Conclusion: Our study corroborates previous findings that interobserver variation in NCP estimation is high, leading to potential misinterpretation of results and inadequate patient management. An important source of error lies in the difference between tumour area *versus* percentage of tumour cells. Indeed, upon revision of our four cases with higher discrepancies, 3 corresponded to colon adenocarcinomas with abundant mucin and/or dense lymphoplasmacytic infiltrate, and to a melanoma with extensive necrosis. Thus, careful macrodissection privileging tumour-rich areas, development of standardized methods of evaluation and, crucially, implementation of pathologists' training programs is vital. Furthermore, the development of digital automated analysis algorithms may improve the consistency of this assessment.

E-PS-16-054
An audit of non-small cell lung cancer molecular testing in Galway University Hospital
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Background & Objectives: Testing for somatic mutations which drive lung cancer proliferation has allowed for significant advances in the treatment of the disease, in addition to PD-L1 testing for immune checkpoint therapy. We audited the reported non small cell lung cancers (NSCLC) of University Hospital Galway for 2024.
Aims: To audit the reported histology classification, molecular and PD-L1 status of samples, including cases classified as inadequate.

Methods: A list of all specimens diagnosed with NSCLC in 2024 was obtained from the laboratory information system. Information on specimen type, diagnosis and predictive marker testing was obtained from reports and molecular audit trails.
Results: 215 cases were reviewed. 51.7% (n=109) were male, and 49.3% (n=106) were female. 68.4% (n=147) were sampled from the primary tumour, 19.5% (n=42) from lymph nodes, and 12.1% (n=26) were metastatic deposits from other organs.
67.9% (n=146) were adenocarcinoma, and 26.5% (n=57) were squamous cell carcinoma. 86% (n=14) of adenocarcinoma specimens had molecular testing completed. Of the 21 specimens that did not, 24% (n=5) had insufficient material, 38% (n=8) had molecular testing done on a previous sample, and 38% (n=8) had no identifiable reason.
83.7% (n=180) of NSCLC had PD-L1 testing done. 16.2% (n=35) did not have PD-L1 testing, of these, 3.3% (n=7) had insufficient material, 7% (n=15) had testing done on previous specimens, and 6% (n=13) had no identifiable reason for not testing.
148 specimens had molecular testing in total. Of these, 52.7% (n=78) had a molecular alteration.
Conclusion: The majority of NSCLC undergo testing as per recommendations. 5.5% of adenocarcinoma specimens had no molecular testing without an identifiable reason.
6% of specimens had no PD-L1 done without identifiable reason.
This will be further investigated to assess if testing should have been completed for these specimens.

E-PS-16-056
Analysis of genomic alterations in metastatic and non-metastatic pleural mesotheliomas
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Background & Objectives: Molecular alterations are important in terms of both diagnosis, treatment and prediction of prognosis in cancer. Genomic changes in the pathogenesis of mesothelioma are copy number loss, gain and rarely mutations. In this study, we aimed to determine the differences between the genetic profiles of metastatic and non-metastatic mesotheliomas with the cohort in the ciobioportal dataset.
Methods: Since it was aimed to investigate genomic changes with more up-to-date data, three datasets consisting of a total of 60919 cases from 2021 and later were selected. 244 cases diagnosed with mesothelioma were included in the study. The most frequently mutated genes and the genes showing the most frequent copy number changes and structural changes were analysed in the series. Clinicopathological parameters and molecular changes were compared between the 195 metastatic and 49 non-metastatic case groups.
Results: The first five genes with the most frequent mutations in 244 cases were BAP1 (36.5%), NF2 (23%), TP53 (11.1%), SETD2 (10.7%) and LATS2 (7.8%); the first five genes with copy number changes were CDKN2A (32.4%), CKDN2B (31.1%), BAP1 (14.8%), TEK (4.5%) and NF2 (4.5%); and the first three genes with structural changes were BAP1 (4.1%), PBRM1 (1.6%) and NF2 (1.2%). The fourth and fifth most frequently mutated genes were LATS2 and TERT in non-metastatic group. The most frequent copy number alterations in the non-metastatic group showed some differences. Of the 195 cases, 99 had lung, 38 had bone, 32 had liver and 8 had brain metastases. In cases with bone and brain metastases, biphasic and sarcomatoid type was more common. NF2 mutation was significantly higher in cases with bone metastases. Microsatellite instability was seen at a higher rate in cases with liver metastases ($p<0.05$ $q<0.05$).
Conclusion: In this study, statistically significant and remarkable features were highlighted in whole genome analysis data in mesotheliomas, which are quite rare.

E-PS-16-058
A novel *SOX5::NTRK3* fusion in a patient with neuroendocrine tumour of the lungs: a case report
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Background & Objectives: Low- and intermediate-grade neuroendocrine tumours of the lungs, commonly referred to as typical and atypical carcinoids, represent a rare but clinically significant subset of lung neoplasms. Neurotrophic tyrosine receptor kinase (NTRK) gene fusions are well-established oncogenic drivers found in various solid tumours. However, NTRK fusions are reported in only 0.5% of non-small cell lung cancers and are even rarer in pulmonary carcinoids.
Methods: We present the case of a 48-year-old female patient diagnosed with bilateral typical carcinoid tumours. Tumour biopsy samples underwent targeted next-generation sequencing (NGS) using both DNA- and RNA-based approaches. NGS was performed with the QIAseq Targeted DNA IO Panel TMB and QIAseq RNA Fusion XP - Solid Tumour Panel (Qiagen), with sequencing carried out on the SURFseq 5000 platform (GeneMind).
Results: RNA analysis identified a novel *NTRK3* fusion involving the *SOX5* (SRY-Box Transcription Factor 5) gene as the fusion partner. This oncogenic rearrangement fuses the 5′ region of *SOX5* with the 3′ region of *NTRK3*, preserving the entire tyrosine kinase domain of NTRK3. No additional clinically relevant mutations were detected. The patient is currently undergoing treatment with somatostatin analogue (Sandostatin).
Conclusion: This case report describes a novel SOX5::NTRK3 fusion in a pulmonary neuroendocrine tumour, expanding the known spectrum of *NTRK3* rearrangements. Its identification underscores the value of molecular profiling and may inform personalized treatment decisions. If standard therapy fails, NTRK inhibitors could offer a targeted alternative.

Funding: MH CZ—DRO (FNOL, 00098892)

E-PS-16-059
Using next-generation sequencing (NGS) to further understand vascular anomalies: insights from the initial tests conducted at a Portuguese university hospital centre
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Background & Objectives: Next-generation Sequencing (NGS) has emerged as a powerful tool in the genetic analysis of malignant neoplasms, allowing a better understanding of the genetic landscape of the tumours and contributing to the diagnosis, prognostication and treatment planning. Similarly, NGS has also emerged as a powerful tool to further unravel vascular anomalies, which are developmental defects of the vasculature, encompassing a heterogeneous group of disorders. Vascular anomalies, which harbour considerable phenotypic and genetic heterogeneity, are more frequently sporadic and are associated with somatic mutations and/or double-hit mechanisms.
Methods: To share our initial experience with NGS testing for vascular anomalies we retrospectively collected cases from January 2022 until

now, which underwent routine NGS testing using the Oncomine Precision Assay (OPA) in the Genexus (Thermo-Fisher Scientific) platform or a 38-gene custom-made panel in the MiSeq (Illumina) platform.
Results: In this pilot study we were able to include 25 patients, with a slight preponderance of female patients and age ranging from 1 to 55 years old. The great majority of the cases were arteriovenous malformations (AVMs). Genetic abnormalities could not be identified in the majority of the cases. However, several cases harboured pathogenic variants of the PIK3CA gene. GNAQ pathogenic variants were also rarely identified.
Conclusion: Our experience highlights the utility of NGS in the holistic evaluation of the complex vascular malformations, paving the way for improved diagnostic accuracy and offering potential targets for personalized treatment strategies. Moreover, our findings emphasize the need for comprehensive NGS panels covering all potentially relevant genes in the context of vascular anomalies, allowing us to expand our understanding of the molecular mechanisms driving these complex disorders.

E-PS-16-060
Next-Generation Sequencing (NGS) in precision oncology: decoding the puzzle of primary vs. metastatic tumours
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Background & Objectives: The integration of advanced molecular techniques into Anatomical Pathology has revolutionized patient care by enabling personalized treatment strategies, prognostic predictions, and improved diagnostic accuracy. Next-generation sequencing (NGS) allows for the identification of unique genetic alterations and variants that may serve as distinguishing markers for primary versus metastatic cancers.
Methods: We present two cases where NGS played a pivotal role in diagnosing two synchronous lung adenocarcinomas and in distinguishing between primary lung versus metastatic colon adenocarcinoma.
Results: **Case 1:** A 64-year-old female smoker underwent a left lower lobectomy for two nodular lesions (3.5 cm and 1.5 cm). The histopathological analysis revealed two moderately differentiated adenocarcinomas harbouring architectural patterns with both similar and distinct features. NGS revealed an EGFR p.E746_A750del mutation in the 3.5 cm tumour and a KRAS p.G12C mutation in the 1.5 cm tumour, favoring two synchronous lung adenocarcinomas.
Case 2: A 77-year-old woman with a history of colorectal adenocarcinoma presented with a 6 cm nodule in the lung left upper lobe. The histopathological analysis showed an intestinal-type, TTF-1 negative adenocarcinoma. The medical team was initially uncertain about the metastatic nature of the lung lesion. Therefore, NGS analysis was performed on both the colon surgical specimen and lung tumour biopsy. The NGS study demonstrated that the same genomic variants of the *TP53*, *PIK3CA* and *NRAS* genes were present in both the colon and lung tumours. This finding strongly suggested that the lung tumour originated from the colon, supporting a diagnosis of metastatic colon cancer rather than a primary lung adenocarcinoma.
Conclusion: Both cases highlight the critical role of NGS in solving histopathological dilemmas. By identifying shared genomic alterations or showing distinct genetic profiles, NGS not only helped to clarify the tumour origin, but also helped to define therapeutic decisions, underscoring its potential in improving diagnostic accuracy and in defining patient-specific treatments.

E-PS-17 E-Posters Nephropathology

E-PS-17-001
Microscopic manifestation of kidney damage in the catastrophe of the century
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Background & Objectives: Turkey is located in an earthquake-prone region. On February 6, 2023, a devastating earthquake struck Kahramanmaraş, affecting approximately 14 million people. While extensive studies have been conducted on patient follow-up in basic and advanced life support, nephrology, and intensive care units, there is a lack of research on the renal histopathology of earthquake victims. This study aims to fill this gap in the literature by examining renal biopsy findings in affected patients.
Methods: Between February 6, 2023, and May 15, 2024, kidney needle biopsies from 40 earthquake victims aged 0-85, who presented to our clinic from 11 affected provinces, were retrospectively analysed. Demographic data such as age and gender, along with laboratory findings, were collected from the hospital information system.
Results: The mean age of the cases was 35.05 years, with 25 males and 15 females. The majority (24 cases) were from Hatay. A history of being trapped under rubble was present in 20% of cases. Histopathological examination revealed common findings such as tubulitis, tubular epithelial cell shedding, inflammatory cell infiltration, tubular casts, interstitial fibrosis, tubular atrophy, and glomerulosclerosis. Diagnoses included Proliferative Glomerulonephritis (10 cases), Focal Segmental Glomerulosclerosis (7), Necrotizing Crescentic Glomerulonephritis (6), Minimal Change Disease (3), Membranous Nephropathy (2), AA Amyloidosis (2), Membranoproliferative Glomerulonephritis (2), and Lupus Nephritis (2). Additionally, single cases of Hypertensive Nephropathy, Nephrocalcinosis, Pyelonephritis, Diabetic Nephropathy, and Cryoglobulinemic Glomerulonephritis were identified. Vascular changes, tubulointerstitial nephritis, and vasculitis secondary to hypertension were also observed.
Conclusion: Earthquakes are significant natural disasters that contribute to morbidity and mortality not only through direct trauma but also by disrupting the management of chronic conditions such as diabetes, hypertension, chronic obstructive pulmonary disease, and end-stage renal disease. This study highlights the renal complications resulting from various etiological factors, particularly crush syndrome, in earthquake victims.

E-PS-17-002
Thrombotic microangiopathy with extensive mesangiolysis as a first clinical presentation of plasmacytoma
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Background & Objectives: Thrombotic microangiopathy (TMA) is a rare condition characterized by systemic microthrombi causing end-organ ischemia. It can be primary, resulting from complement abnormalities, or secondary, associated with infections, malignancies, or connective tissue diseases. While renal impairment is common in multiple myeloma, TMA as its initial presentation is rare. We present a unique case where TMA was the first indication of plasmacytoma.

Methods: A 37-year-old male, who had recently recovered from infective myocarditis, underwent kidney biopsy due to a three-month history of nephrotic-range proteinuria and arterial hypertension. His kidney function was normal and urinary sediment was unremarkable. Immunoserological tests were within reference ranges. The complete blood count was normal, with no signs of systemic haemolysis. However, serum electrophoresis revealed a monoclonal IgG lambda. Kidney histopathology showed glomerular TMA with chronic mesangiolysis, while extraglomerular vessels remained unaffected. Immunofluorescence findings were minimal and nonspecific, and electron microscopy confirmed mesangiolysis with minimal podocyte effacement. The initial presumed aetiology was infection-triggered (myocarditis-related) TMA.
Results: Despite treatment with corticosteroids, complement inhibitors, and rituximab, proteinuria persisted, and kidney function deteriorated. A repeat biopsy revealed features of chronic TMA. Further imaging, including PET-CT and MRI, identified a metabolically active lesion in the right clavicle and surrounding soft tissue. Biopsy confirmed plasma cell proliferation with lambda light chain restriction, leading to a revised diagnosis of plasmacytoma. The patient was treated with daratumumab, bortezomib, and lenalidomide. At the last follow-up, two years after diagnosis, he remained clinically stable without progression of plasmacytoma.
Conclusion: This case highlights the diagnostic challenge of TMA as a rare initial manifestation of plasmacytoma. The absence of classical symptoms delayed the diagnosis, underscoring the importance of thorough follow-up and repeated investigations when renal dysfunction persisted despite initial treatment. Early recognition and appropriate management of underlying haematological malignancies in TMA cases can significantly improve patient outcomes.

E-PS-17-003
Clinicopathological analysis of 23 renal amyloidosis cases: a single-centre experience
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Background & Objectives: Renal involvement is a major cause of mortality in systemic amyloidosis. In renal amyloidosis, the glomeruli are the most common site of amyloid deposition, and nephrotic syndrome is the typical clinical presentation. Differentiation between AA and AL amyloidosis is performed using immunofluorescence (IF) and immunohistochemistry (IHC) techniques. Kidney biopsy plays a critical role in diagnosis and, by applying scoring and grading to biopsy findings, helps in predicting the clinical course of the disease.
Methods: This study includes all cases of biopsy-proven renal amyloidosis diagnosed between January 2018 and December 2023. The analyses involved light microscopy, Congo red staining under polarized light, IF, IHC for amyloid A, kappa, and lambda, and bone marrow examination. The classification, scoring, and grading of glomerular amyloid deposition were conducted according to the guidelines of Sen S et al
Results: A total of 23 cases of renal amyloidosis confirmed by biopsy were identified, of which 18 were primary and 3 were secondary. In two cases, the distinction between primary and secondary amyloidosis could not be established. The average age at diagnosis was 52.2 years. Edema was the most common presenting symptom. Secondary amyloidosis was predominant, accounting for 78.26% of cases. Among the secondary causes, tuberculosis, rheumatoid arthritis, and familial Mediterranean fever (FMF) were each found in five cases. Plasma cell neoplasia was detected in only one of the three primary amyloidosis cases. In two cases, differentiation between primary and secondary amyloidosis was inconclusive. The grading of renal biopsy findings correlated well with the class of glomerular involvement.
Conclusion: The combination of clinical history, IF, and IHC is essential for accurate amyloid typing. Grading of biopsy findings provides a detailed guide for assessing disease severity based on a broad range of morphological features and biochemical values. Correct amyloid typing is also crucial for selecting appropriate treatment strategies.

E-PS-17-004
Histopathological scoring and staging in renal aa amyloidosis: correlation with clinical parameters and prognostic implications
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Background & Objectives: AA amyloidosis is the predominant subtype of systemic amyloidosis in developing countries and frequently involves the kidneys, resulting in proteinuria and progressive renal dysfunction. However, the prognostic utility of standardized histopathological scoring systems remains understudied. The aim of this study is to evaluate renal AA amyloidosis cases using a structured histologic scoring and staging system and to correlate pathologic findings with clinical parameters and renal outcomes.
Methods: This retrospective cohort included 74 renal biopsies diagnosed as AA amyloidosis between 2011 and 2025. Biopsies were assessed via light microscopy, immunofluorescence, and immunohistochemistry. Histopathological staging was performed using the Renal Amyloid Prognostic Score (RAPS), as described by Sen and Sarsık, incorporating glomerular, vascular, and interstitial amyloid deposition, as well as inflammation, fibrosis, and glomerulosclerosis. The cohort included five biopsies from transplant kidneys, and four biopsies were second procedures performed on previously diagnosed patients (including one transplant case). Clinical data were available for 69 patients; five were assessed solely based on pathological parameters. Renal survival was defined as the time from biopsy to initiation of renal replacement therapy (RRT).
Results: Of the 74 patients, 68% were male. The most common underlying disease was Familial Mediterranean Fever (41%). RAPS staging revealed: Stage 1 (1%), Stage 2 (38%), and Stage 3 (57%). End-stage renal disease developed in 25 patients (36%), who had higher RAPS stages and more severe baseline renal impairment. Glomerular amyloid load correlated with proteinuria, while interstitial fibrosis, inflammation, and vascular/interstitial amyloid deposition were associated with lower eGFR values.
Conclusion: Structured histopathological staging in renal AA amyloidosis reflects the extent of renal damage and correlates with clinical severity at diagnosis. This approach may support risk stratification and guide clinical management, particularly in regions where AA amyloidosis is prevalent.

E-PS-17-005
Clinicopathological characteristics of IgA nephropathy and their and correlation with MEST C scores: a single centre cohort study from Sri Lanka
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Background & Objectives: IgA nephropathy (IgAN) is a poorly studied disease in a Sri Lankan setting and the value of MEST-C score in the Sri Lankan population has not been elucidated. The objective was to characterize clinical presentations and morphological patterns of

IgAN in a cohort of patients in Sri Lanka and correlate the clinical parameters with MEST-C scores.
Methods: 106 cases of IgAN diagnosed at a tertiary care centre from 2019 to 2024 were studied. Clinical data was retrieved from requested forms. Renal biopsies were reviewed by two pathologists for assessment of morphological patterns and MEST-C score. Correlation between clinical parameters and MEST-C score were assessed with multivariate regression analysis.
Results: Majority were male (n=63;59.4%); mean age 36.3 years (SD 12.7, range 14-69 years). Most had proteinuria (n=104,98.1%); sub-nephrotic (n=55;53.8%), nephrotic (n=49;45.7%) and haematuria (n=90;84.9%) microscopic (n=70;77.7%, macroscopic (n=20;22.3%) at presentation. Ten (9.8%) presented with rapidly progressive glomerulonephritis. Majority (n=58;54.8%) were CKD stage 3 or above. MEST-C scores were M1(n=97;91.5%), E1 (n=42;39.6%), S1 (n=37;34.9%), C1(17;16%) C2 (09;8.5%), T1 (32;30.2%) T2 (26;24.5%).
MEST-C sum score ≥3 correlated with eGFR(p=0.024) and serum creatinine (S.Cr)(p=0.034)
T score correlated with eGFR(p=0.012), C (p=0.027) and T (0.019) score with S.Cr, M(p=0.031) and E (p=0.029) scores with serum C3 level, serum albumin level with S (p=0.020). C3 staining intensity correlated with T(p=0.017) and eGFR(p=0.025).
Conclusion: Clinical presentations and the pattern of injury in IgAN matched other countries. However, majority were CKD stage ≥3 at presentation. The most important predictor of eGFR was T score. Glomerular C3 deposition appears to play a prognostic role.

E-PS-17-006
Beyond what we know: the role of glomerular C4d staining in transplant glomerulopathy
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Background & Objectives: Late antibody-mediated rejection (AMR) diagnosis is an ensemble of criteria based on the presence of peritubular C4d (C4dptc), histological findings and donor-specific antibodies (DSA). However, the significance of C4d expression in glomerular capillaries (C4dgcap) and the mesangium (C4dgmes) remains undefined. The aim of this study is to review the transplant glomerulopathy (TG), highlighting AMR cases, and the association between C4dgcap expression and DSA.
Methods: We reviewed the TG biopsies from May 2023 to December 2024, finding 70 cases. Cellular rejection, membranous nephropathy and lupus nephritis were excluded, a total of five cases.
Results: Among 65 TG biopsies, 24.6% (16/65) were diagnosed with AMR. In non-AMR cases (46/65, 70.7%), 60.9% (28/46) showed an absolute lack of C4d staining in the glomerular compartment. C4d positivity at the glomerular compartment (18/46, 39.1%) was subcategorized into C4dgcap in 15 cases (15/46, 32.6%), with a range of expression between 2 to 35% and a weak-moderate intensity and C4dgmes in six cases (6/46, 13%), between 5 to 50% with a moderate intensity. Regarding the positive DSA (30/65, 46.1%), 40% presented a positive C4d staining (12/30), all of which were C4dcap, with a range of expression between 5 to 100% and predominantly moderate intensity. Only one case exhibited C4dgmes staining (25%, weak intensity). Among DSA-negative cases (30/65, 46.1%), 15 exhibited glomerular C4d staining (15/30, 50%), C4dgcap was predominantly weak (between 2 to 25%) except for two cases which were AMR with stronger staining (~80%). Additionally, six cases displayed mesangial staining (between 5 to 50%, moderate intensity).
Conclusion: C4dgcap staining was more prevalent and intense in DSA-positive cases, whereas DSA-negative and AMR-negative cases showed lower expression staining in both intensity and percentage of involvement. In contrast, C4dgmes was observed in a significant proportion (mean 40%) of DSA-negative cases with moderate intensity, though its significance remains unclear.

E-PS-17-007
The kidney and substance abuse – a toxic relationship
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Background & Objectives: A 37-year-old female patient with a history of multi-drug abuse, and chronic hepatitis C presented to the department of nephrology with proteinuria and chronic kidney disease (CKD G3A2). The patient was under methadone substitution therapy (Substitol) for her multi-drug abuse. Blood pressure at time of presentation was 165/100 mmHg. Her baseline creatinine was within normal range until 2022 and then slowly increased over the course of two years to 1.83 mg/dl (eGFR was 37 ml/min/1,73m^2 (CKD EPI)) at current presentation. Proteinuria rose to 0.7 mgProtein/mgCreatinine during the same timeframe.
Methods: A renal biopsy was performed for investigation of progressive renal dysfunction.
Results: Histology revealed a glomerulopathy with membranoproliferative pattern of injury with conspicuous vacuolization of mesangial matrix and endocapillary cells. There were no immune deposits detected by immunohistochemistry. Electron microscopy confirmed mesangial, endothelial and also podocytic vacuoles that sometimes contained amorphic or lamellar electron dense material. This pattern was suggestive of Polyvinylpyrrolidone (PVP)-associated glomerulopathy.
Conclusion: PVP is a hydrophilic polymer widely employed as a carrier in pharmaceutical and biomedical preparations and has been previously described as a cause of CKD in patients after intravenous misuse of methadone syrup. The source of PVP in our case, however, was enigmatic as EU regulations banned PVP from methadone preparations in 2014. Upon further inquiry, the patient eventually admitted to having dissolved Oxazepam (Anxiolit forte) and Flunitrazepam (Rohypnol) tablets for intravenous injection. The manufacturer confirmed that both drugs contain PVP, thus making these the likely source of PVP. Renal function in our patient remained stable at an eGFR around 35 ml/min/1,73m^2 under supportive therapy with RAS and SGLT2 inhibitors.
To our knowledge this is the first described case of an intravenous injection of dissolved Oxazepam and Flunitrazepam tablets as a source of PVP causing CKD.

E-PS-17-009
Membranous glomerulonephritis superimposed on diabetes mellitus: description of 3 cases
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Background & Objectives: Membranous glomerulonephritis (MGN) is a disease characterized by subepithelial immune deposits with thickening of the glomerular capillary walls. We present 3 cases of MGN in patients with type 2 diabetes mellitus who presented with nephrotic proteinuria, where renal biopsy enabled a precise diagnosis.

Methods: The medical records of three patients with type 2 diabetes mellitus and progressive renal insufficiency with nephrotic proteinuria were retrospectively analysed. Renal biopsy was performed to assess suspected diabetic nephropathy and evaluate the possible coexistence of another glomerulopathy. Light microscopy (haematoxylin-eosin, PAS stain, Masson's trichrome, silver methenamine), immunofluorescence, and electron microscopy studies were conducted for a conclusive diagnosis.
Results: Case #1: A 42-year-old male with insulin-requiring type 2 diabetes mellitus and subnephrotic proteinuria progressing to nephrotic range, with generalized oedema. Biopsy showed findings consistent with MGN and class IV diabetic nephropathy.
Case #2: A 64-year-old male with type 2 diabetes mellitus, hypertension, dyslipidemia, and nephrotic-range proteinuria with renal deterioration. Biopsy confirmed MGN and class IIb diabetic nephropathy.
Case #3: A 69-year-old male with type 2 diabetes mellitus, hyperuricemia, and benign prostatic hyperplasia. Persistent subnephrotic proteinuria without evidence of diabetic retinopathy. Biopsy identified MGN and class I diabetic nephropathy.
Conclusion: These cases emphasize the importance of renal biopsy in diabetic patients with significant proteinuria and atypical features. The coexistence of MGN and diabetic nephropathy highlights the complexity of differential diagnosis. The identification of other glomerulopathies in diabetic patients allows for more targeted and specific treatments. It is crucial to evaluate nephrotic proteinuria in patients without diabetic retinopathy and with unusual clinical findings, avoiding the assumption that diabetic nephropathy is the sole cause of renal impairment.

E-PS-17-011
Relationship between clinico-biological parameters, histological semi-quantitative scores and T lymphocyte subsets in lupus nephritis
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Background & Objectives: Renal biopsy, the gold standard for lupus nephritis (LN) diagnosis, allows classification and assessment of disease activity and chronicity status. Our study focuses on the relationship between clinico-biological and histological characteristics in LN, aiming for better disease course prediction.
Methods: We analysed 53 LN cases confirmed by renal biopsy, classified as class II (2 cases), III (4 cases), IV (19 cases), V (22 cases), and VI (6 cases). Clinico-biological parameters were collected and rSLEDAI was calculated. Histological assessment used semi-quantitative scores for renal corpuscle (RC_S) and tubulo-interstitial component (TI_S). T lymphocyte subsets were immunohistochemically marked and counted. Data were statistically analysed.
Results: Among LN classes, statistical analysis showed significant differences in clinico-biological parameters (serum creatinine, eGFR [CKD-EPI], serum C3 complement, triglycerides) and semi-quantitative scores (RC_S, TI_S) (ANOVA test). We found: a significant, positive, moderate correlation between RC_S and rSLEDAI, but no significant correlation between TI_S and rSLEDAI (Pearson's correlation); no significant relationships between RC_S and TI_S, respectively, and CD4+ T lymphocyte counts (global, intraglomerular, periglomerular, and interstitial) (Spearman's correlation); a significant, positive, strong correlation between RC_S and total and interstitial CD8+ T lymphocytes, and a moderate correlation with periglomerular and intraglomerular ones (Spearman's correlation); a significant, positive, moderate correlation between TI_S and CD8+ lymphocytes in all considered areas (total, intraglomerular, periglomerular, and interstitial) (Spearman's correlation).
Conclusion: The correlative analysis of clinico-biological parameters, paraclinical and morphological indexes of activity and chronicity and T lymphocyte subsets supports the variability among LN classes. The intensity of glomerular and interstitial changes is influenced by CD4+ and CD8+ T lymphocytes, which act in the pathogenic mechanism of LN. Disease course is directly related to the severity of histological lesions. Refining clinico-pathological criteria for disease staging allows for better prognostic assessment and optimal treatment decisions.

E-PS-17-012
Role of endocapillary, extracapillary and interstitial inflammatory cells in development of IgA nephropathy
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Background & Objectives: IgA nephropathy (IgAN) is the most common glomerulonephritis worldwide and there are a lot of mechanisms that drive progression. The aim of our study is to investigate endocapillary, extracapillary and interstitial inflammatory cells in development of IgAN.
Methods: We investigated 39 patients with IgAN and compared the composition of inflammatory cells in the crescents, endocapillary loops and interstitium using immunohistochemistry markers against T-lymphocytes, macrophages and dendritic cells. The correlation between the number of different cells and location and patient clinicopathological data were evaluated.
Results: Immunohistochemistry analyses demonstrated that predominant cellular type in three locations were CD68+macrophages, followed by CD8+ and CD4+T-lymphocytes (18.4+/-4.2 vs. 6.8+/-3.8 vs. 4.1+/-2.1 cells/mm^2, respectively). Cases with high endocapillary infiltration with CD68+macrophages had higher infiltration with CD68+ and CD83+cells in the crescents (χ^2=7.63, p=0.044). In addition, the infiltration with CD68+macrophages and CD83+dendritic cells were higher in patients with class IV compared to class III and V (by Haas classification) (χ^2=1.29, p=0.002). Finally, CD8+T-lymphocytes in interstitium were correlated with the level of erythrocyturia and proteinuria.
Conclusion: Our results suggest the relationships between different inflammatory cells and their localizations are "key factor" involved in development of IgAN and could be strong predictor of disease progression.

Funding: 1) This research was funded by the Bulgarian Ministry of Education and Science (MES) in the frames of the Bulgarian National Recovery and Resilience Plan, Component "Innovative Bulgaria", Project No. BG-RRP-2.004-0006-C02, "Development of research and innovation at Trakia University in service of health and sustainable well-being". 2) This research was funded by the Medical Faculty, Trakia University-Stara Zagora, Bulgaria, under Project No. 4/2023

E-PS-17-014
Analysis of Serum Amyloid P component (SAP) and Apolipoprotein E (ApoE) expression in renal AL amyloidosis
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Background & Objectives: Our previous study has identified that AL-kappa (AL-κ) presents with higher serum creatinine and includes

a higher subset of cases with PAS-positive amyloid deposits (1). The serum amyloid P component (SAP) and Apolipoprotein E (ApoE) are signature proteins in all types of amyloidosis. This study aims to evaluate differences in the immunohistochemical expression of amyloid-associated proteins (SAP and ApoE) between AL-κ and AL-lambda (AL-λ).
Methods: Kidney biopsies previously diagnosed as AL-κ or AL-λ amyloidosis were retrospectively reviewed. Cases were selected from a prior study and included only those with at least four open glomeruli and adequate tissue for immunohistochemical staining. PAS staining status was recorded, and immunostaining for ApoE and SAP was performed. Glomerular staining was evaluated using a semiquantitative scale from 0 to 3+.
Results: A total of 85 cases were analysed: 16 AL-κ and 69 AL-λ. PAS-positive amyloid was identified in 50.0% of AL-κ cases and 18.8% of AL-λ cases. ApoE positivity was observed in 81.3% of AL-κ and 98.6% of AL-λ cases, with a statistically significant difference ($p = 0.022$). SAP positivity was noted in 75.0% of AL-κ and 79.7% of AL-λ cases ($p = 0.94$). When comparing PAS-positive and PAS-negative groups across both types, no significant differences were found in ApoE ($p = 0.45$) or SAP ($p = 1.00$) expression.
Conclusion: ApoE and SAP are frequently expressed in glomerular deposits of both AL-κ and AL-λ amyloidosis. While ApoE staining is significantly more frequent in AL-λ, PAS staining status does not correlate with differential expression of ApoE or SAP. We speculate that peptide ApoE interact more with λ than κ light chain. However, further studies including mass spectrometry are needed to better understand the underlying mechanisms contributing to the differences in ApoE and SAP expression between AL-κ and AL-λ amyloidosis.

Reference: https://doi.org/10.1093/ajcp/aqad017

E-PS-17-015
Histopathological evaluation in *post-mortem* renal biopsies of patients with COVID-19 and comorbidities: a case-control study
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Background & Objectives: Among the main systemic complications of severe cases of COVID-19, there is acute kidney injury. The objective of this study is to describe the histopathological changes in *post-mortem* kidney biopsies from patients who died as a result of the disease caused by SARS-CoV-2. These changes were evaluated through a case-control study conducted in a tertiary hospital in Brazil.
Methods: The study group, called 'COVID', consisted of kidney biopsy samples obtained from deceased patients with COVID-19, with a "Control" group included for comparison. The samples were selected based on sex, age and similar comorbidities, with emphasis on diabetes mellitus (DM) and systemic arterial hypertension (SAH). The morphological evaluation was carried out by pathologists using pre-established criteria, with glomerular, tubulointerstitial and vascular characteristics among the parameters.
Results: Tubular atrophy and interstitial fibrosis, markers of chronic kidney injury, were observed with equal frequency in both groups, probably due to the initial pairing of the samples. Regarding DM, the findings mentioned are in line with what would be expected from chronic exposure to hyperglicemia. In relation to SAH, the main identification was vascular damage, particularly arteriolosclerosis/arteriosclerosis. Acute tubular injury was the most observed feature in patients in the COVID group, probably related to ischemic damage.
Conclusion: The research demonstrated that the main change identified in the renal parenchyma of patients with COVID-19 is acute tubular injury, a fact expected considering the context of severe systemic ischemia to which these patients are subjected, with the other findings being consequences of chronic damage, mainly due to systemic diseases such as DM and SAH.

E-PS-17-016
SARS-CoV-2 infection could act as a trigger for TMA in patients with an underlying complement defect. Case report
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Background & Objectives: TMA is an endothelial lesion present in a wide range of serious diseases with very different aetiologies, manifested by microangiopathic haemolytic anaemia, thrombocytopenia and renal and neurological symptoms.
A 25-year-old woman was admitted with TMA and acute kidney injury (AKI), suggestive of atypical haemolytic uremic syndrome (aHUS). Early treatment with ravulizumab was initiated.
Methods: During follow-up, the patient's renal function persisted, with urinary abnormalities (Alb/CrCl ratio 536 mg/g, microhematuria), C3 consumption, and undetectable haptoglobin levels despite continuing ravulizumab therapy.
Results: Renal biopsy (RB) was performed. 29 glomeruli were found, 3 of which were sclerosed without crescents and frequent membrane ruptures. Presented a very mild proliferative component at the mesangial level, global and fairly diffuse endotheliosis with areas of mesangiolysis and microaneurysms, and occasional microthrombi. Immunofluorescence was negative for all antiserums. Ultrastructurally, exhibited intense endothelial degeneration without deposits. Diagnosis was glomerular and arteriolar thrombotic microangiopathy with acute and chronic findings in a well-preserved renal parenchyma. Genetic study was performed, revealing a pathogenic variant of complement factor H (CFH), preventing the expression of factor H (FH) proteins, in addition to risk polymorphisms for aHUS in the monocyte chemoattractant protein (MCP) gene.
Conclusion: Hypotheses have been developed that propose that "two triggers" are required for the development of aHUS, such as the combination of genetic background and a triggering factor. In our case, the patient meets both criteria since she presents a genetic factor, such as the presence of a genetic mutation that inactivates the gene encoding CFH, preventing the expression of FH proteins, and risk polymorphisms for aHUS in the MCP gene; and a triggering factor, such as COVID infection. There is data in the literature that supports the theory that SARS-CoV-2 infection could act as a trigger for TMA in patients with an underlying complement defect, although the mechanism that causes it is unknown.

E-PS-17-017
Subpopulations of T cells in acute cellular rejection of kidney transplant - pilot study
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Background & Objectives: The interstitium of a healthy kidney contains scattered mononuclear cells. In acute T-cell mediated rejection

(ATCMR) following kidney transplantation, the interstitium becomes oedematous and infiltrated with lymphocytes, creating a site of intense cellular immune activity. Regulatory FoxP3+ T lymphocytes may play a role in moderating the inflammatory response, potentially exerting an anti-inflammatory effect. We aimed to investigate if the immune response in ATCMR depends on CD4/CD8 ratio and the presence of the FoxP3 regulatory lymphocytes, and if there was influence on graft survival.

Methods: Kidney transplant biopsies were analysed from 25 patients, with a median time from transplantation to biopsy of 3 months. The biopsies were immunohistochemically stained for CD4, CD8, and FoxP3. T cell counts were quantified relative to the cortex area.

Results: The median age of patients was 55 years, with creatinine levels of 147.0 µmol/L at biopsy and 125.5 µmol/L one year later. Graft function was maintained in 91.3% of patients, while 2 patients (8.7%) died. The median CD4/mm² was 81.11, CD8/mm² was 49.34, and the CD4/CD8 ratio was 1.86. FoxP3+ cells were found in 2 patients (8%). Patients with graft dysfunction were 20 years older and had higher creatinine levels at biopsy compared to those with normal graft function (p=0.049). Those with graft loss had nearly double the number of CD4 cells. FoxP3-positive patients had higher creatinine levels one year later (p=0.044). A positive correlation was found between age and the CD4/CD8 ratio (ρ=0.560, p=0.004), and between CD4 and CD8/mm² (ρ=0.608, p=0.001).

Conclusion: Our findings suggest that CD4-mediated immunity is more prevalent in older patients, potentially increasing their risk of graft dysfunction. The findings regarding FoxP3 cells differ from the limited literature, which suggests better outcomes in FoxP3 infiltrated samples, emphasizing the need for further, more comprehensive investigations.

E-PS-17-018

C3-dominant glomerulonephritis with membranoproliferative pattern secondary to chronic Q

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Background & Objectives: Membranoproliferative glomerulonephritis is a pattern of glomerular injury on light microscopy characterized by proliferative endocapillary lesions in glomerulos tuft and double contour of the glomerular basement membrane. The classification of MPGN is pathophysiology-based and dependent on immunofluorescence staining.

Methods: We present a case of a 62-year-old man with progressive kidney dysfunction, haematuria, and proteinuria. His medical history consist of chronic kidney disease, hypertension, and a biological aortic prosthesis complicated by infectious endocarditis due to Cardiobacterium hominis, diagnosed and treated with antibiotics 2.5 years previously. Additionally, he was diagnosed with chronic Q fever one month before referral to Nephrology department, and he started doxycycline therapy at that time.

Results: A renal biopsy revealed hypersegmented glomeruli with mild to moderate expansion of the mesangial matrix, slight mesangial cellularity increase, and marked endocapillary hypercellularity, mainly from mononuclear cells. Silver staining showed double segmental contours in the basement membrane, interspersed with oedema and rare mononuclear cells. Two glomeruli exhibited capillary wall lysis, fibrinoid necrosis, and cellular crescents. Tubules and interstitium showed mild degenerative and reactive changes. Arterioles and arteries demonstrated mild hyalinosis and fibroplasia, without vasculitis.

Immunofluorescence revealed dominant granular and pseudolinear deposits in the capillary wall and mesangium for C3 (++++),with some deposits of IgM, C1q, and light chains kappa and lambda. Immunohistochemical testing for C4d was positive. It was assumed a C3-dominant glomerulonephritis with a membranoproliferative pattern, secondary to chronic Q fever.

The patient started immunosuppressive therapy while continuing antibiotics. His renal function stabilized, and immunosuppressive treatment was gradually reduced.

Conclusion: Q fever, caused by Coxiella burnetii, can rarely progress to chronicity specially in patients with cardiac anomalies or prosthetic devices. There are only a few reported cases of Q fever in which patients developed glomerulonephritis and even rarer cases a membranoproliferative glomerulonephritis.

E-PS-17-019

The intensity of glomerular C3 deposition predicts IgA nephropathy progression

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Background & Objectives: IgA nephropathy (IgAN) is the most common primary glomerulonephritis, with a variable course, leading to end-stage renal disease in 20-40% of patients within 20 years.

KDIGO emphasizes the role of complement activation in IgAN progression. Despite well-documented histological deposition, clinical correlations remain limited. We assessed the prognostic value of C3 deposit intensity in initial IgAN biopsies at our centre.

Methods: We retrospectively analysed biopsy-proven IgAN cases (1998–2018) with at least 5 years of follow-up. A Pathologist and Nephrologist reviewed biopsies per Oxford criteria. C3 deposition was semi-quantitatively scored (1+, 2+, 3+) by a blinded Pathologist using immunofluorescence.

Results: Of 108 patients, 103 (95%) had C3 deposition and were categorized by intensity: mild (1+, n=46), moderate (2+, n=34), and high (3+, n=23). No significant differences were found in eGFR, proteinuria, or MEST-C score. However, renal survival was significantly shorter in the high-intensity group (10 years) than in the moderate (16 years) and mild (23 years) groups (Log-Rank test, p=0.029).

In a multivariate logistic regression model adjusted for clinical (age, eGFR, 24h proteinuria) and histological variables (C3 groups, MEST-C components E, S, T, and C), predictors of RRT included lower eGFR at T0 (p<0.001), high-intensity C3 deposition (p=0.006), and MEST component E (p=0.034). Cox regression showed a higher risk of RRT in patients with high-intensity deposits vs. mild (HR 2.93, 95% CI: 1.075–4.808, p=0.028). Lower eGFR at T0 (HR=0.971, 95% CI: 0.957–0.978, p<0.001) and endocapillary hypercellularity (HR=2.909, 95% CI: 1.068–6.384, p=0.012) were also independent predictors of earlier RRT initiation.

Conclusion: Our study highlights the prognostic importance of C3 deposition intensity in IgAN. High-intensity deposits were significantly associated with an increased risk of progression to RRT, which could serve as a biomarker for risk stratification and targeted therapies.

E-PS-17-020

Unmasking the unexpected: incidental discovery of renal cell carcinoma in a transplant biopsy for rejection

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Background & Objectives: Renal transplant-associated malignancies are rare; their development is most often a consequence of immunosuppression, and they pose a diagnostic challenge by overlapping with allograft pathology. We present a 46-year-old female transplant recipient whose renal biopsy, performed for clinical allograft dysfunction, revealed an incidental malignancy.
Methods: A renal biopsy was performed due to allograft dysfunction. The specimen was processed for light microscopy using routine and special staining (H&E, PAS, trichrome, methenamine silver) and immunofluorescence (anti-Cd4). Microscopic examination for allograft dysfunction focused on glomerular, tubular, interstitial, and vascular changes according to Banff 2022 criteria. Immunohistochemical markers (CK7, CD10, CD117, vimentin and AMACR) were employed for accurately diagnose origin and histological tumour type.
Results: Histopathological examination showed: chronic active T-cell mediated rejection grade 1B, based on the following Banff lesion scores: 3 for total inflammation (ti), 2 for inflammation in area of interstitial fibrosis and tubular atrophy (i-IFTA), and 3 for tubulitis (t), associated to I-IFTA, based on Banff lesion score 3 for tubular atrophy (ct). Additionally, a small patch (less than half of the width of biopsy) of epithelial tumour proliferation was incidentally discovered, exhibiting a histological pattern suggestive of clear cell renal cell carcinoma. The unexpected neoplastic component was further evaluated by immunohistochemistry, revealing intense CK7 and vimentin positivity; CD10, CD117 and AMACR negativity. This atypical profile supported the diagnosis of clear cell papillary renal cell tumour (ICD-O: 8323/1), considered as borderline malignancy.
Conclusion: This case is unique due to incidental discovery of a rare tumour type in a check-up renal allograft biopsy. Tumour size was extremely small, and imaging indicated the absence of any proliferative changes of renal parenchyma. Knowledge on tumour indolent behaviour influenced the patient's decision to keep the functional allograft. In the last 6 months, she underwent regular clinical and imaging monitoring, associated with immunosuppression adjustment – maintaining stable general condition.

E-PS-17-021
LECT2 amyloidosis: a diagnostic challenge – a four-case series with bone marrow involvement in one patient
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Background & Objectives: LECT2 (leukocyte cell-derived chemotaxine-2) amyloidosis is a rare and often underdiagnosed subtype of amyloidosis that usually presents with renal-limited disease. This case series highlights four renal biopsy-confirmed cases of LECT2 amyloidosis, including one with extrarenal involvement and accompanying monoclonal gammopathy.
Methods: Four renal biopsies diagnosed as LECT2 amyloidosis between 2022 and 2024 were retrospectively reviewed. Immunohistochemical and immunofluorescence studies were performed to characterize amyloid deposits. Clinical and laboratory data were retrieved when available.
Results: Three male patients (aged 70, 54, and 48) were referred from external centres with no available clinical information. All showed amyloid deposition in the glomerular mesangium, arteriolar walls, and interstitium, with exclusive LECT2 positivity on immunohistochemistry. No staining was observed for AA, kappa, lambda, transthyretin, gelsolin, or β2-microglobulin.
The fourth case was a 65-year-old woman with no known comorbidities, presenting with nephrotic-range proteinuria (4471 mg/day). Her renal function tests were normal. Kidney biopsy revealed diffuse amyloid deposition in the kidney parenchyma which was positive for LECT2 by immunohistochemistry. However, immunofluorescence showed a lambda monotypic light chain restriction. Subsequent bone marrow biopsy was also characterized by lambda-restricted monotypic plasma cell proliferation and, notably, diffuse LECT2 deposition in the vascular walls. Bone marrow remission was achieved with six cycles of Daratumumab plus CyBorD therapy, however, proteinuria persisted at 2340 mg/day.
Conclusion: Although often considered renal-limited, LECT2 amyloidosis may involve other organs, as demonstrated by vascular LECT2 deposition in the bone marrow of one of our patients. The presence of monoclonal gammopathy may lead to misclassification of the disease as AL amyloidosis and interferes with the correct diagnosis. Accurate subtyping through detailed immunophenotyping is essential to ensure appropriate management and avoid unnecessary treatment.

E-PS-17-022
A case of Monoclonal immunoglobulin disease (MIDD) versus proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID) with overlapping features on renal biopsy
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Background & Objectives: Monoclonal immunoglobulin disease (MIDD) and proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID) are uncommon diseases with deposition of monoclonal immunoglobulins in the glomeruli.
Methods: We describe a 55-year-old female who presented with nephrotic syndrome and microscopic haematuria and impaired renal function.
Results: On presentation; urine PCR was 1052mg/mmol with serum albumin of 20g/L. Serum Creatinine was 137umol/L. There was no paraprotein or elevation of serum free light chains. Anti-PLA2R, ANA, anti-GBM, ANCA, FR, cryoglobulins, HBS antigen, HbC antibody, HIV were negative. Kidney biopsy showed a membranoproliferative pattern of glomerulonephritis on light microscopy. Immunoperoxidase staining showed mesangial and capillary wall IgG, C3 and C1q without IgA and IgM. Kappa and Lambda were not interpretable due to background staining. Immunofluorescence of paraffin sections after protease digestion showed strong capillary wall and mesangial IgG, C3, C1q and kappa with weak segmental capillary wall IgA, IgM and Lambda. electron microscopy showed subendothelial linear as well as conventional deposits and mesangial deposits. No substructure was noted. No extra-glomerular deposits were seen. An immune complex mediated membranoproliferative pattern of glomerulonephritis with IgG kappa restriction was diagnosed with the differential diagnosis of PGNMID and MIDD. Haematological investigations did not identify a paraprotein or a plasma cell clone. The patient is responding well to high dose steroids.
Conclusion: There is clinical and morphologic overlap between PGNMID and MIDD. The presentation with nephrotic syndrome is common to both. This case had powdery electron dense deposits characteristic of MIDD along with conventional deposits more often seen in PGNMID. Extraglomerular deposits which are more common in MIDD were not seen. The absence of a identifiable clone is more common in PGNMID. Thorough evaluation of renal biopsy with light, immunofluorescence and electron microscopy is essential for diagnosis. Immunofluorescence of paraffin sections after protease digestion is an invaluable salvage technique to demonstrate clonality of deposits.

E-PS-18 E-Posters Neuropathology

E-PS-18-001
The experience of the Mohammed VI University Hospital of Marrakech in the detection of the methylation status of the O6-methylguanine-DNA methyltransferase gene in IDH wild-type glioblastomas by methylation-specific qPCR: about twenty-two cases
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Background & Objectives: Gliomas are classified according to the fifth edition of the World Health Classification in 4 grades (1 to 4). Now, they are classified by site as well as by histological and molecular characteristics. IDH wild-type glioblastoma was considered the most aggressive glioma and is classified as grade 4 according to WHO 2021. The objective of this work is to report the experience of the Mohammed VI University Hospital in Marrakech in detecting the methylation status of the O6-methylguanine-DNA methyltransferase (MGMT) gene promoter in IDH-wild-type glioblastomas with observation of the expression of IDH1, ATRX and P53 by immunohistochemistry.
Methods: Our study involved twenty-two formalin-fixed, paraffin-embedded (FFPE) tissue blocks, the immunohistochemical study of which led to the diagnosis of glioblastoma. We examined the methylation status of the MGMT gene promoter using a specific real-time methylation PCR technique (MS-qPCR).
Results: All studied cases presented wild-type form of IDH1, loss of ATRX expression was recorded in eleven samples. In ten cases, the mutated form of p53 was expressed. The level of p53 expression varied from intense (>80% of tumour cells) to weak (<10% of tumour cells), and a staining less than 10% was considered non-mutated.
In our study, when analysing the methylation profiles of the MGMT gene promoter, we found that nine cases, presented positive methylation with a methylation rate that varies between 0.184% and 27% with a hypermethylation threshold is greater than 0.1%.
Conclusion: This study identifies MGMT promoter methylation in nine cases with positive result out of twenty-two cases of wild-type IDH glioblastomas, with the observation of the expression profile of three proteins (IDH1, ATRX and p53) by immunohistochemistry. Our study is the first in Morocco, but it should be extended to large prospective studies to confirm the results and draw definitive conclusions to suggest potential targets and appropriate therapeutic strategies.

E-PS-18-002
Diagnostic trap - primary mesenchymal intracranial chondrosarcoma
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Background & Objectives: Primary intracranial mesenchymal chondrosarcoma (PIMC) is an exceedingly rare tumour, accounting for 0.1-0.15% of all intracranial tumours. Due to its clinical behaviour, imaging appearance, localisation, and even histopathological features, it can closely resemble the much more common meningioma.
Methods: We present the case of a 35-year-old male patient who presented with cephalalgia, right hemianopsia, and seizures, progressively worsening over several months. Seven months earlier, the patient underwent surgery for a right posterior fossa (RPF) compressive mass, which was diagnosed as an atypical meningioma by a secondary centre. On current presentation, CT imaging revealed an expansive lesion in the RPF with bilateral extension and significant contrast enhancement, raising suspicion of recurrence. Emergency surgery was performed.
Results: Macroscopic examination revealed multiple pink, fleshy fragments with a soft consistency. Microscopic analysis showed an intensely vascularized mesenchymal proliferation composed of large and medium-sized, primitive-appearing, uninucleated, monomorphous cells arranged in sheets. Frequent typical mitoses, calcifications, and vascular spaces were noted within the tumour. Foci of chondroid transition were observed, with cells separated by an amorphous basophilic substance. Immunohistochemistry showed positivity for Ki67 (60%), OLIG2, S100 (in chondroid foci), CD99, NKX2.2, and SOX9. Tumour cells were negative for GFAP, Synaptophysin, IDH1, and ERG. These features support a diagnosis of primary mesenchymal intracranial chondrosarcoma.
Conclusion: PIMC is a rare and aggressive tumour that mimics the characteristics of meningioma, presenting a significant diagnostic challenge. Close attention and immunohistochemistry are essential in distinguishing this entity from more common diagnoses in order to avoid significant diagnostic pitfalls.

E-PS-18-003
Rare anatomical locations of Pleomorphic Xanthoastrocytoma: a report of two cases
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Background & Objectives: Pleomorphic xanthoastrocytoma (PXA) is a rare tumour of the central nervous with glial origin. It commonly occurs in young patients and it is most frequently located supratentorially, particularly in the temporal lobe.
Methods: We report two cases of PXA with unusual tumour locations, affecting a paediatric and an adult pacient.
Results: Case 1: A 4-year-old girl presented with right-sided hemiparesis as the initial symptom. Brain magnetic resonance imaging (MRI) revealed a tumour in the left parieto-occipital region, measuring 77 mm, with hyperintensity on T2-weighted images and hypointensity on T 1. Imaging showed that the tumour exerted a compressive effect on the ipsilateral lateral ventricle (LV), causing compensatory dilation of the right LV and a 7 mm midline shift to the right.
Case 2: A 59-year-old man presented with motor deficits in the lower limb as the initial symptom. MRI described an intradural, intramedullary lesion spanning a cranio-caudal segment of 33 mm, corresponding to the vertebral bodies C4-C6, with an teroposterior diameter of 11.5 mm at the C5 level, showing hyperintensity on T2.
In both cases, complete surgical resection was performed. Histopathologic examination revealed characteristics of World Health Organisation (WHO) grade pleomorphic xanthoastrocytoma, No necrosis or mitotic activity were detected. Immunohistochemical findings supported the diagnosis.
Conclusion: These cases illustrate PXA with parieto-occipital and cervical spinal cord locations, which are rare, with very few cases reported in the literature. The severe clinical presentation in both cases highlights the atypical nature of these tumour locations and the significant neurological impact they can have, despite their WHO grade 2 histological characteristics.

E-PS-18-004
Mature teratoma of the conus medullaris: a rare entity in an uncommon location
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Background & Objectives: Teratomas are tumours of germ cell or dysembryogenic origin, arising from aberrant tissue that includes elements from the ectoderm, mesoderm, and endoderm. They most

commonly occur in gonadal regions, as well as in the sacrococcygeal and mediastinal areas. Spinal teratomas are extremely rare, and those affecting the conus medullaris are particularly uncommon, usually seen in children. Sporadic cases in adults require heightened clinical vigilance due to their potential for neurological impairment and impact on quality of life.
Methods: A 37-year-old patient with no significant medical history presented with vesicosphincter disturbances, characterized by urinary retention, but without motor or sensory deficits. Magnetic resonance imaging (MRI) revealed an intramedullary lesion at the T12-L1 level, appearing hyperintense on both T1- and T2-weighted sequences. Based on these findings, surgical resection was performed. Intraoperatively, the lesion was observed to be adherent to the conus medullaris and an adjacent nerve root.
Results: Gross examination revealed a cystic mass containing a viscous, yellowish fluid. Histologically, the tumour demonstrated a heterogeneous composition of mature tissues, including adipose tissue, respiratory epithelium, acinar structures, squamous epithelium, and glial tissue with reactive gliosis, along with focal calcifications. No immature or malignant components were identified. The diagnosis of mature teratoma was confirmed.
Postoperatively, the patient experienced significant improvement in lumbosciatica; however, sphincter dysfunction persisted, requiring ongoing rehabilitative therapy.
Conclusion: Although rare, conus medullaris teratomas can affect patients across various age groups and lead to progressive neurological symptoms. Histopathological examination confirms the diagnosis. The benign nature of these lesions generally confers a good prognosis following complete surgical excision with tumour-free margins. Nonetheless, long-term follow-up is essential to monitor for potential recurrence, particularly in cases where immature or malignant components may be present.

E-PS-18-005
The unexpected evolution of an unusual polyphenotypic cerebral tumour
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Background & Objectives: The fifth edition of the WHO Classification of Tumours of the CNS introduces major changes that emphasize the importance of integrated molecular studies into definitive diagnosis. However, some cases fail to be classified even when proper and extensive testing is performed.
Methods: We present the case of a 52 y.o. patient, who presented with a five-month history of dizziness. Imaging revealed a fronto-temporal nodular mass which was initially resected and diagnosed. After recurrence one year later, it was also resected and submitted to the pathology laboratory for histological examination, immunohistochemisty and molecular studies.
Results: Histological examination of the first lesion revealed a well-circumscribed, non-infiltrating tumour composed of a mixture of spindled and epithelioid cells with gland-like structures and necrosis. Immunohistochemistry reveals a polyphenotypic pattern, with positivity for glial markers (GFAP and Olig2) and epithelial markers (Cytokeratin AE1/AE3, CK7 and CK20). The overall histologic and molecular findings did not differentiate between poorly differentiated well-circumscribed, high grade glial tumour and metastatic carcinoma of unknown origin. The recurrent lesion showed an infiltrating hypercellular proliferation composed of moderately-to-severely atypical cells, with positivity for GFAP and Olig2. Some well-demarcated foci of epithelioid and monster cells were also present and showed focal loss of GFAP and Olig2. Cytokeratin AE1/AE3 was negative. The overall findings were consistent with a glioblastoma with an epithelioid component, and we concluded that the prior lesion was in fact a high-grade glial tumour with unexpected immunohistochemical findings.
Conclusion: Despite adequate pathological workup, the tumour could not be initially classified within a standard WHO diagnosis. Even though the sharp demarcation, the presence of atypical epithelioid cells and the aberrant expression of specific epithelial markers such as CK7 and CK20 suggest at first a metastasis, the diagnosis of a glial tumour should be retained.

E-PS-18-006
Diagnostic challenges in pseudotumoral infections of the central nervous system
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Background & Objectives: Some central nervous system (CNS) infections pose significant diagnostic challenges due to their diverse clinical presentations and radiological mimics. Many cases are incidentally diagnosed following surgical intervention for presumed neoplastic lesions. This study aims to present the clinicopathological characteristics of various infectious CNS lesions diagnosed in our pathology department.
Methods: We conducted a retrospective study of 27 cases of infectious CNS lesions diagnosed between 2005 and 2024.
All cases underwent surgical resection or biopsy, followed by histopathological examination using H&E staining.
Special stains such as PAS, and Grocott were applied when necessary.
Results: Patients ranged in age from 3 to 75 years, with a mean age of 34,8 years and with a male-to-female sex ratio of 1.25.
Fifteen patients were from rural area.
The most common presenting symptoms included headaches, focal neurological deficits, visual disturbances, and signs of intracranial hypertension. Radiological imaging frequently suggested tumoral processes, with lesions mimicking gliomas, meningiomas, or other expansive intracranial masses. Cystic lesions (n=8) were predominantly seen in hydatidosis cases, whereas abscess-like (n=4) formations were more characteristic of amebiasis and other fungal infections.
Histopathological examination confirmed the diagnosis in all cases. Tuberculosis cases (n=9) exhibited epithelioid granulomas with central caseous necrosis. Hydatidosis cases (n=10) demonstrated characteristic laminated eosinophilic membranes with daughter cysts containing protoscolices. Amebiasis cases (n=4) showed necrotizing inflammation with trophozoites in tissue sections. Fungal infections, including aspergillosis (n=1), mucormycosis (n=1), and phaeohyphomycosis (n=1), displayed angioinvasion and tissue necrosis.
The single case of actinomycosis showed suppuration and granulomatous inflammation surrounding actinomycotic granules.
Conclusion: CNS infectious lesions remain a formidable diagnostic challenge, often mimicking neoplasms and leading to delayed diagnosis. This case series underscores the importance of integrating histological, special stain, and molecular findings to ensure accurate diagnosis. Recognizing these infections, particularly in endemic regions, is crucial for appropriate management.

E-PS-18-008
Cystic glioblastoma multiforme mimicking neurocysticercosis: a rare presentation in Indian subcontinents
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Background & Objectives: Cystic glioblastoma multiforme (GBM) is a rare disease. Cystic GBM may mimic Neurocysticercosis (NCC) & other cystic benign lesions of CNS thereby causing diagnostic dilemma. Differential diagnosis of cystic brain lesion includes parasitic

lesions (e.g. NCC, echinococcosis), benign CNS neoplasms and less likely GBM, tuberculosis, fungal infections, and benign cystic lesions (epidermoid cyst, simple cyst). Cystic GBM have better prognosis.
Methods: 38 yrs. male with history of headache and intermittent fever for 13 days. CT scan revealed two peripherally enhancing lesion in right fronto-partial region and left frontal region with features and mass effect suggesting the possibility of parasitic lesion Neurocysticercosis (NCC). CSF & serological tests were negative for NCC. Bilateral frontal craniotomy with excision of SOL was done dueto mass effect. Preoperatively thin membranous cystic SOL filled with yellowish black fluid was found. Cyst wall was adherent and cleavage plane was present cyst and brain parenchyma, confirming the diagnosis of Neurocysticercosis. Total excision of both cysts was done &sent for HPE.
Results: Histopathology showed large cyst &lining of the cyst wall showed inflammation and oedema. Glial tissue bordering cyst lining showed anaplastic astrocytic tumour cellular pleomorphism, multinucleated giant cells, angectatic blood vessels, focal necrosis with cellular palisading thereby confirming the diagnosis of cystic glioblastoma multiforme.The patient was then put on radiotherapy and has received 2 cycles of radiotherapy since then.
Conclusion: Neurocysticercosis is a common parasitosis of CNS in endemic areas. In our case cystic multiple lesions without any solid component suggested the possibility of Neurocysticercosis however serological tests and CSF were negative for NCC. Histopathology played an important role in confirming the diagnosis of cystic GBM. To conclude, Cystic GBM should be kept as differential while evaluating cystic lesions of brain as it may mimic some common benign lesions. Cystic GBM have better prognosis and survival as compared to classical GBM.

E-PS-18-009
Cauda equina's neuroendocrine tumour: a series of 3 cases
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Background & Objectives: Cauda Equina Neuroendocrine Tumour (CENET) is a rare, low-grade intradural spinal tumour typically attached to the filum terminale. It presents with non-specific symptoms like back pain and radiculopathy and MRI can help in diagnosis. In this study, we included present three cases of this rare entity from our institution.
Methods: Available blocks and glass slides were retrieved from the archives for reevaluation and additional immunohistochemical applications.
Results: Patient 1 is a 37 year old woman who presented with lower back pain, right foot weakness, and numbness. Patient 2 is a 45 year old man who presented with a 1.5-month history of radiating pain from the right hip to the calf with no other neurological deficits. Patient 3 is a 71 year old man who had a five-year history of arm pain and radiating pain from the left hip to the lateral thigh and knee. All lesions appeared hypointense on both T1- and T2-weighted imaging. Histopathological examination revealed tumoral cells forming a nest pattern within a prominent vascular framework, surrounded by spindle-shaped sustentacular cells. The tumour cells were characterized by abundant eosinophilic cytoplasm, well-defined nuclear contours, and salt-and-pepper chromatin typical of chief cells. No cellular atypia or necrosis was observed. The tumour cells exhibited a low proliferative index, with mitotic counts of 1, 0, and 4 per 10 HPF, respectively. The tumour exhibited patchy PanCK positivity, with paranuclear dot-like staining observed in Patient 1. EMA, GFAP, GATA3 and PHOX2B were negative. S100 was positive in sustentacular cells, and both chromogranin and synaptophysin showed positivity in chief cells.
All three cases underwent resection and the prognosis was favourable with no recurrence.
Conclusion: Despite its favourable prognosis, CENET is often clinically indistinguishable from other spinal tumours and requires careful histopathological evaluation for accurate diagnosis.

E-PS-18-010
Neuropathology on AI models: how reliable can it be in generating differential diagnoses from stroke histopathology slides
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Background & Objectives: Accurate diagnosis of stroke-related neuropathological changes, particularly hypoxic-ischemic injury, remains a cornerstone of neuropathology. With the emergence of artificial intelligence (AI) language models, there is increasing interest in evaluating their potential to assist in neuropathological assessments. This study investigates the reliability of various ChatGPT models in generating differential diagnoses based on a histopathology slide of acute neuronal injury from stroke.
Methods: A histopathology slide demonstrating hypoxic-ischemic injury with characteristic "red neurons" in the hippocampus was selected from the University of Utah WebPath database (https://webpath.med.utah.edu/CNSHTML/CNS048.html). Five different ChatGPT models (GPT-4, GPT-4o, GPT-4o mini, GPT-3 mini, GPT-3 mini-High) were presented with the same prompt: "Based on what you see on this pathology slide, give three possible differential diagnoses and point to the most likely one." The AI-generated responses were analysed for diagnostic accuracy, reasoning, and alignment with the known pathology.
Results: The ground truth diagnosis was hypoxic-ischemic injury, an early-stage neuropathological hallmark of stroke. However, only GPT-4o included hypoxic-ischemic encephalopathy as a differential diagnosis, while the majority of models—particularly GPT-3 mini and GPT-3 mini-High—prioritized Creutzfeldt-Jakob Disease (CJD) due to their interpretation of spongiform changes. GPT-4 suggested reactive gliosis and neoplastic processes (astrocytoma, meningioma) as possible diagnoses, demonstrating variability in diagnostic reasoning across models. None of the AI models definitively identified stroke-related hypoxic injury as the most likely diagnosis.
Conclusion: OpenAI specifies that its different model variants excel in distinct task domains (e.g., reasoning, summarization), yet their performance in neuropathological differential diagnosis of stroke pathology remains inconsistent. This study highlights both the potential and current limitations of AI models in assisting neuropathological evaluations, particularly for cerebrovascular events. Further refinement and domain-specific training are essential to enhance AI reliability in neuropathology.

E-PS-18-011
Meningiomas: analysis of a series of 78 cases at the pathological anatomy department of the Mohammed VI University Hospital of Marrakech
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Background & Objectives: Meningiomas are the most common primary tumour of the central nervous system, arising from the arachnoid cap cells associated with the dura mater or choroid plexus , a ccounting for37,6%% of all CNS tumours. The aim of this work is to report the

experience of the Mohammed VI University Hospital in meningeal tumours.
Methods: We report a retrospective study of a series of 78 cases of meningioma diagnosed in oure stablishment between January 2014 and December2024
Results: There were 32men and 37women, one of who was diagnosed on an autopsy. The age of our patients varied between 44 and 91years. Most patients reported non-specific clinical signs such as headaches and seizures. All patients underwent brain imaging, the appearance of which was in favour of a meningioma located at the level of the cerebral convexity in 60 cases,at the level of the base of the skull in17cases and one case at the level of the optic nerve. The histolopathological and immunohistochemical study showed 75 cases of grade 1 meningioma according to WHO 2021 and distributed as follows: meningothelial in 45cases, transitional 16 cases,fibrous subtype in 11cases, psamomatous in 3 cases and 3 case of atypical grade2meningioma.
Conclusion: Meningioma are among the most common adult brain tumours whose prognosis depends on the extent of resection and histopathological grade. They must be classified according to the WHO 2021 recommendations taking into account histopathological criteria in grade1,2,3

E-PS-18-013
Astrocytoma, IDH-mutant with primitive neuronal component
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Background & Objectives: Astrocytoma, IDH-mutant is the most common primary brain tumour in young adults, with peak incidence between the ages of 30 and 40. This genetically defined tumour is morphologically characterized by diffuse infiltration with fibrillary astrocytic, gemistocytic, or oligodendroglial differentiation. Only rarely does it exhibit a primitive neuronal component (PNET), which we aim to describe.
Methods: Our cohort was established through a nationwide search of pathology archives for diffuse gliomas with PNET differentiation. Only cases (n=18) with confirmed IDH mutation by immunohistochemistry or sequencing were included in the study. Formalin-fixed, paraffin-embedded tumour tissue samples were macrodissected, and each PNET and glial component was analysed using immunohistochemistry, next-generation sequencing, and methylation profiling.
Results: The cases in our study predominantly exhibited dual glial and embryonal morphology, while only a few demonstrated pure PNET differentiation. The PNET component showed reduced GFAP expression and expressed at least one neuronal marker, typically synaptophysin. A subset of cases displayed true large-cell/anaplastic features and cell wrapping. Furthermore, the PNET component exhibited a distinct epigenetic signature from the glial component and selectively harboured MYCN amplification and RB1 alterations.
Conclusion: All studied cases were high-grade tumours, characterized by a high total number of copy number variations, with MYCN amplification and RB1 loss being common features. These findings highlight the distinct molecular and epigenetic characteristics of the PNET component compared to the glial counterpart.

Funding: This work was supported by Czech Health Research Council (NW25-03-00131) and Masaryk University (MUNI/A/1621/2024)

E-PS-18-014
Molecular study of macrophage activity in wall of intracranial aneurysms: results of a pilot study
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Background & Objectives: Our team previously identified changes in quantity and subtype ratio of macrophages in walls of ruptured and unruptured intracranial aneurysms (IA), however, their role in process of aneurysm formation and rupture remains unclear. Therefore, we studied RNA expression of genes involved in the process of extracellular matrix remodelling.
Methods: Walls of neurosurgically resected IAs (both ruptured and unruptured) were formalin-fixed and paraffin embedded. We used circle of Willis arteries from cadavers as control samples and processed them with formalin-fixation and paraffin embedding. RNA was isolated from paraffin blocks. Gene expression of *CD163, MMP2,* and *TIMP1* was measured by quantitative real-time PCR and relative gene expression was calculated using *B2M* housekeeping gene expression as a reference. Statistical significance was calculated using t-test.
Results: A total of 16 IA samples (unruptured $n = 10$, ruptured $n = 6$) and 7 control samples were included in the study. Relative expression of *CD163*, *MMP2,* and *TIMP1* genes was significantly higher in aneurysm walls compared to control samples ($p < 0.001$). Relative expression of *CD163* was significantly higher ($p = 0.029$) in ruptured IAs compared to unruptured ones. Relative expression of *MMP2* was significantly lower ($p = 0.008$) in ruptured IAs compared to unruptured ones. The difference in *TIMP1* expression between ruptured and unruptured IAs was not statistically significant ($p = 0.232$).
Conclusion: The presented pilot study confirms that macrophage count and matrix metalloproteinase expression in aneurysm walls are higher than in normal vessel walls. We found that expression of matrix metalloproteinase *MMP2* was higher in unruptured aneurysms compared to ruptured ones, which is in contradiction to our expectations of its role in aneurysm rupture.

Funding: Supported by grant NU22-08-00124

E-PS-18-015

Progressive Multifocal Leukoencephalopathy: a case series of four patients with diverse clinical presentations

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Background & Objectives: Progressive Multifocal Leukoencephalopathy (PML) is a deadly demyelinating disease of CNS commonly related to immunosurpression. This study presents the histopathological findings of four patients with distinct clinical backgrounds.
Methods: Slides were reevaluated and additional IHC was performed.
Results: Patient-1, 61-year-old female with a history of goiter and Sjögren, presented with numbness in her arm that progressed to paralysis. Imaging revealed a mass in the right frontal lobe
Patient-2, a 60-year-old male with no previous complaints, presented with disorientation to time and place. Imaging revealed a contrast-enhancing lesion at the left temporo-occipital junction, extending into lateral ventricle.
Patient-3**,** 36-year-old female, presented with dizziness. Twenty days later, she developed speech delay and impaired balance. Imaging revealed multiple subcortical hyperintense lesions in the left part of pons, left temporal, right parietal, and left frontal regions.
Patient-4, a 40-year-old woman, developed speech difficulties and tremor. Lesions were identified in the right frontal and parietal regions. She has been under follow-up for Neuro-Behcet. JC-virus reactivation was attributed to adalimumab therapy.
For all four patients, the CSF analyses were inconclusive
All histopathological examinations revealed a brain parenchyme severely damaged by infiltration rich in macrophages, lymphoplasmacytic cells and few Creutzfeldt cells. Background neuropil damage and scattered large atypical glial cells with prominent nucleoli were present. Intranuclear viral inclusions with darker nuclear contours with central, ground-glass type amphophilic pattern were seen in both the infiltrated areas and surrounding cells resembling oligodendroglia. SV40 was diffusely positive**.** CD68 was positive in macrophages. IDH-1 mutation and ATRX loss was not observed. P53 expression was increased in the atypical nuclei and inclusions. The Ki-67 was high, reflecting increased lymphoid activity and proliferation. Diagnosis of PML was established in all patients.
Conclusion: Variable aetiology and clinical presentation of PML along with possible inconclusive CSF analyses, suggest that the diagnostic yield of biopsy can outweigh its invasiveness.

E-PS-18-016

Assessment of primary tumour and metastatic focus in gynaecological tumours that spread to the central nervous system

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Background & Objectives: Nearly half of female mortality are caused by gynaecological tumours, particularly cervical cancer, in conjunction with breast cancer. Brain metastases are quite uncommon in women, despite the fact that gynaecological tumours are rather common. The development of metastases always results in death. Although many metastatic foci respond well to treatment, brain metastases do not.
Methods: Ten patients who had surgery for gynaecological tumours at our centre between 2010 and 2023 had samples taken of the central nervous system in the years that followed. A review that included histopathological data and other prognostic factors was carried out in addition to demographic data.
Results: The average age of our patients was 52.6±6.7 years. The most prevalent primary tumour diagnosis was ovarian(n=6, 60%), and the most frequent ovarian tumour was serous carcinoma(n=4, 66. 7%). Primary tumours of the endometrium, cervix, and vagina were also identified. The average size of the primary tumours was 51.5±44.7 mm. In terms of tumour necrosis rates for primary tumours, the lowest value was 0%, while the highest was 80%. The average duration of metastasis for primary tumours was 52±53.6 months. While the majority of metastasis localisation occurred on the right side(n=6, 60%), half of the cases were found in the frontal lobe. The largest recorded size of the metastatic deposit was 39.8±14.7 mm, and most of them were unifocal(n=7, 70%). The rate of necrosis in metastatic foci was comparable and slightly elevated. The predominant pattern of metastasis was infiltrative (n=8, 80%). The mean overall survival was 68.7±66 months.
Conclusion: In the realm of brain metastases, median survival is generally short, often lasting only months. This study assessed the distinction between primary tumours and brain metastases. In future studies, our goal is to improve our understanding of the differences between the primary tumour and the metastatic site.

E-PS-18-018

Detection of genetic alterations via molecular cytogenetic analyses in a case series of paediatric glioma patients: a pilot study

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Background & Objectives: Gliomas represent the most common central nervous system tumours in children, presenting diagnostic and therapeutic challenges due to their molecular heterogeneity. The identification of molecular biomarkers is crucial to improve diagnosis, predict treatment responses, and develop new therapeutic strategies, especially in low- and middle-income countries. This study evaluated the most frequent molecular alterations in a cohort of paediatric patients diagnosed between 2016 and 2020 at a referral hospital.
Methods: Tissue samples from 50 children who were diagnosed with glioma between 2016 and 2020 and treated at HOMI-Fundación Hospital Pediátrico La Misericordia, Bogotá, Colombia were analysed via tissue microarrays and fluorescence in situ hybridization (FISH). We evaluated tumours for the presence of *KIAA1549::BRAF* fusion, *CDKN2A* deletion, *EGFR* and *N-MYC* amplification, and 1p/19q codeletion. The expression of H3K27me3 was evaluated via immunohistochemistry.
Results: The mean patient age at diagnosis was 8.05 years; 54% were females, 44% had high-grade gliomas, and 56% had low-grade gliomas. Genetic alterations were detected in 18% of the tumours, the most frequent being the *KIAA1549::BRAF* fusion (12%), of which 80% were diagnosed with pilocytic astrocytoma. A significant relationship was observed between infratentorial location and fusion, although no significant correlation was found between survival and the presence of fusion, a trend towards decreased mortality was observed in this group. Alterations in the expression of H3K27me3 (8%), alterations in *EGFR* (4%), homozygous deletion of *CDKN2A*

(2%) and heterozygous loss of 1p (2%) were detected. There was no amplification of N-MYC in any tumour.
Conclusion: Despite the relatively small sample size, the findings are consistent with the literature; despite the economic limitations to apply the WHO 2021 criteria, the methodology employed offers an affordable and accurate approach. These results highlight the need for comprehensive biomarker analysis to improve diagnostics, personalized treatments, and develop new therapies.

E-PS-18-019
Diagnostic value of the immunohistochemical marker H3K27Me in identifying midline low-grade gliomas with unfavourable prognosis
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Background & Objectives: The H3K27M mutation is a crucial pathogenetic event in the development of diffuse midline glioma (DMG), which is classified as high-grade glioma (HGG). Rarely DMG may have morphology consistent with low-grade glioma (LGG). However, the H3K27M mutation has also been described in rare cases of midline pilocytic astrocytoma (PA) and ganglioglioma, leading to their unfavourable behaviour. Therefore, extremely important to identify patients with midline LGG with a potential unfavourable prognosis before molecular study.
Methods: Allele-specific PCR identified the H3F3A p.Lys28Met mutation in five cases of LGG with midline localization. In three cases, the following diagnoses were initially established: PA (n=2), LGG (n=1), diffuse LGG (n=1). In one case the diagnosis of DMG was suspected based on the loss of H3K27Me expression by immunohistochemistry (IHC). Retrospective IHC analysis for H3K27Me was subsequently performed in the other four cases.
Results: The study included 4 girls and 1 boy (aged 3.11 to 15.2y., median 12.1y.). In all cases there were midline tumour localization: medulla oblongata/pons (n=2), thalamus, basal nuclei (n=3). Histology revealed hypo- (n=3) or moderately (n=2) cellular neoplasm, with monomorphic ovoid cells with finely dispersed nuclear chromatin and scant eosinophilic cytoplasm among eosinophilic fibrillary matrix. There were no mitosis, necrosis and endothelial proliferation. In three cases, tumour was well-circumscribed. In two cases, it had diffuse growth, which was confirmed by NF-staining. The Ki-67 proliferation index varied from 1 to 5%. IHC with H3K27Me showed total loss of expression in two cases and mosaic expression in three cases. The median follow-up was 2.1 y. (range: 1.2 – 4.6y.). One patient died (follow-up 4.6y), four - alive, three of which receive palliative treatment.
Conclusion: IHC staining with H3K27Me is highly recommended for all patients with low-grade midline glioma to identify unfavourable LGG which biologically correspond to DMG.

E-PS-18-020
Atypical meningiomas: a clinicopathological study of 30 cases
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Background & Objectives: Atypical meningiomas (AM) represent 25 % of all meningiomas and correspond to grade 2 meningiomas in the 2021 WHO classification of central nervous system tumours. We aimed to investigate the clinical and pathological features of AM.
Methods: This is a retrospective study of 30 cases of AM recorded at the department of pathology of the university hospital of Sfax in Tunisia during a period of 16 years (2009-2024).
Results: The mean age was 51.7 years (30-73 years). Men were mostly affected (sex ratio = 1.3). Symptomatology was dominated by headaches and intracranial hypertension syndrome. Only one case was the result of progression of grade 1 meningioma; all other cases were de novo. The most frequent localization was the frontal lobe (53.3%), followed by the parietal, temporal and occipital lobes (16.6%, 13.6% and 12.2% of cases respectively). One case involved the olfactory nerve. Histologically, cellularity was often high (73% of cases). High mitotic index (>4 mitoses/10CFG) and necrosis were observed in 57.6% and 53.8% respectively. Cerebral invasion was present in 30%. Ki67 index (achieved in 8 cases) was greater than 10% in 3 cases. Partial removal was observed in 20% of cases. The course was marked by recurrence in 30% of cases. No transformation to grade 3 was observed.
Conclusion: AM occur de novo or as a result of the progression of grade 1 meningiomas (30% of cases). They are distinguished by a high recurrence rate (30% to 50%) and a more aggressive progression compared to grade 1 meningiomas. The main prognostic factor for recurrence remains the quality of surgical resection; the recurrence rate is lower in case of complete resection than partial resection. The other histoprognostic factors correlated with high relapse are the high mitotic index, high Ki67 index (>10%), and cerebral invasion, which stratifies patients who are candidates for adjuvant therapy.

E-PS-18-021
IDH-mutant gliomas: Is 1p/19q Co-deletion essential in canonical oligodendroglial phenotype?
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Background & Objectives: Oligodendrogliomas are molecularly characterized by combined *Isocitrate Dehydrogenase* (*IDH*) mutation and co-deletion of chromosome arms 1p and 19q (1p/19q codeletion). This study aims to determine the frequency and utility of 1p/19q co-deletion in IDH-mutant gliomas with classical oligodendroglial morphology.
Methods: This is a retrospective observational study of IDH-mutant gliomas Data was retrieved from the Electronic medical record and molecular pathology database over six years (2017-2022).
Results: Of the total 1276 *IDH*-mutant gliomas, 502 were of classical oligodendroglial morphology (IDH1R132H, IDH2R172K, IDH2R172W and IDH2172M), 591 were of astrocytic morphology and 183 were of admixed morphology. 331(65.94%) oligodendroglial tumours were evaluated for 1p/19q FISH, 13.6% (n=45) were uninterpretable. 278 (83.99%) cases showed 1p/19q co-deletion, molecular results while 2.4% (n=8) did not show co-deleted status. 46(25.1%) cases with admixed morphology were evaluated for 1p19q co-deletion, 20 (43.5%) were codeletion (none of which showed ATRX protein loss of expression). Of total astrocytic (n=591) cases, 11(1.8%) cases showed ATRX protein expression and were evaluated for 1p/19q FISH, one (9.1%) showed 1p/19q codeletion.
IDH-mutant, 1p/19q codeleted oligodendrogliomas were more common in older patients (41-65 years). A male predominance and

supratentorial involvement were noted. IDH1 mutation was more common (95.22%) than IDH2(4.78%). None showed p53 protein immunoexpression like TP53 mutant phenotype. None of the non-oligodendroglial tumours showed IDH2 mutations.
Conclusion: IDH-mutant diffuse glioma with classical oligodendroglial morphology and retained ATRX protein expression are invariably 1p19q co-deleted; while the astrocytic morphology and retained ATRX expression rarely show 1p19q co-deletion. However, cases with admixed morphology with IDH-mutation and retained ATRX expression do not show any consistent pattern. These findings shows a little incremental utility of additional FISH evaluation for1p19q co-deletion in IDH-mutant gliomas with classical oligodendroglioma, especially in real world scenario.

E-PS-18-022
Histopathological spectrum of neurenteric cysts: a report of two cases
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Background & Objectives: Neurenteric cysts (NC) are rare, non-neoplastic developmental lesions caused by incomplete resorption of the neurenteric canal, a temporary connection between the yolk sac and amniotic cavity during early embryogenesis. These lesions commonly present during late childhood or early adulthood, with the spinal canal being their most common location. This study aims to analyse cases from our centre, focusing on imaging characteristics, histopathological features, and clinical follow-up.
Methods: After diagnosing the latest case in our centre, records from 2015 to 2024 were reviewed, resulting in two cases of NC. Clinical data and follow-up information were retrieved from the patients' electronic medical records.
Results: We report two cases of symptomatic NC, both belonging to male patients. The first case involves an 8-year-old child with a 25 millimeters cystic expansive lesion in the medulla oblongata. Histologically, the cyst was lined by a single simple columnar and cubical epithelium, rich in mucin-producing cells with some goblet cells, without atypia. The second case involves a 47-year-old adult with progressive paresthesias and a well-circumscribed intramedullary cystic lesion with a solid component in C4-C5 of 16 millimeters. Histologically, the cyst exhibited a lining of a non-atypical pseudostratified, ciliated columnar epithelium, poor in mucin-producing cells. Cyst fluid composition analysis was not performed.
Conclusion: Our observation reveals the histological variability of NC, ranging from simple columnar to pseudostratified ciliated epithelium, with varying mucin production. This spectrum highlights the critical importance of meticulous histopathological examination in differentiating NC from other cystic spinal lesions.

E-PS-18-023
The implications of the updated WHO classification of CNS tumours on paediatric brain tumours diagnosis. A South African perspective
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Background & Objectives: Primary Central Nervous System (CNS) tumours are the most common solid tumours in children. Their prognosis mostly relies on the age at presentation, histological classification and molecular characteristics.
The objective of this study was to present the prevalence and histological subtypes of paediatric brain tumours and address the implications of the latest WHO classification of CNS tumours.
Methods: A retrospective and descriptive study of cases diagnosed with CNS paediatric tumours between 2012 and 2021. The laboratory information system provided the clinicopathological characteristic data. Histological diagnoses were reviewed using the 2021 WHO Classification of tumours of the CNS.
Results: A total of 73 cases were recorded, with a mean age of 7 years, and a male predominance. Supratentorial tumours were prevalent (n=35, 48%) compared to infratentorial tumours (n=27, 37%), while the rest were unclassified. As per the WHO classification, gliomas, glioneuronal tumours, and neuronal tumours were the predominant category (n=25, 32.4%), followed by embryonal tumours (n=17, 23.3%), while choroid plexus tumours and other CNS embryonal tumours were the least prevalent (n=3, 4.1% each). The predominant tumour type was medulloblastoma (n=17, 23.3%), which was also the most prevalent malignant tumour. The most prevalent benign tumour was pilocytic astrocytoma (n= 12, 16.7%).
Conclusion: The study established baseline data for paediatric CNS tumours in our centre and Pretoria, crucial for developing guidelines for effective treatment. It will also accelerate the implementation of molecular studies in South Africa, enabling best practices in management according to the latest WHO classification of CNS tumours.

E-PS-18-024
Abnormal vimentin and histone H3 p.K27me3 immunohistochemical expression patterns as potential surrogate markers for 1p/19q-codeletion in adult-type diffuse gliomas
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Background & Objectives: Oligodendrogliomas and astrocytomas are diffuse-type gliomas of adulthood with overlapping molecular and histological features. The presence of *IDH* mutation is an essential diagnostic criterion for both. 1p/19q-codeletion is used to differentiate between these tumours. Molecular tests are generally less accessible and more expensive with a longer turn-around time compared to immunohistochemical tests. The aim was to determine if vimentin and histone H3 p.K27me3 (H3me3) immunohistochemical stains can be used as surrogate markers instead of 1p/19q-codeletion to differentiate between oligodendrogliomas and astrocytomas and to examine the correlation between these markers and different histological parameters.
Methods: Totally, 43 tissue blocks from adult patients with *IDH*-mutant diffuse gliomas from the Department of Pathology, University of Debrecen were analysed in this study. Cases were categorized into two cohorts based on 1p/19q-codeletion status: oligodendrogliomas (25 cases) and astrocytomas (18 cases). Vimentin (clone: V9) and histone H3 p.K27me3 (clone: EPR18607) immunohistochemical stains were performed according to the manufacturing instructions. The percentage of positive tumour cells for H3me3 and percentage of positive tumour area for vimentin were then estimated. Vimentin and H3me3 expression were correlated with 1p/19q status and conventional histological parameters including plexiform vessels, perinuclear halo, calcification, microcystic area, gemistocytic and minigemistocytic appearance, mitosis index, grade and p53 expression.
Results: The percentage of H3me3 positive tumour cells was significantly higher in astrocytomas comparing with oligodendrogliomas (mean 77.78% *vs* 13.75%, $p<0.0001$, Mann-Whitney test). The percentage of vimentin positive area was significantly larger in astrocytomas comparing with oligodendrogliomas (mean 80% *vs* 13%, $p<0.0001$, Mann-Whitney test). Loss of vimentin and H3me3 expression showed significant correlation with 1p/19q-codeletion ($p<0.0001$ for both, Fisher's exact test). Perinuclear halo, plexiform

vessels and gemistocytic morphology showed significant positive or negative correlation with both vimentin and H3me3 expression.
Conclusion: Vimentin and H3me3 immunohistochemical stains serve as potential surrogate markers for the differential diagnosis of oligodendrogliomas and astrocytomas.

E-PS-18-025
A rare *cauda equina / filum terminale* tumour: once diagnosed, expect at least 2 in a row (it can happen to you too)
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Background & Objectives: The last WHO Classification of Tumours involving CNS (2021, 5th Edition) mentions "nearly 300 cases have been reported since their initial description in 1970" for neuroendocrine tumours of the cauda equina region, formerly known as paragangliomas. We experienced and signed out this type of tumour twice in one month, November, last year.
Methods: Tissue fragments from two middle-age patients (male, 46 y-o and female, 44 y-o) with intradural extramedullar lumbar (L1-L3) mass were formaline fixed, paraffin-embedded and routinely stain. Additionaly, automated immunohistochemistry, using polymer detection system and DAB visualisation was performed.
Results: For both cases there were similar histopathological aspects: apparently encapsulated tumour proliferation, composed of trabeculae, rosettes, nests and (pseudo)papillae of relatively cohesive medium-sized, polygonal or discretely elongated neoplastic cells, showing rich, eosinophilic cytoplasm and pleomorphic nuclei: some rounded vesicular, other elongated hyperchromic, and still other with fine "salt and pepper" chromatin; mitotic activity was unidentified in the usual staining. Vascularization was rich with a network of capillaries either with "chicken-wire" or hemangiopericytic pattern, but also telangiectatic spaces filled with red blood cells. Associated: interstitial oedema, stromal hyalinization emerging from the meningeal / dural insertion.
The same similarity was found for the immune profil of the neoplastic cells: positive for panCK(AE1/AE3) as paranuclear granules and synaptophysin (diffuse and intense), negative for: GFAP, EMA, GATA3 and S100 (except for a few flattened cells at the periphery of neoplastic nests - sustentacular cells). The proliferation marker Ki67 was low: 1%, respectively 3%.
Conclusion: By fulfilling the WHO's criteria for diagnosis, we signed out the cases as cauda equina-filum terminale neuroendocrine tumour, G1 (well-differentiated). Being aware of its differences (histogenetically and molecularly) from paraganglioma outside the CNS, we informed our colleagues (neurosurgeons and oncologists) that total excision was curable, so there is no need for adjuvant therapy.

E-PS-18-026
Clinical and imaging mimic of posterior fossa' meningioma: medulloblastoma in young-to-middle of adulthood patients
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Background & Objectives: When a neurosurgeon receives a cranian MRI interpretation of a 30 - 40 years old patient, as posterior fossa mass, apparently extraaxial, with tentorium insertion, the first thought can be: meningioma. Then, the intra-operative aspects not as expected, plus the frozen-section' diagnosis signed as: "malignant, high grade, small, blue cells" definetively changed, that first thought.
Methods: Tissue fragments from 3 middle-age patients (one male, 38 y-o and two females, 32 y-o, respectively, 45 y-o) with cranian posterior fossa mass were formaline fixed, paraffin-embedded and routinely stain. Silver impregnation for reticulin and automated immunohistochemistry (with polymer detection system, DAB visualisation) were made. Further, we have submitted representative paraffin-embedded tissue for each case to second opinion (in a reference centre for CNS tumours).
Results: H&E stain suggested a malignant tumour proliferation with the histopathological characteristics of a primitive / embryonal tumour, invading the meningeal sheath and cerebellar cortex in all 3 cases. The neoplastic cells (small, blue, round-oval, relatively monotonous, discohesive) were arranged in trabeculae and nodules relatively well delimited by a desmoplastic stroma. Silver staining highlights the rich reticulin network with complete surrounding of the neoplastic nodules. Immunohistochemically, neoplastic cells in the cellular nodules are positive for synaptophysin; GFAP variable and only in the internodular / trabecular cells; proliferation marker Ki67 was positive exclusively in internodular cells ranging from 15% to 35%. All 3 cases were confirmed in the reference centre as medulloblastoma, with the expansion of immunohistochemical testing as surrogates for molecular classification (p53, YAP1, beta-catenin), more precisely: SHH-activated medulloblastoma, TP53 wild-type, G4.
Conclusion: Even is known that medulloblastomas can arise at all ages, we had to face such diagnosis involving patients in their 4th and 5th decade of life, with a misleading imaging / preoperative aspect as meningiomas. The shift of their prognosis towards sever one was accordingly.

E-PS-18-027
Mycobacterial spindle cell pseudotumor (MSP) of the spinal cord: a case report and literature review
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Background & Objectives: MSP is a rare, benign and diagnostically challenging manifestation caused by various species within the genus Mycobacterium, but most commonly by non-tuberculous mycobacteria (NTM) and affect primarily immunocompromised individuals. It causes tumour-like growths, affecting different parts of the body, but exceptionally the spinal cord, with only one case previously described in the literature.
Methods: We are reporting the only case of MSP of the spinal cord diagnosed in our hospital and describe clinical, radiological, histopathological, immunophenotypic and microbiologic features. This is a 79 year-old male from Guinea-Conakry with recently diagnosed active tuberculosis (M. tuberculosis positive tested by polymerase chain reactions (PCR) method) under treatment and history of chronic lymphocytic leukaemia diagnosed 2 years before and prostatic adenocarcinoma operated 12 years ago, with sudden legs hypoesthesia and weakness.
Results: The 7 mm D11 spinal cord mass observed in magnetic resonance imaging was resected and macroscopically showed a 1,3x0,7x0,5 cm whitish lesion with fibrous consistency. Histologic examination revealed a bland spindled and epithelioid histiocytic proliferation focally arranged in a fascicular and storiform architectural pattern, that effaced the background architecture and associated with mixed inflammatory infiltrate including lymphocytes and occasional neutrophils. Granulomas, multinucleated giant cells and caseous necrosis were absent. Immunohistochemical stains were positive for CD68 and negative for neural, epithelial, muscular and vascular markers. Acid-fast

staining shows acid-fast bacilli and the case was positive for NTM by PCR method. At the time of this work, the patient continues with the antimicrobial therapy and started a rehabilitation programme.
Conclusion: MSP is a rare benign lesion and to our knowledge, this is the second case described in the spinal cord. Its morphological pattern could mimic neoplastic lesions and represent a diagnostic challenge for pathologists unfamiliar with this lesion. Although immunostaining could be helpful, its morphology awareness will avoid confusion and will allow an accurate diagnosis and management.

E-PS-18-028
Pineal parenchymal tumours: a tunisian bicentric retrospective study
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Background & Objectives: Pineal parenchymal tumours (PPT) are a rare group of tumours originating from the pineal gland's parenchyma. These tumours pose significant diagnostic and therapeutic challenges. This study aimed to analyse the clinical, radiological, and histological features of PPT treated surgically over a 26-year period, focusing on cases from the Neurosurgery Departments of the National Institut of Neurology in Tunis and Habib Bourguiba Hospital in Sfax.
Methods: A retrospective, bicentric study was conducted, reviewing 75 cases of pineal region tumours between 1998 and 2023. Of these, 13 cases were identified as PPT. Clinical records, radiological findings (CT and MRI scans), and histological diagnoses were analysed. Histological subtypes were classified according to the World Health Organization (WHO) grading system.
Results: The study identified 13 cases of PPT, accounting for 18% of all pineal region tumours. Radiologically, CT and MRI scans showed homogeneous lesions with intense contrast enhancement, particularly in pineocytomas and intermediate-grade pineal parenchymal tumours. Histological analysis revealed four cases of pineocytoma (Grade 1), one intermediate-grade pineal parenchymal tumour (Grade 3), and eight cases of pineoblastoma (Grade 4). No cases of papillary pineal tumour or SMARCB1-mutated myxoid desmoplastic pineal tumour were found. Notably, no pleomorphic component was observed in the pineocytomas. Adjuvant treatments, including radiotherapy (38.5%) and chemotherapy (23%), were applied, with varying outcomes. Recurrence was noted in one patient with pineoblastoma.
Conclusion: This study emphasizes the clinical and histological diversity of PPT and the importance of a multidisciplinary approach to diagnosis and treatment. The findings highlight the need for personalized treatment strategies, including adjuvant therapies, to optimize patient outcomes. Further research into the molecular characteristics of PPT could offer deeper insights into their pathogenesis and management.

E-PS-18-029
Diffuse Midline Glioma, H3 K27-altered, of the pineal gland
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Background & Objectives: Diffuse midline glioma (DMG), H3 K27-altered, represents an aggressive subtype of diffuse gliomas affecting midline brain structures, developed most commonly in the brainstem, thalamus, and spinal cord. Although primarily a paediatric tumour, occurrences in adults are increasingly recognised. Its incidence is estimated to be 0.54 cases per 1 million person-years overall. High-grade features such as brisk mitotic activity, necrosis, and microvascular proliferation may be present but are not required for diagnosis, as the WHO 2021 classification assigns a grade 4 to this entity by default due to the detection of H3 K27M mutations. In this report, we present a case of DMG, H3 K27-altered, originating uncommonly from the pineal gland in a 40-year-old male.
Methods: Histopathological examination assessed the morphology of the neoplasm while immunohistochemical analyses evaluated the status of IDH 1 or 2, Histone H3.3, ATRX, Olig-2, FOXG1, Ki-67 and BRAFV600E.
Results: Microscopy revealed high-grade features. Immunohistochemistry showed GFAP and Olig2 positivity with loss of FOXG1 and ATRX expression. The H3.3 K27M mutation-specific antibody demonstrated strong nuclear positivity while the H3 K27me3 trimethylated protein was retained. Staining for H3.3 G34R, H3.3 G34V, and BRAFV600E was negative. IDH1R132H and IDH1/2 mutations were absent while Ki-67 reached up to 40%.
Conclusion: This case offers additional insight into the rare presentation of pineal-region DMG, H3 K27-altered, arising in an adult patient, expanding the limited literature beyond the paediatric population. Midline tumours represent a diverse spectrum, ranging from indolent, low-grade neoplasms to aggressive, high-grade malignancies, like DMGs which carry a poor prognosis of a 2-year survival rate of <10% independently of the anatomical area. Clear distinction from other circumscribed or diffuse midline gliomas through the detection of the H3 K27M mutation is essential. This heterogeneity highlights the critical role of biopsy and molecular profiling balancing diagnostic accuracy against the significant risks of intervening in midline structures.

E-PS-18-030
Role of IL-22 and CD163+ cells in the inflammatory microenvironment of Glioblastoma multiformae
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Background & Objectives: Glioblastoma multiformae (GBM) is one of the most aggressive tumours of the central nervous system. Current therapeutic approaches have reached low efficiency in preventing its progression and poor prognosis. The subpopulations of macrophages expressing the surface marker CD163 are pivotal cells in the inflammatory microenvironment of GBM. Additionally, IL-22 produced by several subsets of lymphocytes, has been reported as a promising new immune target in the complex molecular network of GBM and might be involved in the differention of $CD163^+$ macrophages.
Methods: A group of 41 patients diagnosed with GBM and 41 control individuals from the Bulgarian population were studied. Serum IL-22 concentration was assessed via the ELISA method. Immunohistochemistry was performed for assessing the density of $CD163^+$ cells in biopsy tissue of patients.
Results: We found that IL-22 concentration was significantly higher in patients compared to the controls with mean levels of 321.93±37.07 pg/mL and 222.74±25.65, respectively (p=0.006). In males (298.41±36.16 pg/mL) the serum levels of IL-22 were higher compared to females (244.88±28.26), p=0.131. The density of CD163+ cells in the tumour was also significantly higher in male patients compared to females (p=0.022). Regarding the clinical characteristics of GBM cases we observed increased IL-22 levels in patients with low neutrophil-to-lymphocyte ratio (NLR) (362.04±57.51) compared to patients with high NLR (275.49±43.59), p=0.040. The tumour tissue, both nest (21.11±5.97) and border (49.23±12.97), was also significantly enriched in $CD163^+$ cells in patients with low NLR, p=0.036 and p=0.012, respectively.
Conclusion: The preliminary results of our study indicate that serum IL-22 might be involved in modulating the inflammatory tumour microenvironment and could be associated with the recruitment and stimulation of CD163+ macrophages in the progression of GBM.

Funding: This research was funded by the Bulgarian Ministry of Education and Science (MES) in the frames of the Bulgarian National Recovery and Resilience Plan, Component "Innovative Bulgaria", Project No. BG-RRP-2.004-0006-C02, "Development of research and innovation at Trakia University in service of health and sustainable well-being", and by the Medical Faculty, Trakia University-Stara Zagora, Bulgaria, under Project No. 9/2023

E-PS-18-031

The association between TPT1 and paediatric astrocytomas: a study based on SNPs and immunohistochemistry evaluation

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Background & Objectives: Central nervous system tumours, including astrocytomas, are solid neoplasms with high rates of incidence and mortality in childhood. Diagnostic tools include morphological characteristics, but molecular methods have been increasingly used. Translationally controlled tumour protein (TCTP), encoded by *TPT1* gene, is a multifunctional protein which plays an important physiological role in the cell cycle. This protein has been associated with several neoplasms, including astrocytomas in adults. However, its role in paediatric astrocytomas is still unknown.

Methods: We aim to evaluate in 75 cases of paediatric astrocytomas, grades 1 (n=56) and 4 (n=19), according to the WHO classification, the frequency of three single nucleotide polymorphisms (SNP) in *TPT1* (rs1062420 [C/T], rs2234222 [T/C] and rs9595305 [T/C]), correlating it with TCTP expression, through genotyping and immunohistochemistry analyses, as well as with clinical variables.

Results: The most revealing result refers to an anatomic association. Most grade 1 astrocytomas were infratentorial whereas most grade 4 were supratentorial (p=0,006). Regarding the SNPs, results were also interesting, though not statistically relevant. As for rs1062420 [C/T], all the cases showed homozygosis or heterozygosis for T polymorphic allele, regardless of grade. Another interesting finding was that rs2234222 [G/C] showed a low incidence of C polymorphic allele (only 12% of cases, n=9). TCTP expression assessed by morphometry showed no statistic difference; grade 1 (Mean±SD 13720,24±7084,549) and grade 4 (Mean±SD 15664,03±6418,956).

Conclusion: This study sought an association between TCTP pathway and the tumorigenesis of paediatric astrocytomas. Our results reinforce the biological difference between low and high grade astrocytomas in the paediatric population. And regarding the three SNPs evaluated in this study, they do not seem to be involved in grade 1 or grade 4 astrocytomas. Further studies should be conducted for different SNPs as well as correlations with outcome, since they could still act as prognostic markers.

E-PS-18-032

P53 expression and its correlation with Ki-67 and clinical parameters in paediatric medulloblastomas from Southern Brazil

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Background & Objectives: Central nervous system tumours, including medulloblastomas, are solid neoplasms with the highest incidence and mortality rates in childhood. Medulloblastomas are aggressive WHO grade 4 tumours, diagnosed based on histopathological and molecular characteristics. Mutations in *TP53* gene are diverse, with missense mutations of single nucleotide polymorphism (SNP) being common. In southern Brazil, about two decades ago, the R337H variant was described, present in germline mutations. Establishing an association between medulloblastomas and *TP53*-R337H could provide novel insights on this neoplasm in the population of southern Brazil.

Methods: We evaluated in 48 cases of paediatric medulloblastomas, the expression of p53 through immunohistochemistry, as a potential sign of an underlying mutation, correlating it to ki67 and clinical variables.

Results: We found that regardless of histology, most cases presented normal p53 protein expression, indicating wild *TP53* (p=0,033). The lack of abnormal p53 expression indicates wild-type *TP53*, but it does not exclude underlying mutations, especially SNPs such as R337H. Regarding ki67, most classic medulloblastomas had ki67≤50%, whereas all anaplastic medulloblastomas had ki67≥75% (p=0,044). We also found a correlation between necrosis and ki67. Most cases with necrosis had ki67≥50% and most cases without necrosis had ki67≤50% (p=0,049). Seven deaths were recorded among the patients and most of them had the classic morphology. This finding was not statistically relevant. Nonetheless, it is noteworthy that most deaths had classical morphology but probably did not belong to the WNT-activated molecular group since this group usually has an excellent prognosis. Correlations with clinical parameters showed no significant results.

Conclusion: This study sought the expression of p53 through immunohistochemistry as a potential sign of *TP53* mutation. Results were negative, but associations statistically relevant between medulloblastomas, ki67 and necrosis have been made. Further studies should be conducted on the role of *TP53*-R337H mutation in medulloblastomas in the southern Brazilian population.

E-PS-18-033

Factors associated with overall survival in breast cancer patients with leptomeningeal carcinomatosis: a single institutional retrospective study

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Background & Objectives: Despite significant improvements in breast cancer (BC) treatment, the prognosis of patients with a leptomeningeal spread of tumour cells, termed as leptomeningeal carcinomatosis (LC), remains extremely poor.

This study aimed to investigate factors affecting overall survival (OS) in patients with LC related to BC.

Methods: Data analysis of our cerebral-spinal-fluid (CSF) cytology database was performed in the period between 2005 and 2021, identifying 34 patients who have undergone at least one CSF-cytology-sampling in the context of suspicion of BC-LC. Amongst them, 20 patients met diagnostic criteria for LC diagnosis (positive CSF cytology and/or neuroimaging in the presence of suggestive neurological symptoms). We used log-rank test and multivariate Cox-regression-analysis to compare patients' OS.

Results: The median age at diagnosis of LC was 49 years. Half of patients had a high-performance-status (PS) and prior or concurrent brain metastases (BM). The median OS was 5 months. In terms of management of LC, the majority of patients received a systemic treatment (ST) and a combination of at least 2 treatment modalities namely_ intrathecal treatment, ST and radiotherapy (70% and 75%, respectively).

On univariate analysis, 4 factors were associated with prolonged OS: high-PS (p=0,05), absence of BM (p=0,002), administration of ST (p=0,003), and the use of multimodal treatment (p=0,003). After multivariate analysis, we identified only 2 independent good prognostic

factors i.e. the absence of brain metastases, and the use of multimodal therapeutic approach.
Conclusion: LC represents a dreadful complication of BC, causing a drastic decline in BC patients survival rates. At this stage, median OS usually does not outreach 6 months. The results of our study confirmed that high-PS, absence of BM, use of ST, and of combined modality therapy are factors associated with prolonged OS. Only 2 factors (BM and number of treatment modalities) proved to be still prognostic after cox-regression-analysis.

E-PS-18-034
Prognostic significance of genetic biomarkers in glioblastoma IDH wild-type: a retrospective survival analysis
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Background & Objectives: Glioblastoma, IDH wild-type, is the most aggressive primary brain tumour, characterized by a poor prognosis despite standard treatments. Genetic and molecular alterations play a critical role in tumour progression and patient survival. This study investigates the association between key biomarkers (EGFR, MGMT, mTERT, CDKN2A, p53, and PTEN) and survival outcomes.
Methods: A retrospective analysis was conducted on 92 patients diagnosed with glioblastoma, IDH wild-type. Descriptive statistics and cross-tabulations were used to assess the distribution of genetic markers and their correlation with survival. Pearson's Chi-Square and Fisher's Exact Test were applied to determine statistical significance. Kaplan-Meier survival analysis was performed to evaluate overall survival.
Results: EGFR alterations were present in 31.8% of cases, while MGMT promoter methylation was detected in 61.3%. The mTERT mutation had the highest prevalence (77.3%). No statistically significant associations were found between CDKN2A loss and p53 ($p = 0.159$), MGMT ($p = 0.926$), or mTERT ($p = 0.523$). However, a significant correlation was observed between CDKN2A loss and EGFR alterations ($p = 0.039$). Survival analysis revealed that 60.9% of patients were deceased at the time of data collection, while 32.6% remained alive with disease (AWD). Poor overall survival was significantly associated with MGMT promoter methylation ($p = 0.046$, Kaplan-Meier analysis), and a trend toward worse survival was noted in patients with CDKN2A loss ($p = 0.191$).
Conclusion: Molecular alterations are highly prevalent in glioblastoma, IDH wild-type, though their impact on survival remains complex. The observed association between CDKN2A loss and EGFR alterations suggests a potential prognostic role, warranting further investigation in larger cohorts to refine therapeutic strategies.

E-PS-18-035
Epithelioid angiosarcoma of the CNS with regional loss of INI1 expression
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Background & Objectives: Epithelioid angiosarcoma can be a diagnostic challenge especially in small biopsies. We describe a case of epitheliod angiosarcoma of the central nervous system (CNS) in a patient with cerebrospinal fluid leakage and clinical history of prolonged media otitis. The tumour showed regional loss of INI1 expression, with retained INI1 positivity in other tumour areas. This has profound implications in the differential diagnosis with neoplasms with loss of SMARCB1/INI1 expression at presentation or recurrence. Furthermore as shown in this report epitheliod angiosarcoma can be included in the group of neoplasms with variable, mosaic or regional expression of SMARCB1/INI1 protein.
Methods: Mayer Haematoxylin-Eosin sections of CNS open biopsy material were stained on Ventana HE 600 platform.
Immunohistochemistry was carried out on Bond III and Ventana platforms with the following antibodies: AE1/AE3, CAM5.2, MNF116, Desmin, EMA,GFAP, HMB45, mIDH1, INI1, CD3, CD79a, CD31, Ki67, Melan A, MyoD1, Myogenin, p53, S100, SMA, SOM-R2, SOX10, VImentin, WT-1, CD34, CD45, CD99,C D117,CD68, CD138, CDK4, Chromogranin A,DOG1, ERG, MDM2, MPO, NF, OCT3/4, PAX8, SALL4, Synaptofysin, STAT6 and TLE1.
Results: The tumour cells showed positivity for CD31, ERG and Vimentin, showing only faint cytoplasmatic positivity for p53 and CD99. Ki67 index was 75% in tumour cells. Regional loss of SMARCB1/INI1 expression was observed.
Conclusion: Partial loss of INI1 protein's expression can be seen in epithelioid angiosarcoma, and further perplex the already difficult diagnostic process in small biopsies from the CNS.

E-PS-18-036
Improving glioma diagnosis in Morocco: evaluation of a competency-based neuropathology masterclass
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Background & Objectives: Adult gliomas, the most common primary tumours of the central nervous system, pose a complex diagnostic challenge, accentuated by the 2021 WHO classification integrating morphological and molecular criteria.
To evaluate the effectiveness of a competency-based neuropathology masterclass in improving the diagnostic accuracy of gliomas among Moroccan residents and pathologists.
Methods: A quasi-experimental study was conducted with 26 participants, including a pre-test, a structured masterclass (theoretical course and practical workshop with virtual slide simulation), and a post-test. Statistical analysis used the Wilcoxon signed-rank test to compare scores before and after the intervention. A satisfaction survey was also conducted.
Results: A significant improvement in diagnostic skills was observed, with mean scores increasing from 61.54% to 81.92% (gain of 20.38 points, $p = 0.0002$). The proportion of participants achieving high scores (80-100%) increased from 11% to 73%. Comparison with a control group confirmed that the improvement was attributable to the intervention. The satisfaction survey revealed a high engagement rate, with 76.9% of participants expressing strong agreement on the relevance and clarity of the training.
Conclusion: This study demonstrates the effectiveness of a neuropathology masterclass in improving the diagnostic accuracy of gliomas in Morocco. These results highlight the importance of such initiatives in harmonizing diagnostic practices and potentially improving patient care for glioma patients.
Perspectives: Extending this approach to other training modules and diversifying case studies are recommended to strengthen national neuropathological expertise.

E-PS-18-037
A case of Gerstmann-Sträussler-Scheinker disease associated with a rare mutation
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Background & Objectives: Gerstmann-Sträussler-Scheinker (GSS) disease is a rare, autosomal dominant inherited prion disorder characterized by progressive cerebellar ataxia and/or cognitive decline/dementia. Its incidence is estimated at 1-10/10^8 population. It was reported in families by Dimitz in 1913, Gerstman in 1928, and by Gerstman, Sträussler and Scheinker in 1936. The most common mutation is p.P102L. This report highlights a less common clinical presentation and a rare mutation in GSS disease.
Methods: The patient was a 54-year-old man who died after a 12-month course of rapidly progressive dementia, difficulty ambulating, and bowel and urinary incontinence. Neurological evaluation favoured corticobasal degeneration, frontotemporal dementia, and Creutzfeldt-Jakob Disease (CJD). After further workup, which included brain imaging, electroencephalography, positive 14-3-3 protein and negative RT-QuIC (Real-Time Quaking-Induced Conversion) on cerebrospinal fluid, CJD could not be definitively confirmed or excluded.
Results: A brain-only autopsy was performed due to concern for CJD. Neuropathologic evaluation showed spongiform change in many areas of gray matter and numerous large amyloid-type plaques with dense central cores. Immunohistochemistry performed by the National Prion Disease Pathology Surveillance Centre showed positivity for prion protein (PrPSc) in the plaques. Genetic testing revealed a pathogenic variant in the *PRNP* gene c.350C>T (p.A117V); the polymorphism at codon 129 in the *PRNP* gene was methionine/valine (129MV).
Conclusion: This case highlights the variability of GSS disease, particularly in presentations involving less common *PRNP* mutations such as p.A117V. While the hallmark symptoms of progressive cerebellar ataxia and cognitive decline were present, the rapid progression and prominent dementia observed underscore the influence of genetic variations on disease phenotype. The clinical overlap between GSS and CJD presents a diagnostic challenge and emphasizes the importance of neuropathologic evaluation and genetic testing in cases of dementia. Further study on rare *PRNP* mutations is needed to elucidate the impact of genetic variation on disease progression and to advance diagnostic and therapeutic approaches.

E-PS-18-038

Unravelling sarcoglycanopathies: correlations between muscle histopathology and disease severity

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Background & Objectives: Sarcoglycans are transmembrane proteins critical for muscle cell integrity. Their loss causes sarcoglynopathies, a subset of limb-girdle muscular dystrophies (LGMD) with variable phenotypes. This study describes the histopathological findings of a large cohort of sarcoglynopathies and studies the association of these findings with disease severity.
Methods: Muscle biopsy data was collected, including the sampled muscle, disease duration at biopsy (time from symptom of onset to the date of biopsy), key findings from haematoxylin-eosin (H&E) staining, and results from immunohistochemistry (IHC). Kaplan-Meier analysis was used to estimate the time to loss of ambulation. To further stratify disease severity, we calculated the 25th and 75th percentiles of ambulation loss timing.
Results: Data on 25 muscle biopsies was collected (8 LGMDR3, 8 LGMDR4, 8 LGMDR5, and 1 LGMDR6). Mean age at biopsy was 17.52 ± 11.89 years. All biopsies underwent H&E staining, while 21 patients had additional analysis using IHC. Histopathological analysis revealed varying degrees of myopathic changes, including rounded fiber atrophy, fiber size variability, increased internal nuclei, endomysial fibrosis, and fatty infiltration. Patients with severe disease who lost ambulation within eight years of disease onset exhibited moderate to severe fatty replacement, with a Spearman's correlation coefficient between severity and H&E staining of 0.51 ($p = 0.029$). In alpha patients, there was a significant reduction of IHC staining for α-sarcoglycan in severe cases ($r = 0.91$, $p = 0.03$). No significant correlation was found between β-sarcoglycan or γ-sarcoglycan IHC staining and disease severity ($p = 0.35$ and $p = 0.29$ respectively).
Conclusion: Histopathological and protein expression analyses largely mirrored clinical severity, with more pronounced fatty replacement in patients experiencing rapid loss of ambulation. Among the sarcoglycans, α-sarcoglycan reduction correlated most clearly with disease severity on immunohistochemistry, suggesting that α-sarcoglycan quantitation may serve as a relatively robust marker for disease progression.

E-PS-19 E-Posters Ophthalmic Pathology

E-PS-19-001

Clinicopathological features and prognostic factors in uveal melanoma: a retrospective analysis of 69 cases

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Background & Objectives: Uveal melanoma (UM) is the most frequent primary intraocular malignancy in adults, with histopathological features playing a crucial role in determining prognosis. This study aims to assess the clinicopathological characteristics, tumour staging, and clinical outcomes in a cohort of 69 UM cases diagnosed over 13 years.
Methods: We conducted a retrospective analysis on 69 enucleation specimens diagnosed with UM between 2012 and 2025 at the Hospital Italiano de Buenos Aires. Tumours were categorized by histological subtype, growth pattern, T stage, extrascleral invasion, lymphovascular invasion, and vascular loops. Clinical records were reviewed to assess patient outcome, including metastatic progression and survival, with follow-up data available for 55% of cases.
Results: The cohort's mean age was 58 (14–90 years), with 38 males and 31 females. Thirteen patients had glaucoma, and 11 had undergone prior brachytherapy. The most common histological subtype was mixed (61%), followed by spindle cell (17%) and epithelioid (17%). Three cases were completely necrotic, so the histological subtype could not be determined. The growth patterns included dome-shaped (48%), mushroom-shaped (32%), diffuse (3%), and others (17%). Lymphovascular invasion and vascular loops were observed in 25% and 13% of cases, respectively, and were significantly associated with poor overall survival ($p<0.05$). T stage also correlated strongly with survival ($p<<0,01$).
Among patients with available follow-up data (median 34 months), 39% developed distant metastases, with the liver being the most frequent site, followed by lungs and bones.

Conclusion: This study provides valuable insights into the clinicopathological features of UM, emphasizing the prognostic significance of T stage, lymphovascular invasion, and vascular loops. These factors were strongly associated with overall survival. Although the study is limited by the challenges of long-term follow-up in referral-based populations, the findings contribute to the understanding of UM and may help guide future risk stratification and treatment strategies.

E-PS-19-002

Recurrent adenoid cystic carcinoma of the left orbit: a case report

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Background & Objectives: Adenoid cystic carcinoma (ACC) is a rare malignant neoplasm that primarily originates in the salivary glands but also manifests in other regions, including the orbit. Orbital ACC accounts for 1% and usually originates from the lacrimal gland. Few cases have been reported without lacrimal gland involvement. ACC is known for slow growth and often poses a challenge in diagnosis due to its ability to mimic other conditions. There are many differential diagnoses for orbital masses, and distinguishing ACC from similar lesions is often difficult.
This case report aims to highlight the clinical and histopathological features of recurrent ACC of the left orbit.
Methods: We report the case of a recurrent CAK diagnosed at our department. Clinical, radiological, and histopathological data were analysed from pathology reports and the patient's medical records. The patient presented with recurrent exophthalmos a period of 4 years following the initial diagnosis and treatment.
Results: A 74-year-old male patient, with history of diabetes and hypertension, presented with left exophthalmos. An initial biopsy confirmed ACC. A subsequent resection of the tumour with clear margins was performed. Four years later, he returned with similar symptoms. An MRI revealed a 36x22mm tumour in the left extra-conal space. The patient underwent left orbital exenteration with lymph node dissection. Pathological examination revealed a tumour infiltrating the upper eyelid, iris, irido-corneal angle, posterior chamber of the left orbit, and the sclera, with numerous perineural invasions and vascular emboli. Lymph node dissection revealed the presence of a metastatic lymph node. The tumour was classified as pT3N1.
Conclusion: This case emphasizes the importance of considering ACC in the differential diagnosis of orbital masses. Recurrent exophthalmos should raise suspicion for ACC, and accurate histopathological evaluation is crucial for definitive diagnosis. Early detection and treatment of recurrence are key to managing this aggressive tumour.

E-PS-19-003

Beneath the surface: the silent rise of conjunctival melanoma from a nevus

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Background & Objectives: Conjunctival melanoma is a rare and aggressive ocular malignancy that arises from melanocytes in the conjunctival epithelium. Its incidence is rising globally, attributed to genetic, environmental, and precursor lesion-related factors. This case highlights the pathological and clinical features of a 47-year-old Caucasian male diagnosed with melanoma involving the palpebral conjunctiva, originating from a pre-existing nevus.
Methods: The patient presented to the clinic with a mass on his left lower eyelid, near the lash line, which had gradually increased in size over the past three months. The lesion had mainly caused mild irritation and a foreign body sensation in his eye. No history of eye surgeries, trauma, infections, or family background of melanoma.
Results: Upon examination, the patient displayed a pigmented lesion with irregular borders, ranging in colour from brown to black, with visible blood vessels on the surface, giving it an ulcerative appearance. Microscopically, the examined tissue revealed a malignant melanocytic tumour composed of medium to large polygonal cells with hyperchromatic, pleomorphic nuclei, some displaying prominent acidophilic nucleoli. Areas of distinctive brown pigment have been noted. These nevoid neoplastic cells, organized into nests, extended from the conjunctival epithelium into the underlying stroma, exhibiting pagetoid spread. Signs of mitotic activity and numerous apoptotic bodies further complicate the picture. Encouragingly, no lymphovascular or perineural invasion was present, indicating a less invasive case.
The presumptive diagnosis of melanoma was later confirmed through immunohistochemical analysis, which revealed strong positivity for PRAME (Preferentially expressed Antigen in Melanoma, >75%), HMB45, SOX10, Ki67 (>30%), and p16.
Conclusion: Although conjunctival melanomas are rarer than their cutaneous counterparts, it is crucial to remain vigilant for any unusual nevi in the ocular region. While this case has progressed favorably, it should not be seen as the norm, but rather as an exception to this potentially alarming condition.

E-PS-19-004

Case report: orbital myeloid sarcoma as initial presentation of Acute Myeloid Leukemia in a 13-year old patient

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Background & Objectives: Myeloid sarcoma is a rare extramedullary manifestation of acute myeloid leukaemia (AML) that can present in various anatomical locations, including the orbit. We report a case of a 13-year-old patient who initially presented with an orbital mass, which was later diagnosed as myeloid sarcoma with underlying AML.
Methods: A 13-year-old previously healthy child presented with a rapidly enlarging, painless orbital mass causing mild proptosis and swelling. There were no systemic symptoms such as fever, weight loss, or night sweats. Orbital imaging (MRI) revealed a well-defined, enhancing soft tissue mass measured 2.9x4.0x4.5 cm, involving upper and postero-lateral wall of right orbit with extension to the retrobulbar adipose tissue.
The tumour excision consists of the diffuse infiltration of medium- to large-sized atypical cells with a high nuclear-to-cytoplasmic ratio and prominent nucleoli. The tumour cells was positively stained with Myeloperoxidase, TdT, CD34, CD31. The negative stains were CD3, CD4, CD7, CD8, CD20, CD23, CD30, BCL6, CD7, LCA, PAX5, CyclinD, Langerin, Vimentin, Actin, Desmin, MioD1, Myogenin, CD1a, S100. These findings were consistent with a diagnosis of myeloid sarcoma. A bone marrow examination was not performed initially.
Results: Myeloid sarcoma is a rare and often misdiagnosed entity, particularly in paediatric patients with no prior history of leukaemia. Early recognition is crucial, as isolated myeloid sarcoma often progresses to overt AML. Standard treatment typically involves systemic AML-directed chemotherapy rather than localized therapy alone. Cytogenetic and molecular studies are essential for risk stratification and prognosis, but they were not performed in this case.
Conclusion: This case emphasizes the importance of including myeloid sarcoma in the differential diagnosis of paediatric orbital tumours. Immunohistochemical markers play a key role in distinguishing MS from other small round blue cell tumours. Early systemic workup and initiation of chemotherapy are essential to improve outcomes.

E-PS-19-005

Microcystic adnexal carcinoma of eyelid and orbit: an update and management

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Background & Objectives: Primary skin cancers include melanocytic and the vast non-melanoma skin cancer group. The former group is dominated by melanoma the latter by basal and squamous cell carcinoma. A small fraction comprises appendageal tumours also know as adenexal tumours. Malignant adnexal tumours are frequently located in the head and neck. Skin appendageal tumours do not form a single form. Microcystic adnexal carcinoma, of the overarching group of apocrine and eccrine differentiation, is very rare low-grade malignant skin tumour with a high rate of misdiagnosis and a preponderance for local recurrence but seldom nodal or distant metastasis first described by Goldstein in 1982.
Methods: A 66 year old man presented with a slow-growing asymptomatic nodule of left inferior medial eyelid and submitted to radical excision extended to bone of orbit floor and reconstructed with cadaver bone fixed by micro-crews and micro-plates. The tumour recurred three years after in lateral part of inferior eyelid. The tumour was widely excised, lateral canthus anchored to reverse temporal flap and cheek rotation/advancement flap was employed for soft tissue reconstruction.
Results: Histopathological examination showed a dermal neoplasm with infiltrative growth pattern and deep invasion of subcutaneous adipose tissue and skeletal muscle. The tumour lacked any connection to the epidermis and consisted of horn cysts. Ductal structures, nests and strand of neoplastic cells embedded in a fibrosclerotic stroma. Epithelial membrane antigen (EMA) , cytocheratin (CK), CK 15, and carcinoembryonic antigen, Ber-EP4, are helpful in histologic differentiation diagnosis.
Conclusion: Microcystic adnexal carcinoma is a rare but commonly misdiagnosed frequently recurrent malignancy which poses a significant diagnostic and treatment challenge to clinicians. Microcystic adnexal carcinoma of the eyelid and orbit requires multidisciplinary approach to diagnosis and management.

E-PS-19-006

Conjunctival squamous cell carcinoma in situ: a rare entity not to be missed

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Background & Objectives: Conjunctival squamous cell carcinoma in situ (SCC in situ) is a rare but significant pre-invasive neoplasm of the conjunctiva. It is often associated with risk factors such as excessive UV exposure and can occur in the presence of pre-existing lesions, such as pterygium. The histological diagnosis of SCC in situ can be challenging due to subtle cytological and architectural atypia, without invasion of the basement membrane.
This case highlights the diagnostic difficulties of SCC in situ in the context of an advanced pterygium and illustrates the histopathological features that are critical for accurate identification.
Methods: A 50-year-old female, followed for advanced right eye pterygium, underwent surgical resection of the affected tissue. The excised fragment was submitted for histopathological examination. The histological features were analysed using standard staining techniques.
Results: Histologically, the conjunctival epithelium was acanthotic, with architectural disorganization affecting the full height of the epithelium in some areas. Moderate cytological atypia with upper-layer mitoses were observed, but there was no invasion of the basement membrane. The underlying stroma was inflammatory. These findings were consistent with a diagnosis of SCC in situ, without evidence of stromal invasion or basement membrane breach.
Conclusion: Conjunctival SCC in situ presents a diagnostic challenge, particularly in the setting of advanced pterygium. While the absence of basement membrane invasion is a key feature, the identification of architectural and cytological abnormalities is critical for diagnosis. A precise diagnosis is essential to prevent progression to invasive carcinoma. Close correlation between histological examination and clinical presentation is crucial for proper management of such lesions.

E-PS-19-007

Histopathological findings of corneal amyloidosis

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Background & Objectives: The eye is a target organ for amyloidosis, with partial or broad compromising. Stromal corneal dystrophies (CD) are the leading group of diseases that are the source of amyloid, which can be either primary-localized or secondary corneal amyloidosis. Chronic ocular irritation, inflammation, or infection can lead to secondary localized corneal amyloidosis. The aim of the present study is to provide a histopathologic description of corneal amyloidosis in the context of the clinical diagnosis of CD in a single tertiary centre in Türkiye.
Methods: A total of 27 corneal buttons, obtained through penetrating keratoplasty from 20 adult patients diagnosed with CD between 2000 and 2025, were analysed. Congo-red stain positivity served as the primary inclusion criterion. The parameters assessed in each corneal button included epithelial and stromal characteristics, corneal thickness, and the localization, distribution, and thickness of amyloid deposits.
Results: The male-to-female ratio was 12:8, with a median age of 53±15.6 years (range: 21-83). Among the samples, 22 were naïve corneal buttons, and 5 were regrafts. The median corneal thickness was 0.6 mm (IQR: 0.39–1.90), while the median amyloid deposit thickness measured 0.1 mm (IQR: 0.01–1.10).
Linear subepithelial deposits alongside small stromal amyloid deposits were commonly observed in naïve corneal buttons. Large subepithelial amyloid deposits were prominent in regrafts. Two naïve corneal buttons exhibited keratohyalin deposits (Masson-trichrome positive), and one showed macular corneal degeneration; they all had amyloid deposits. Epithelial hyperplasia, atrophy, and stromal changes, such as cellularity, vascularization, and inflammation, varied across samples.
Conclusion: This study highlights the histopathological and clinical characteristics of corneal amyloidosis. Histopathological examination of corneal buttons from keratoplasty procedures provides valuable insights into accurate diagnosis and facilitates timely clinical management of amyloidosis.

E-PS-19-008

A rare case of primary cutaneous T-cell lymphoma mimicking eyelid carcinoma: diagnostic and therapeutic challenges

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Background & Objectives: Primary cutaneous T-cell lymphomas (CTCLs) are rare lymphoproliferative disorders, particularly when arising in the periocular region. Their clinical appearance often mimics more common eyelid malignancies such as squamous cell carcinoma

(SCC) or keratoacanthoma, making early diagnosis and management challenging.
Methods:
We present the case of a 70-year-old man with a solitary, enlarging lesion (16 mm × 16 mm) on the lower left eyelid. The initial differential diagnosis included SCC and keratoacanthoma. The lesion was surgically excised in its entirety, and the defect was reconstructed using a full-thickness skin graft.
Results: Histopathological examination unexpectedly revealed a T-cell lymphoma. Immunophenotyping confirmed a diagnosis of CD30-positive primary cutaneous T-cell lymphoproliferative disorder. Differential considerations included mycosis fungoides, primary cutaneous anaplastic large-cell lymphoma, and lymphomatoid papulosis. Staging with PET scan showed no systemic involvement or lymphadenopathy. The lesion was excised with clear margins, and no adjuvant systemic therapy was initiated. The patient remains under close surveillance in the haematology clinic, with chemotherapy reserved for any signs of recurrence.
Conclusion: This case illustrates the diagnostic complexity of rare eyelid lesions and reinforces the importance of histopathological and immunophenotypic analysis. Early recognition and multidisciplinary management are crucial for optimal outcomes in atypical CTCL presentations.

E-PS-19-009
Heterogeneity in uveal melanoma: a retrospective study about monosomy of Chromosome 3 and vascular density
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Background & Objectives: The increasingly accurate definition of parameters of prognostic significance in melanoma of the uvea represents a topical challenge. The availability of advanced therapies (among others targeting tumour neoangiogenesis) requires detailed histological evaluation of melanomas of the uvea.
Methods: From our archive (eight evaluable cases), we wanted to evaluate not only the presence or absence of Chromosome 3 monosomy (FISH analysis) in uveal melanoma cases, but also the percentage of cells with Chromosome 3 monosomy in the areas with epithelioid and spindle-shaped morphology.
We evaluated (immunohistochemistry with CD34) the maximum density of vessels and their appearance in both melanoma components.
Results: The mean vascular density (hot spot evaluation, number of vessels per HPF) is 21/HPF in the epithelioid tumour component compared to 11/HPF in the spindle-appearing component.
The morphology of the blood vessels in the areas of epithelioid appearance appears more complex with greater variability in calibre than in the spindle-shaped areas.
Of the cases evaluated for Chromosome 3 monosomy: in one third of the cases a discrepancy, within the same melanoma, was observed between the epithelioid component (with presence of monosomy) versus the spindle-shaped component (negative for monosomy).
In the remaining two-thirds of the cases studied, although there was concordance for the result of chromosome 3 monosomy (two cases with and two cases without chromosome 3 monosomy), the percentage of cells with Monosomy 3 in the epithelioid areas compared to the spindle areas was 35% to 18%.
Conclusion: Although the limited number of cases does not allow for general considerations, these data further underline the importance of tumour heterogeneity within uveal melanoma when evaluating parameters such as chromosome 3 monosomy and blood vessel density in these cases of melanoma.

E-PS-20 E-Posters Other Topics

E-PS-20-001
Insights into congophilic angiopathy: three case reports
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Background & Objectives: Cerebral amyloid angiopathy (CAA) is a cerebrovascular disorder characterized by amyloid-β (Aβ) deposition in cortical and leptomeningeal vessels, leading to intracerebral haemorrhages (ICH) and cognitive decline. Severe cases show fibrinoid necrosis, microaneurysms, vessel rupture, and perivascular gliosis. Neuroimaging often reveals white matter hyperintensities and cerebral microbleeds as severity biomarkers.
Methods: We present three cases of CAA-related ICH, illustrating clinical and pathological variability. Histology was performed with haematoxylin-eosin and Congo red staining. The severity of CAA was assessed using Greenberg and Vonsattel histopathological grading criteria.
Results: Case 1: 79-year-old female, left frontal haemorrhage on CT, no MRI. Symptoms: acute headache, vomiting. No prior amyloid pathology or dementia. Histology: vascular thickening, fibrinoid necrosis in leptomeningeal vessels (Grade 4 CAA).
Case 2: 69-year-old female, left parieto-occipital haemorrhage on CT, no MRI. Symptoms: hemiplegia, aphasia. No amyloid pathology or dementia history; on antiplatelets. Histology: vascular thickening in leptomeningeal vessels (Grade 2 CAA).
Case 3: 73-year-old male, left parietal hematoma on CT, no MRI. Symptoms: aphasia, hemiparesis. No prior amyloid pathology or dementia. Histology: vascular thickening, fibrinoid necrosis in leptomeningeal and cortical vessels (Grade 4 CAA).
Conclusion: Histological severity correlated with clinical and radiological findings, with fibrinoid necrosis and vascular thickening linked to extensive vascular involvement and severe presentations. The vessel caliber influenced haemorrhage extent and location. These cases emphasize the importance of integrating histopathology, imaging, and clinical data to refine prognosis and guide treatment. Further studies using advanced neuroimaging are warranted to better assess vascular amyloid burden, haemorrhagic risk, and cognitive decline.

E-PS-20-002
Lafora disease: a case series of a rare entity
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Background & Objectives: Lafora disease (LD) is a rare form of progressive myoclonal epilepsy of autosomal recessive inheritance, having characteristic intracellular inclusions which are referred to as Lafora bodies. Lafora bodies present in neurons and in many other cell types cause a dysfunctional activity inside the cell. This study attempts to relate together the clinical and pathological findings in three cases of LD with the importance of their making a diagnosis of LD through axillary skin biopsy.
Methods: A retrospective study was done on the clinical information and histopathological data with three patients diagnosed as LD from the clinical records at Fattouma Bourguiba University Hospital.
Results: The mean age at diagnosis was 33.7 years. All patients were female and classified as having drug-resistant progressive myoclonic

epilepsy. One patient was also found to have cerebellar ataxia and visual hallucinations, while a strong family history of LD was noted in another patient whose sibling was diagnosed with LD at the age of 40. PAS-positive small rounded intracytoplasmic inclusions (Lafora bodies) were seen with great frequency in each axillary skin biopsy from the apical cells of the sweat ducts and in myoepithelial cells surrounding the apocrine glands.
Conclusion: Lafora disease is an extremely rare form of terrible, progressive, myoclonic epilepsy caused by mutations in either EPM2A or EPM2B encoding Laforin or Malin, respectively. Despite the absence of established family history concerning LD in these patients, and obvious onset of symptoms during adolescence, this case series stresses the importance of axillary skin biopsy in early diagnosis for the patients who suffer from Lafora disease. Primarily, early diagnosis will create opportunities for genetic counselling and supportive management, which eventually would help in the optimal management of afflicted individuals, improving outcomes in this difficult disorder.

E-PS-20-003
Diagnostic and therapeutic challenges in multiple primary malignant tumours
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Background & Objectives: Advances in the diagnosis and treatment of malignancies have led to a rise in the occurrence of multiple primary neoplasms, which develop independently throughout a patient's lifetime, each with its own distinct origin and progression. This study aims to explore the relationships between different types of cancers, the prevalence of synchronous and metachronous malignant tumours, and the diagnostic and therapeutic strategies used for managing these cases.
Methods: This retrospective study analysed medical records of patients with at least two primary cancers, admitted to the Radiotherapy Department at Timisoara Municipal Hospital between 2020 and 2024. Relevant data were collected from patient histories and medical documents.
Results: The study included 51 patients (25 women, 26 men) diagnosed with two or more primary malignant tumours. The average age at diagnosis was 69 years (range: 43–87). Of the cases, 46 involved two distinct cancers, while 5 had three malignant tumours, with metachronous tumours being more common than synchronous. The most frequently affected sites were the colorectum, prostate, breast, and endometrium. Rare cases included sarcoma, salivary gland tumours, and maxillary cancers. Histopathological analysis revealed the following types: NOS, mucinous, and adenoma-like adenocarcinomas for colorectal cancers; invasive carcinoma NOS for breast cancers; endometrioid, squamous, and serous carcinoma for uterine cancers; acinar adenocarcinoma for prostate cancers. Most tumours were moderately differentiated, with some showing poor differentiation.
Treatment involved surgery, chemotherapy, hormonal therapy (for breast and prostate cancers), and radiotherapy (both curative and palliative).
Conclusion: This study underscores the elevated risk of second primary cancers, particularly among older patients who benefit from early cancer detection and effective treatments that extend their lifespan. Women often had both breast and uterine cancers, while men commonly presented with prostate and colorectal cancers. These findings highlight the critical need for continuous surveillance in cancer survivors.

E-PS-20-004
Evaluating pathology residency training in Romania: a survey-based approach
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Background & Objectives: Pathology is a specialty that requires extensive hands-on training, beyond what textbooks can provide. To gain insight into the romanian residency training experience and satisfaction, we designed a survey to evaluate key aspects of residents' professional development.
Methods: We designed two questionnaires using an online platform, SurveyMonkey, ensuring the anonymity of responses. The first was a 6-item version for first-year residents, and the second was a 19-item version for residents in years 2 to 5, with a total of 22 questions across both versions. The survey began with 3 demographic questions for all participants. First-year residents answered 3 additional questions, while residents in years 2 to 5 answered 16. The survey included 12 multiple-choice questions assessing satisfaction on a 5-point scale, 4 yes/no questions, and 3 check-box questions with options and free-text suggestions. The questionnaires were distributed via email and shared through the Romanian National Society of Pathology's (UNIPAT) official WhatsApp group.
Results: 89 responses were received, with a 91% completion rate. Of 81 completed responses, 12.35% were from first-year residents, and 87.65% from residents in years 2-5. Among first-year residents, 80% cited work-life balance and personality fit as the main reasons for choosing pathology, with other reasons including remuneration and minimal patient contact. Among residents in years 2-5, 46.47% rated training quality "acceptable". Research and academic opportunity satisfaction was low, nearly 60% finding them insufficient or unsatisfying. Despite high satisfaction with workplace colleagues, personnel, and residency coordinators, more than 70% of participants stated being unable to discuss career paths and opportunities with their supervisor, while up to 75% considered working in Romania after completing their training unlikely or improbable.
Conclusion: By identifying strengths and weaknesses in Romania's pathology residency training, this study aims to foster dialogue to enhance mentorship and programs, ensuring the healthcare system benefits from skilled pathologists.

E-PS-20-005
Multiple peritoneal adenomatoid tumours mimicking peritoneal carcinomatosis during hiatus hernia repair: a case report
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Background & Objectives: Peritoneal adenomatoid tumour (PAT) is a very rare, benign neoplasm. Adenomatoid tumour more frequently involves the uterus, Fallopian tubes and paratesticular region. Despite being considered of mesothelial origin, very few cases were reported in extragenital abdominal serosa. Multiple tumours are even rarer and raise suspicion for malignancy. We present a case in which intraoperative findings suggested peritoneal carcinomatosis, but was ultimately diagnosed as multiple peritoneal adenomatoid tumours (mPATs).
Methods: A 62-year-old female with multiple comorbidities, including hypertension and congestive cardiac failure, presented with gastrointestinal reflux disease secondary to a hiatus hernia. Surgical repair was indicated after failure of conservative management. During surgery,

several peritoneal lesions with suspicion for carcinomatosis were discovered. Abdominal and pelvic organs showed no macroscopic lesions. Excision biopsies of the lesions were sent to our department for histopathological evaluation.
Results: We received two irregular omental fragments, with velvety serosal surfaces, measuring 3.5 cm and 2.5 cm in the maximum dimensions, respectively. Serial sectioning revealed multiple well circumscribed, witish and firm nodules, the largest measuring 1.0 cm in diameter. Microscopically, the nodules consist of a neoplasm composed of uniform cuboidal cells, without pleomorphism, variably arranged in tubular, glandular, and trabecular patterns within a hyalinised stroma. No necrosis or mitotic activity was observed. Immunohistochemistry showed reactivity for calretinin, CK5, and D2-40, and lack of immunoreactivity for BerEP4, GATA-3, PAX8 or ER. Immunoreactivity for BAP1 was also preserved. Proliferative index was low (<2%). These findings were consistent with the diagnosis of mPATs.
Conclusion: This case highlights the diagnostic challenge of mPATs, which can clinically mimic peritoneal carcinomatosis. While benign, awareness of this entity is crucial for accurate diagnosis and management. Multidisciplinary discussion is recommended for rare presentations and histopathological assessment coupled with clinical surveillance is fundamental for such patients.

E-PS-20-006
Incidence of cardiac tumours in a tertiary care hospital
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Background & Objectives: Cardiac tumours are rare but have high morbi-mortality, requiring timely detection and treatment. They are classified as malignant or non-malignant, with primary tumours being mostly benign (90%), while secondary tumours are more common. Advances in molecular and imaging techniques have enhanced their detection and understanding.
Methods: Between 1997 and 2024, 53 cardiac tumours were diagnoed in our hospital: 47 primary and 6 secondary. The most common benign primary tumours were papillary fibroelastoma (35%), myxoma (30%), and lipoma (3%). In children, 4 rhabdomyomas and 1 hemangioma were found. Among malignant tumours, there were 4 sarcomas and 1 with uncertain metastatic potential.
Results: Papillary fibroelastoma was the most common benign primary tumour (40%), mainly affecting the aortic and mitral valves, with most cases being incidental. Myxoma was the second most frequent (34%), predominantly in women, mostly found in the left atrium. Cardiac lipoma accounted 4% of benign tumours, located in the left ventricular wall. In children, rhabdomyoma was the most common, diagnosed prenatally and removed without complications, while one haemangioma was found in a patient with hypoplastic left heart syndrome. Among malignant tumours, 4 sarcomas and 1 inflammatory myofibroblastic tumour were identified. The most common subtype was undifferentiated pleomorphic sarcoma. Secondary cardiac tumours included metastases from melanoma and squamous cell carcinoma, as well as cases of intramyocardial leiomyoma (associated with EBV), T-cell lymphoblastic leukaemia, peripheral T-cell lymphoma, and high-grade large B-cell lymphoma.
Conclusion: The incidence of primary cardiac tumours has increased, while biopsies for secondary tumours have declined due to advancements in multimodal imaging, reducing the need for invasive procedures. Secondary tumours indicate advanced metastatic disease with poor prognosis. Biopsies in high-risk cardiac areas pose significant risks, and metastatic tumours are often biopsied at safer sites outside the heart. As a result, metastatic cardiac tumours, though more common, are typically managed without confirmatory biopsy.

E-PS-20-007
***ALK* rearrangements is very rare in peritoneal mesothelioma**
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Background & Objectives: Peritoneal mesothelioma (PeM) is a rare malignancy with a generally poor prognosis. Anaplastic lymphoma kinase (*ALK*) alterations (activating mutations, amplifications, and fusions/rearrangements) occur in 3% of cancers, though *ALK* fusions/rearrangements are less common. There are several ongoing studies suggesting that the potential for ALK fusion as a tumour-agnostic biomarker.
Methods: In total, 46 patients with PeM were evaluated in the present study. Expression of ALK and/or rearrangement of *ALK* was evaluated by immunohistochemistry (IHC) (D5F3, Ventana) and confirmed ALK rearrangemant by fluorescence in situ hybridization (FISH) using a break-apart probe (ZytoVision)
Results: Among the 46 PeM patients, there were 25 males and 21 females, with a median age of 63,7 (range: 28–83). Histologically, 38 patients were epithelioid, 4 were biphasic and 4 were sarcomatoid subtype. Focal and weak ALK positivity was found in only one case and no ALK rearrangement was detected by FISH.
Conclusion: ALK alterations are extremely rare in PeMs and making studies in these diseases difficult.

E-PS-20-008
Well-differentiated papillary mesothelial tumour of the peritoneum in advanced age
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Background & Objectives: Benign mesothelial tumours are rarer than malignant mesotheliomas and are often found in the peritoneum as incidental findings in women. They include the adenomatoid tumour (AT), the well-differentiated mesothelial tumour (WDPMT), the mesothelioma in situ (MIS), and the solid papillary mesothelial tumour (SPMT). Well-differentiated papillary mesothelial tumour (WDPMT), formerly known as well-differentiated papillary mesothelioma, is a histologically distinctive mesothelial tumour of uncertain malignant potential found in the pleura, peritoneum, and tunica vaginalis.
Methods: We present a case of a 77-year-old Caucasian femalewith a single papillary tumour measuring 15 millimeters at the colon ascendens. The specimens were routinely stained with haematoxylin and eosin. Moreover,Periodic acid–Schiff (*PAS*) was processed. Additionally, the specimens were immunohistochemically stained with primary antibodies Pan-cytokeratin (Roche), cytokeratin 5/6 (Roche), cytokeratin 7 (Roche), cytokeratin 20 (Roche), calretinin (Roche) and KI-67 (Roche).Furthermore, immunohistochemically staining with primary antibody PAX8 (Roche) was performed.
Results: The tumour is composed of papillae with myxoid cores covered by a single layer of generally bland, flattened to cuboidal mesothelial cells. There is no evidence of invasion. Immunohistochemicalanalysis showed that the mesothelial cells expressed calretinin, Pan-cytokeratin, CK 5/6 and CK7, while no expression of CK 20 was detected.
Conclusion: Well-differentiated papillary mesothelial tumour has been included in the WHO classification of gynaecologic tumours since 2020 and in the classification ofthoracic tumours since 2021, replacing the term of well-differentiated papillary mesothelioma. We present a case of a female patient in advanced age, a 77-year-old Caucasian female with a single papillary tumour of 15 millimeters at the colon

ascendens. Due to the probable positive prognosis, no intervention is necessary, but ongoing monitoring is recommended.

E-PS-20-009

Correlation between p53 immunoexpression and *TP53* mutation status in extrapulmonary small cell neuroendocrine carcinomas and its association with patient survival

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Background & Objectives: Extrapulmonary small cell neuroendocrine carcinoma (EP-SCNC) is a rare malignancy with a poor prognosis. Despite its morphological similarity to lung small cell carcinomas, its oncogenesis remains uncertain.
Methods: One hundred and seventy-one EP-SCNC were enrolled in a multicentre study, and all tissue samples underwent an immunohistochemical p53 analysis. One hundred twenty-five samples were molecularly analysed using next-generation sequencing (NGS), comprising DNA and RNA analysis.
Results: p53 normal/wild type expression was detected in 68 cases (39.8%), whereas aberrant expression was detected in 103 cases (60.2%). Molecular *TP53* alteration was detected in 92 out of 125 tumours (73.6%). The *TP53* mutation was shown to be prognostic and associated with shorter overall survival (p=0.041). The multivariate analysis of p53 and *TP53* mutational status found that it impacted overall survival relative to distinct sites of tumour locations ($p = 0.004$ and $p = 0.001$, respectively). Age did not influenced survival in the multivariate analysis of p53 and *TP53* (p=0.002; p<0.001 resp.).
Among tumours with paired immunohistochemical and molecular results, 108 exhibited concordance between the immunohistochemical and molecular analysis, whereas 17 were discordant. Accordingly, p53 aberrant expression was tightly associated with a *TP53* mutation (p<0.001). In discordant cases, molecular analysis revealed no alteration in three tumours with p53 overexpression. In contrast, in 14 tumours with wild-type p53 expression, *TP53* genetic alteration was detected. Possible causes of discordance are discussed in this manuscript.
Furthermore, the incidence of aberrant p53 expression / *TP53* molecular alteration was noticeably lower in EP-SCNC than in small-cell lung carcinomas.
Conclusion: Therefore, in EP-SCNC, other driver mutations than *TP53* alteration should be sought since personalized therapy can improve patient prognosis.

Funding: This work was supported by the Ministry of Health of the Czech Republic and Thomayer University Hospital (FTN, 00064190), the Agency for Health Research of the Czech Republic (project NU22-03-00130), by Charles University (Cooperatio Medical Diagnostics and Basic Medical Sciences)

E-PS-20-010

Developing a risk-based standard operating procedure to streamline multidisciplinary team meeting preparation

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Background & Objectives: Increasing workload and case complexity in multidisciplinary team (MDT) meetings have outpaced resource allocation rendering the current system unsustainable. The Royal College of Pathologists (RCPath) provides best practice guidance, emphasizing the need for a proportionate, risk-based approach to case selection, tailored to local circumstances and workforce capacity.
Methods: Aim: To develop a Standard Operating Procedure (SOP) for a district general hospital to streamline MDT preparation, optimize resource allocation, and enhance reporting efficiency.
Results: Insights: The development process highlighted key challenges in implementation including stakeholder engagement, adaptation to local workflows, and balancing efficiency with clinical governance. Lessons learned are shared to inform future SOP development in similar settings.
Conclusion: The introduction of a structured SOP is expected to significantly reduce MDT preparation time, allowing for improved reporting efficiency and service sustainability. Future work will focus on embedding this model into routine practice, evaluating its long-term impact, and refining the approach based on emerging needs. Additionally, the evolving role of AI-assistance will be a critical consideration in future MDT optimization strategies.

E-PS-20-011

Ethical issues concerning the use of archived human tissue samples for research in pathology

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Background & Objectives: Human tissues collected and archived in usual clinical practice by pathology departments remain a rich and essential source of information potentially available for research. The use of pathology archived tissue samples as research specimen involves a variety of ethical concerns regarding confidentiality and autonomy, especially that informed consent is practically impossible to obtain retrospectively. Our objective is to assess the knowledge and attitude towards the use of archived human tissue samples for research in pathology among the Lebanese population.
Methods: The study was conducted at the Pathology department of Sacred-Heart Hospital in Baabda, Lebanon over a period of two months. Upon consent, hundred patients who have undergone biopsy or surgery with a pathology specimen sent to the laboratory were invited to complete anonymously a validated questionnaire made of 14 questions in total.
Results: Seventy six participants would accept and consent on the use of their tissue specimens for research, with no statistical correlation regarding gender, education, religion and age. Interestingly, 71% were not aware about the fate of their tissue specimens after the diagnosis

is issued. Almost all participants (93.4%) would want to be informed if their stored tissues were to be used for research. Reasons for refusal were evaluated and attributed mostly (45.8%) to patient's fear of research results.

Conclusion: Our study shows that almost all responders wish to be informed prior to the use of their tissue for research purpose. Therefore, our results highlight the need for drafting and establishing national laws and ethical procedures in medical pathology departments in respect to obtaining a clear informed consent and regulating the use of diagnostic specimens for future research studies and education purposes.

E-PS-20-012

The changing landscape of immunohistochemical testing using pan-cytokeratin antibodies in diagnostic histopathology. A survey of results from the UK NEQAS ICC & ISH external quality assessment programme

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Background & Objectives: Antibodies to cytokeratin (CK) proteins were amongst the first to be employed in diagnostic histopathology. Wide-spectrum (pan) CK-antibodies reactive to commonly expressed CK protein family members continue to be universally used to identify tumours of epithelial lineage to this day.

UK NEQAS has conducted external quality assessment (EQA) surveys to test the quality of pan-CK testing by immunohistochemistry (IHC) since the early 1990's. We examined the data accrued as a result to look for trends that may inform methodological choices and advance testing quality.

Methods: The most recent four EQA Runs were selected to maximise the applicability of results. Within each run primary antibody, antigen retrieval, detection and automated platform data were examined for associations with improved stain quality outcomes. Run-to-Run results were investigated for time-related trends.

Results: Four EQA Runs conducted in 2008, 2011, 2019 and 2021 were examined (span: 13 years). Number of submissions was 375, 360, 300 and 276 respectively (total: 1,311).

Overall, where information was submitted (1,246, 95.0%), 1,192 (95.7%) used one of three primarys; AE1/AE3 (654, 52.5%), MNF116 (348, 27.9%), AE1/AE3/PCK26 (190, 15.2%). Multiple other antibodies were represented in the remaining submissions (54, 4.3%) - not further described.

There was a marked change in proportional use of antibodies between 2008 and 2021; use of both AE1/AE3 and MNF116 declined from 52.5% to 44.9% and from 35.9% to 22.8% respectively, that of AE1/AE3/PCK26 increased from 5.5% to 29.3%.

Overall, the proportions of users of the three main antibodies that passed assessment were, AE1/AE3: 91.7%; AE1/AE3/PCK26: 93.3%; MNF116: 91.0%.

The proportions of participants passing at the latter two Runs was markedly higher compared to the two earlier Runs; overall 99.6% and 98.4% passed the latter and 91.0% and 87.6% the earlier pairs of Runs.

Conclusion: The quality of pan-CK testing by IHC is high and has improved over time.

E-PS-20-013

Flipped classroom: a successful method in pathology teaching

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Background & Objectives: Flipped learning is currently a focus of attention among educators worldwide. It is part of initiatives aimed at making classes less lecture-based and students more active. In Tunisia, courses at the pathology college are still taught using a passive, transmissive method. The aim of this study was to assess the impact of a flipped classroom dedicated to residents in terms of knowledge acquisition and learner satisfaction.

Methods: On June 7, 2024, a course on thyroid pathology was held, organized at the Faculty of Medicine of Tunis by the Department of Pathology B at Salah Azaiez Institute. This course utilized the flipped classroom model, along with other innovative teaching methods: group work, peer learning, mind mapping, and gamification. Three questionnaires, available online via Google Forms, were used to evaluate the learners' knowledge and satisfaction. Statistical analysis was performed using SPSS software.

Results: All the residents responded to the three questionnaires (n=30). The success rate for the nine questions after the educational intervention was 0%, 96%, 92%, 50%, 62.5%, 12.5%, 71%, 42%, and 0%, respectively. The educational intervention significantly improved the success rate of the residents on questions 2, 3, and 7 (p=0.01, 0.02, and 0.02, respectively). Ninety-five percent of the residents rated the scientific content, activities, and atmosphere as excellent. The overall rating for the course was 4.95/5.

Conclusion: In conclusion, the flipped classroom model enhances the learning experience of pathology residents by providing a framework where theoretical knowledge is reinforced through practical classroom activities, making training more effective and better suited to the demands of the field.

Thus, the future directions of this work are to expand the concept of active learning and improve the validity and reliability of assessment tests.

E-PS-20-014

Evaluation of medical students training in pathology department of Sahloul Hospital

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Background & Objectives: In medicine, combining theory and practice learning, is crucial to student training. The recent reform of medical education includes practical training in pathology.

Our objective is to evaluate the supervision of medical students in our pathology department.

Methods: This study was conducted over a period of five years (2020-2024). It is destined to the fourth-year students of Sousse medical school, as part of an optional two-week course.

During the training, students take part in the various technical stages and gross. They are then supervised by a senior who teaches them short courses analysing real-life situations . At the end of the training period, the students, working in teams, have to give oral presentations . The final assessment of the course takes the form of an Objective Structured Clinical Examination. The quality of this training was assessed by 15 questions focusing on their experience in the laboratory and the impact this had on their training.

Results: Analysis of the questionnaire showed that 95% of the students had a better understanding of pathology. Prior to this experience, 90% of them had no knowledge of the macroscopic examination or the technical stages. Furthermore, 82% of the students did not understand the importance of frozen section examination in patient management.

The senior lecturers' presentations enabled the students to apply their theoretical knowledge more effectively. The flipped classroom approach improved their communication and oral presentation skills, as well as slide presentation rules.

Overall student satisfaction was estimated at 85%. However, 30% of the students wished for more microscopy sessions.
Conclusion: Training in the pathology laboratory has improved the skills of future doctors in terms of knowledge and professional attitudes. We believe that this contribution should not be limited to small groups but should be extended to all students.

E-PS-20-015
International classification of diseases for oncology – 4: bridging cancer registry data with an evolving tumour classification
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Background & Objectives: International Classification of Diseases for Oncology(ICD-O) topography, morphology and behaviour of tumours is used by pathology registries and hospital and population-based cancer registries, for coding data critical for cancer control and research. With advances in tumour classification and definition of new entities, increasing granularity is needed in coding morphology. The fourth edition of ICD-O(ICD-O-4) aims to provide a structure of unique codes to existent and newly defined tumour entities facilitating accurate coding of data by cancer registries.
Methods: In April 2021 the IARC/WHO ICD-O Committee launched a survey questionnaire of all International Association of Cancer Registries(IACR) members to seek an opinion on updating ICD-O-3.2 by adding an extra 5th alphanumeric digit to existing four-character morphology codes, as opposed to introducing the use of International Classification of Diseases-11th(ICD-11) as a primary classification for use in cancer registries. 90%(250/276) of respondents agreed to the proposal. The beta version of ICD-O-4, including the proposed codes for tumours listed in WHO Classification of Tumours-5th edition, was developed by the IARC/WHO ICD-O Committee and published on the IARC-WCT website (https://tumourclassification.iarc.who.int/icdo4/) in 2024 for open consultation.
Results: Changes made to ICD-O-4 include, addition of a 5th alphanumeric digit in the morphology code, introduction of new morphology codes, changes in first four digits of morphology codes used in ICD-O-3.2, changes of behaviour codes(e.g. lymphangioleiomyomatosis changed from /1 to /3), introduction of a new topography code for gastroesophageal-junction(C16.7), detailed codes for extrahepatic bile ducts(C24.2 and C24.3) and cystic duct(C24.4), and change of topography code for anal skin cancer from skin(C44.5) to anus(C21.3).
Conclusion: ICD-O-4 was compiled in response to increased needs for granularity and in consultation with pathologists, epidemiologists, public health researchers and cancer registry community. The five-digit morphology codes enable hierarchical and detailed coding of tumours, while the new topography codes reflect the evidence base on tumour aetiology and staging.

E-PS-20-016
Intraoperative consultations of frozen sections diagnostic accuracies
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Background & Objectives: Differential diagnosis based on the intraoperative frozen sections (IFS) histological examination provide surgeon with assess the operated organ's condition. Time constraints, stressful situations and lack of skills may result in pathologist's wrong interpretations. The aim of our study was to reveal a value of IFS consultation in final diagnosis taking into account possible diagnostic errors.
Methods: The data of 972 patients with IFS examination during their surgery were enrolled in the study. Clinical features of each case, medical records, intraoperative consultations result and histopathology reports were evaluated. For a more reliable analysis of the IFS consultations' accuracy compared with final diagnosis, following point system was introduced: 1 – complete discrepancy of the conclusion, 2 – partial coincidence, 3 – complete coincidence of the conclusions. Spearman coefficient used in statistical analysis.
Results: Present study has shown that examination of IFS requires highly professional training of a pathologist to correctly assess the macroscopic picture and histological characteristics of the tissue sent from the operating room. It has been established that the frequency of intraoperative examinations at the University Clinic varies between 2.5-3 percent of the total number of surgeries with the collection of histological material annually. Both in 2022 and in 2023, the majority of IFS consultations and after routine histological examination ended in complete coincidences (respectively: 87.48% and 88.23%). Discrepancies decreased in a number of pathologies of the following organs: thyroid gland - 23.5%, breast – 13.9%, ovaries – 11.9%, lungs – 11.8%, pancreas – 9.1% and lymph nodes – 4.7%. Spearman's correlation coefficient (p) was 0.370.
Conclusion: IFS morphological diagnosis has an important value and primarily based on effectively identified suspected area by a surgeon. Diagnostic accuracies of the IFS study of malignant neoplasms tissues should be based on coordinated work of a clinician and a pathologist, which contributes to its improvement and increases the effectiveness of treatment.

E-PS-20-017
Annotation discrepancies in prostate cancer gleason grading: implications for deep learning training
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Background & Objectives: Supervised learning is the predominant approach for training deep learning models in Gleason pattern segmentation on histopathology slides. However, precise annotations are essential, and inter-observer variability in the evaluation of Gleason score remains a major challenge, with reported kappa values as low as 0.34 and a concordance rate of 57% at the slide level (Ozkan et al., 2016). This variability raises critical questions on how to construct robust training and test datasets for deep learning applications.
Methods: We collected 200 tumoral prostate slides and had three independent pathologists annotate each slide at the gland group, gland and cellular level using six labels: Gleason 3, Gleason 4, Gleason 5, IDC, HGPIN, ASAP. Annotations were reviewed by senior prostate specialists to ensure consistency. Pathologists underwent specialized training, and both pathologists and data scientists reviewed annotations to align methodologies. A multireader test set was created to estimate local annotation variability, and a consensus ground truth was derived by merging annotations.
Results: Our analysis quantified annotation discrepancies: the concordance area ratio between two pathologists was 33% on average, while 42% of the regions were labeled by only one pathologist. Additionally, 50% of the annotated regions had conflicting labels, with the most frequent confusion occurring between Gleason 3 and Gleason 4 patterns. The derived slide-wise Gleason score yielded an inter-observer kappa of 0.2.

Conclusion: Local gland-level annotation exhibits higher variability than slide-wise Gleason scoring. This variability must be explicitly considered in model training and evaluation to ensure robustness in automated Gleason grading.

E-PS-20-018

An enhanced 10-minute method for Tissue Macroarray construction

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Background & Objectives: Tissue Microarrays (TMA) are common in pathology research for the simultaneous analysis of multiple tissue samples on a single slide. Nevertheless, its small sized cores (0.2–2mm) may limit representativeness. Tissue Macroarrays (Macro-TA), with cores from 3 to 8mm, offer an alternative for small cohorts of cases, better area selection, geographical analyses or histological heterogeneity analyses in samples, biomarker studies, or quality control. Nevertheless, Macro-TA construction has faced challenges in sample orientation, and its preparation is time consuming, often exceeding one hour per Macro-TA. We here present an optimized Macro-TA construction method that ensures precise orientation and localization of samples throughout all the process while significantly reducing construction time.
Methods: Selected samples were identified and marked on HE-stained sections and on donor paraffin blocks. A digital template was designed to detail case identification and layout. A scaffold was created using an inclusion sponge (Deltalab, Spain). Then, a punch-biopsy instrument (Kai Medical, Japan) was used to make perforations on the sponge. An extra half-core perforation notch was made on one corner for orientation control. Then, the perforated sponge was placed in a tissue embedding metal mold. Each tissue core was extracted from the donor block using the punch and retrieved with a metallic probe to minimize tissue handling. Tissue cores were then inserted into the sponge perforations following the digital template. Finally, the mold was filled with paraffin and allowed to solidify.
Results: Each Macro-TA block was constructed, containing from 9 to 48 cores and a total preparation time between 7 and 25 minutes, depending on the diameter of the punch used. The sponge did not interfere in H&E stains or any other technique performed.
Conclusion: This is an improved fast and reproducible new method for Macro-TA construction without the need of specialized instrumentation, facilitating their implementation in diagnostic and research pathology laboratories.

E-PS-20-019

Detection of neutrophil extracellular traps by flow cytometry in patients with systemic lupus erythematosus

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Background & Objectives: NETosis is a process in which activated neutrophils form net-like structures in the extracellular space known as neutrophil extracellular traps (NETs), composed of decondensed chromatin, histones, and granular proteins. In rheumatic diseases, the formation of NETs leads to damage to organs and tissues, accompanied by inflammation and thrombosis. Increased production of myeloperoxidase (MPO), proteinase-3 (PR-3), and neutrophil elastase (NE) is of significant importance in the pathogenesis of systemic vasculitis, while nucleic acids and DNA molecules act as autoantigens in systemic lupus erythematosus (SLE). The aim of the study was to assess the main parameters of neutrophil extracellular trap formation and their changes in patients with systemic lupus erythematosus.
Methods: The study included 64 patients with a median (Me [25; 75 percent]) age of 38.0 [27.5; 46.5], all with confirmed diagnosis of SLE. The median duration of SLE was 9.0 [3.0; 16.0] years, and the disease activity was considered low with an SLEDAI-2K of 4 [2; 11] compared to healthy donors (n=20). The NETs were assessed using flow cytometry by detecting myeloperoxidase in neutrophils after stimulation with phorbol 12-myristate 13-acetate (PMA).
Results: In the results, the flow cytometry study showed that the MPO content in neutrophils from healthy donors in the control group, after stimulation with PMA, was 25.9 [7.7; 42.8], which was significantly lower compared to the SLE patient group, which had a level of 64.2 [38.2; 73.5] (P=0.0006).
Conclusion: In conclusion, neutrophils from SLE patients differ significantly from those of healthy donors, demonstrating impaired phagocytic clearance, increased tendency towards apoptosis, and abnormal oxidative metabolism.

E-PS-20-020

Comparative Experimental Pathology – a success story

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Background & Objectives: Comparative experimental pathology (CEP) deals with analysing and comparing animal models to their corresponding human diseases, revealing parallels, but also differences on tissue level. This is essential in biomedical research in order to use animal models reliably, responsibly, and efficiently. It is also important with respect to the "3Rs" principles. Yet, much biomedical research using animal models is published without the involvement of pathologists with specific knowledge.
Methods: At the Institute of Pathology of the Technical University of Munich, the CEP core facility has been set up and fully integrated into the human general and surgical pathology institute, which is a unique setting in Europe. Since CEP was established in 2016, diverse project requests have been constantly increasing, as has the number of affiliated veterinary and human pathologists with model-specific expertise (e.g., background lesions, species specificities).
Results: Integration of the CEP built synergies between both, human and veterinary pathology. This increased, first, methodological and technical possibilities, and second, the exchange of current scientific knowledge.
Conclusion: With this example, we aim to advocate for more frequent integration of veterinary and comparative pathology into human biomedical research and for making the best use of the resulting synergies.

E-PS-20-021

Precision nutrition: breakthrough of multi-omics precision medicine

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Background & Objectives: Precision nutrition is a pioneering field that offers multidimensional nutrition recommendations tailored to an individuals' genetic and endocrine background. Use of multi-omics platforms encompassing genomics, transcriptomics, proteomics and metabolomics allows analysis of an individual's genetic fingerprint, protein expression and metabolite presence leading to creation of customized dietary quota. The scope of the study is the modelization of a pipeline that leads from collection of biological material from an individual to production of a tailored nutrition plan.
Methods: The approach entails distinct steps towards generation of vast datasets. The first node of the pipeline involves the precise analysis of biological samples (e.g. blood, urine, saliva, feces), by exhaustive multi-omics analysis integrating technologies such as DNA-seq, RNA-seq and Mass Spectrometry. The second and focal pivot of the pipeline is the implementation of bioinformatics tools towards integrative adaptation of previously collected data.
Results: Specifically, data pre-processing, quality control and integration of multi-omics data are combined towards the construction of a model. The final model, through utilization of machine learning algorithms, is used to predict individual dietary responses, risk factors as well as create personal nutrition plans.
Conclusion: Precision nutrition, a sub-domain of personalized medicine, offers a new point of view to disease prevention and regulation. Multi-omics-derived data to are used create a predictive model for nutrition planning, the final goal being optimizing management of cancer and chronic or metabolic diseases, or offering a personalized plan to improve the individual's health status.

E-PS-20-022
Digestive cancer risk associated with quality of water in Boyacá, Colombia
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Background & Objectives: Disinfection By-Products (DBPs) are chemical compounds formed during water treatment when disinfectants like chlorine react with organic matter, posing a cancer risk through genotoxicity, DNA repair disruptions, and chronic inflammation. Regulatory frameworks in Colombia, guided by the Water Quality Risk Index (IRCA) weigh these cancer risks against pathogen-related disease prevention, differing from European approaches. Boyaca, Colombia—an agriculturally driven region with unregulated mining activity—has significant DBP concentrations in its water supply. Such exposure may correlate with elevated rates of digestive cancers, including colorectal and gastric cancers. Aims to create a risk assessment model, based on cancer prevalence in relation to DBP exposure, integrating raw data on cancer incidence and water quality based on water quality index (IRCA) and quantitative measure of DBPs (trihalometanes, haloacetics acids and emergents DBPs) across 15 municipalities.
Methods: A cross-sectional study with a mixed design was conducted. Water consumption data and Boyacá registries on gastric and colorectal cancers were collected, with a one-year exposure adjustment, across municipalities ranging from <5,000 to >100,000 inhabitants (397,014 total; 493 cases annually). Cancer risk from ingestion and dermal exposure—calculated using Tafesse's equation for chronic daily intake—was evaluated. A cancer risk map based on DBP concentrations and digestive cancer rates was created to test the hypothesis linking increased water carcinogens to elevated cancer incidence.
Results: Model show moderate positive correlations between DBP levels and digestive cancer rates across municipalities. Linear regressions modeled gastric and colon/colorectal cancers, with incidence measured at 124.17 per 100,000 and a model risk of 804.30, clearly underscoring public health concerns.
Conclusion: Excessive chlorine use, increases DBP formation, thus the need for optimized water treatment practices and regulatory standards in Boyacá and in Colombia. Taken together, findings support the need of longitudinal designs (cohorts) to more conclusively confirm these associations with cancer incidence

Funding: Minciencias

E-PS-20-023
Optimizing the iDISCO protocol for metastasis analysis in human lymph nodes
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Background & Objectives: Lymph nodes serve as major hubs for metastatic cell growth, secondary dissemination, and immune modulation. Lymph node metastasis (LNM) is crucial for cancer staging, clinical management, and prognosis. Conventional histological methods rely on 2D biopsy sections, which may miss key structural details, limiting insights into micro-metastases and cellular interactions. Three-dimensional (3D) imaging using iDISCO tissue clearing provides a more comprehensive approach. This study aims to optimize the iDISCO protocol for multiplexed 3D imaging of human lymph nodes to investigate metastatic patterns, angiogenesis, and immune cell distribution.
Methods: Human lymph node samples were deparaffinized and processed using a solvent-based clearing approach. The protocol included methanol-based dehydration, bleaching with hydrogen peroxide, rehydration, permeabilization, and blocking. Immunolabeling was performed using four biomarkers—CD3, CD31, Cytokeratin, and Podoplanin. Samples were then dehydrated, delipidated using dichloromethane (DCM), and finally made transparent with dibenzyl ether (DBE). Imaging was conducted using a light-sheet fluorescence microscope equipped with four channels to capture all markers simultaneously.
Results: We successfully established a protocol for multiplexed 3D imaging of human lymph nodes. The optimized iDISCO protocol effectively rendered the samples transparent while preserving structural integrity. This facilitated detailed visualization of metastatic lesions, vascular structures, and immune cell organization. The improved protocol enhances the detection of micro-metastases and enables precise spatial analysis of tumour-immune interactions within lymph nodes.
Conclusion: Our findings demonstrate the advantages of 3D imaging over traditional histological techniques, offering a more detailed and comprehensive approach to studying lymph node metastases. The optimized iDISCO protocol provides a valuable tool for investigating tumour progression and immune response, with potential implications for refining cancer diagnostics and treatment strategies.

E-PS-20-024
Heterogeneity of reparative processes in the Achilles tendon: a comparative analysis of three anatomical zones in the early postoperative period
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Background & Objectives: The aim was to compare the morpho-functional characteristics of three anatomical zones of the Achilles

tendon on the 7th day of healing of the tendon complex after suturing an experimental tendon rupture.
Methods: 23 mature male rabbits (10±2 months, 3.2±0.5 kg) underwent dissection and X-shaped suturing of the tendons of the soleus and calf muscles of the left hind limb. After 7 days, the tendon complex was removed from the surrounding tissues. The sections were stained with haematoxylin-eosin and the Cason method. The proximal, middle and distal tendon zones, and the tendon sheath were studied. Morphometry was performed in Scope Photo 3.0 (10 measurements/field). Statistical processing was performed in jamovi using Mann-Whitney criteria, Chi-square and Spearman correlation.
Results: Heterogeneity of reparative processes was observed after surgery.: the skin and subcutaneous tissue were in the proliferative healing phase, zonal differences were revealed in the tendon complex - the proximal part showed active inflammation (hyperemia, cellular infiltration), the middle part combined exudative inflammation with initial fibroplasia (immature regeneration, decreased optical density of collagen to 0.074±0.03 cu), and the distal part showed exclusively dystrophic changes (fibrinoid swelling, ischemia).
The optical density of collagen was reduced in all zones of the main group relative to the intact one (0.97 ± 0.02 cu): the proximal part (0.089 ± 0.01 cu), the middle part (0.074 ± 0.03 cu), and the enthesis (0.081 ± 0.03 cu). The total area of the vessels of the microcirculatory bed in the proximal part increased due to large vessels (>50 microns) against the background of a decrease in capillaries, small vessels (<30 microns) prevailed in the middle part, postcapillary venules dominated in the enthesis.
Conclusion: The area of the inflammatory infiltrate was 18.9%, the regeneration zone was 34.87% of the surface of the sections, which indicates the competitiveness of the degradation and recovery processes.

E-PS-20-025
Arachnoiditis: an integrative review of cases based on structural anatomy, pathology and clinical manifestations
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Background & Objectives: The arachnoid is described as consisting of an internal layer enriched with reticular cells and collagen, and an external mesenchymal layer. The internal layer interacts with the pia mater and vascular elements, while the external layer is contiguous with the dura mater and subdural space. These structural divisions are essential for maintaining the stability and function of the arachnoid in cerebrospinal fluid dynamics and neural protection, despite its avascular nature. Defined as inflammation of the arachnoid, arachnoiditis not is an infectious meningitis; exhibits varied clinical neurological presentations, frequently mimicking nerve root disorders. With an estimated occurrence of 25,000 cases worldwide annually, its aetiology involves infections, trauma, and exposure to irritants. Aims to review case reports of patients following medical procedures, redefining the understanding of this condition.
Methods: Comparison and review of the clinical and pathological presentation of arachnoiditis in patients who have undergone medical procedures; Cases were obtained on grey literature and medical databases to identify histopathology and common symptoms and signs associated with the condition.
Results: A total of 50 cases of patients diagnosed with arachnoiditis (in pathology specimen) following medical procedures. Among these, 76% were women and 24% were men, with an average age of 41.75 years (standard deviation of 17.11). The age range of patients varied from a minimum of 11 years to a maximum of 76 years. The most frequent trigger for arachnoiditis was the administration of epidural anesthesia during labour or the use of analgesics for chronic back pain.
Conclusion: The most frequently reported signs included motor deficits and sensory disturbances as pain in the lower limbs and in the back. Mechanisms by which anesthetics can cause tissue damage are chemical detergent properties that can lead to cell lysis, and any foreign object, such as needles or catheters, can provoke secondary injuries to the nervous system.

E-PS-20-026
Enhancing laboratory quality through six sigma: a case study on process improvement
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Background & Objectives: Medical laboratories play a vital role in healthcare by providing accurate and timely diagnostic results. However, errors in sample processing, delays in test turnaround times, and inconsistencies in quality can affect patient outcomes. Implementing Six Sigma, a data-driven methodology for process improvement, can help laboratories minimize defects, streamline operations, and enhance overall efficiency. This study examines the impact of Six Sigma in a clinical laboratory, focusing on reducing sample rejection rates and improving turnaround time.
Methods: A retrospective analysis was done in a tertiary medical Centre, Western Maharashtra, India conducted using the Define, Measure, Analyze, Improve, Control, (DMAIC) framework to identify key problem areas. Baseline data revealed a 5% sample rejection rate due to mislabeling, improper handling, and inadequate documentation and samples. Turnaround times also exceeded the standard benchmark, leading to diagnostic delays. A series of interventions, including barcode-based sample tracking, standardized training for laboratory staff, and quality monitoring, were implemented to address these issues.
Results: Post-intervention analysis demonstrated a significant reduction in errors, with sample rejection rates dropping from 5% to 1.39%. Additionally, turnaround time improved by 29%, leading to faster clinical decision-making. The enhanced quality control measures also contributed to greater test accuracy, improved compliance with regulatory standards, and increased patient satisfaction.
Conclusion: This study highlights the effectiveness of Six Sigma in improving laboratory performance and ensuring high-quality diagnostic services. By fostering a culture of continuous improvement, medical laboratories can achieve greater operational efficiency and enhanced patient outcomes. The findings support broader adoption of Six Sigma methodologies across healthcare settings to optimize laboratory processes and drive excellence in diagnostic services. Further research should explore long-term sustainability and the integration of advanced technologies to enhance Six Sigma applications in laboratory management.

E-PS-20-027
Tissue biobanking proficiency testing – a sustainable way to assure high quality standards in biobanking
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Background & Objectives: For tissue-biobanking and its services, e.g. histotechnological processing, tissue analyses and the whole processing chain, proficiency tests are useful tools to test and demonstrate high quality and expertise. This is necessary to avoid alterations in histopathological morphology or on molecular level caused by preanalytical processes, such as transportation, processing and storage.
Methods: For this purpose, the NCT Tissue Bank of Heidelberg University Hospital, in close cooperation with the German Biobank Node (GBN), organizes and performs tissue proficiency tests since 2017.
Results: Seventeen tissue biobanks across Germany participated in the last round robin. The aim of this successfully established nationalwide quality-assurance program for tissue-biobanks is to offer objective review and to evaluate sample quality and processing procedures and it includes the assessment of a histopathological evaluation of tissue biosamples, sampling processes and macroscopic assessment of centrally distributed fresh tissue-samples, its fresh freezing, preparation of cryosections, staining procedures, and DNA/RNA-extraction from cryo preserved tissue including the respective concentration and nucleic acids integrity measurements. The results are jointly evaluated in personal feedback sessions and considered for the design of the following proficiency test.
Conclusion: Here, we present the structured performing and results of the GBN tissue biobank proficiency test. The results are valuable resources allowing refinement and harmonization of tissue-related processes. This is important to ensure consistent high and comparable sample quality, a sustainable use of biomaterials and optimal tissue sample processing in the context of tissue biobanking.

E-PS-20-028
Clinical value of percutaneous CT-guided core biopsy for solid tumours diagnosis
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Background & Objectives: CT-guided percutaneous core biopsy is a highly valuable diagnostic tool al clinical setting. We aimed to evaluate the feasibility, safety, and diagnostic yield of percutaneous CT-guided core biopsy.
Methods: A total of 174 CT-guided percutaneous core biopsies in adult patients with solid tumours of liver, lung, retroperitoneum, pancreas, abdominal cavity, pelvic cavity, kidney, mediastinum and miscellaneous sites, between 2021 and 2023 were done.
Results: Pathological diagnosis was achieved in 166 cases (95.4%). Malignant tumour was diagnosed in 134 (81%) cases. Pathological diagnosis in each biopsy from liver (60), mediastinum (10), kidney (7), and miscellaneous sites (5) was accomplished. In 8 cases (lung 3 of 30, pancreas 2 of 17, retroperitoneum 1 of 23, intra-abdominal cavity 1 of 12, and pelvic cavity 1 of 10), the pathological diagnosis no was succeed. There were no major procedure-related complications.
Conclusion: Percutaneous CT-guided biopsy is an effective and safe procedure for initial diagnosis of patients with solid tumours. Affords a high diagnostic yield (95%) for pathological and immunohistochemical characterization. Anatomical obstacles, corporal movement and respiratory motion of patient are linked to the unsuccessful diagnosis.

E-PS-20-029
Clinicopathological features of the term "undifferentiated malignancy" used by the pathologists and the prevalence rate of BRG1 loss under this diagnosis
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Background & Objectives: Most pathological reports include tumour differentiation and categorized into carcinoma, or sarcoma, etc. However, occasionally, tumour differentiation cannot be confidently told by conventional exams and a term "undifferentiated malignancy" will be used. One of the reasons may be the epithelial-mesenchymal transition (EMT) phenomenon, which obscures epithelial features while obtaining mesenchymal or sarcomatous features. In addition, sarcomas may mimic carcinoma, morphologically or even immunophenotypically. Although there is literature regarding diagnostic approaches, no study has been explored in a clinical cohort.
Methods: Retrospectively, 90 cases were enrolled with a diagnosis of "undifferentiated malignancy" or "poorly differentiated malignancy" at our institution (NCKUH) from January1st, 2000 to August 30th, 2023. The mean age was 58 years, with a male-to-female ratio of 1.7. Clinicopathological features and immunophenotypes were obtained from both electronic records and slide review. Re-classification was done based on current WHO system. BRG1 immunohistochemical stain was added additionally, for which losing expression was prevalent in undifferentiated carcinoma from various origins. Molecular studies were performed in five cases for treatment purposes.
Results: After thorough investigations, the diagnoses included carcinoma (n=71), sarcoma (n=13), melanoma (n=2), germ cell tumours (n=3), and olfactory neuroblastoma (n=1). Liver and lung were the most common origins. Prognosis was extremely poor, most patients died (~80%) with a mean follow-up of 18.2 month. Nine of 75 cases undergone BRG1 staining lost BRG1 expression, which were all carcinomas. The origins included lung (n=5), stomach (n=1), liver (n=1), sinus (n=1) and thyroid (n=1). Two cases revised the original diagnoses into SMARCA4-deficient tumour, including thoracic and sinonasal origins. Five cases had molecular studies, which revealed MET amplification, EGFR amplification, RICTOR amplification, and BRAF V600E mutation but without recurrent genetic changes.
Conclusion: In conclusion, this study helps us to know when pathologists diagnose "undifferentiated malignancy" and unraveled their nature.

Funding: This study is granted by National Cheng Kung University Hospital, Taiwan (grant No. NCKUH-11304031) and approved by IRB (No. B-ER-116-320)

E-PS-20-030
A game-changer in histology, histopathology and cytology learning: virtual microscopy platform developed in an European university consortium
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Background & Objectives: Virtual microscopy (VM) platforms may enhance medical education by providing digital access to high-quality images. By collaboration with other European partners, our team developed a virtual microscopy platform, entitled Virtual Microscopy Histology and Histopathology.
Methods: Developed by a consortium of medical universities in Iasi, Alicante, Plovdiv, and Gdansk, Virtual Microscopy Histology and Histopathology platform uses Aperio AT2 scanners (Leica Microsystems) to digitize slides at 0.25 µm resolution. Hosted on secure, cloud-based servers, it ensures scalability, reliability, and fast access to a large collection of digital slides. The user interface is intuitive and responsive, compatible across desktops, tablets, and smartphones.
Results: Virtual Microscopy Histology and Histopathology platform, launched in September 2024, provides a dynamic and engaging learning environment, allowing users to study both normal and pathological tissue specimens in high detail. Interactive features, including seamless zooming, screenshot-taking, and the ability to add annotations, enhance the learning experience, fostering active engagement. The platform's VM library is organized into 20 chapters to align with

medical curricula, offering comprehensive coverage of histology, histopathology, and cytology. The integrated quiz section, which generates randomized tests with images for recognition, helps students assess their knowledge and reinforce learning. Feedback from users, with more than 90% 5-star rating, highlights its value in promoting self-paced learning and improving diagnostic skills, particularly for students and residents, with multilingual support and easy-to-use interface. The platform continues to grow, regularly adding new content. Plans to expand the pathology section and include more complex cases further strengthen the platform's educational utility.
Conclusion: Virtual Microscopy Histology and Histopathology platform offers an interactive, digital tool for histology and pathology education. It provides a flexible and accessible approach for learners, empowering undergraduate and postgraduate medical students and pathology professionals with advanced diagnostic training through modern technology.

Funding: This study is supported by Erasmus+ project 2022-1-RO01-KA220-HED-000089017

E-PS-20-031
Is it red just dead, or something ahead? A one-centre experience with lymph node necrosis
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Background & Objectives: Isolated lymph node necrosis is an uncommon histopathological finding. In most cases, it is associated with underlying conditions, frequently malignancies. Immunohistochemistry (IHC) use in such cases is controversial but may provide valuable diagnostic insights. This study evaluates the diagnostic utility of IHC in cases of extensive lymph node necrosis and its role in suspicion of malignancy and subsequent diagnosis.
Methods: Over the past 15 years, we retrospectively analysed 43 cases of total or subtotal (up to 95%) necrosis in lymph node biopsies. IHC was performed to assess retained antigen expression. The retained reactions included lymphocytic markers (CD20) and epithelial markers (Pan-Cytokeratin (PanCK), CK7, CK20). Clinical, follow-up data and prior diagnoses were reviewed.
Results: Prior malignancy diagnosis was established in 41.9% of cases, with necrosis primarily linked to therapeutic effects. Follow-up data were unavailable for 14% of cases. In 11.6% of cases, a final malignancy diagnosis was confirmed in subsequent biopsies. Notably, in 32.6% of cases, initial pathological suspicion of malignancy was correctly raised based on IHC findings. These included 10 cases of B-cell lymphoproliferative disorders, predominantly diffuse large B-cell lymphomas (n=5), and carcinomas (n=4). The interval between the initial pathological diagnosis and the final malignancy confirmation ranged from two weeks to two months. One remarkable case involved a patient with a history of B-cell lymphoproliferative disorder and axillary lymph node biopsy showing complete tumour necrosis. Retained PanCK and CK7 expression led to a surprising diagnosis of breast carcinoma, which was not previously suspected clinically.
Conclusion: IHC in necrotic lymph nodes, particularly structural cytoplasmic and membranous markers, can be retained as a valuable diagnostic tool. It aids in identifying tumour cell lineage and some architectural-cytological characteristics, as well as improving patient management.

E-PS-20-032
Weekly nationwide virtual uropathology consensus meetings among Turkish pathologists: a vibrant example of multidisciplinary effort in continuous uropathology education
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Background & Objectives: Consensus meetings are important aspects of daily surgical pathology practice, however, organized nation-wide effort in establishing weekly case-discussion platforms is rare.
Methods: Under the supervision of Turkish Uropathology Working Group, a weekly online consensus meeting is planned. Regardless of the type of the laboratory setting (e.g. academic tertiary setting, community hospitals, private pathology labs, small rural pathology laboratories), practice type (general or subspecialty-type pathology practice), and level of experience (resident, fellow, faculty and/or staff) were invited to the consensus meetings. Zoom platform (Zoom Communications, San Jose, CA, USA) were used to established free-of-charge case discussion platform. All discussed cases were required to be completely de-identified from personal information.
Results: Between July 2024 - February 2025, 32 weekly consensus meetings were performed every Tuesday (of 35 weeks, 91%). Attendees were from 17 different Turkish cities; mean number of attendees in each weekly meeting was 29 (range 5 - 54 attendees). in 32 meetings, a total of 101 cases were discussed with an average of 3 cases per meeting (range 0 - 5). Number of cases based on organs were as follows: Kidney (62, 61.3%), urinary tract (22, 21.7%), prostate (6, 5.9%), testis (5, 4.9%), penis (1, 0.9%), and others (5, 4.9%). Moreover, starting January 2025, brief multidisciplinary (medical oncology, urology, and radiology) sessions on the management of urologic neoplasia were conducted (n = 3), and journal club-style article presentations were performed (n=4; 3 renal tumours, 1 prostatic adenocarcinoma).
Conclusion: Weekly nationwide virtual urology consensus meeting is a great tool for continuous pathology education. It is critically helpful in countries where urologic pathology fellowship training is not formally established, and it is a great tool to consult challenging cases, particularly for pathologists practicing in remote/limited resource setting.

E-PS-20-033
Applications of three-dimensional printing in surgical pathology: new perspectives
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Background & Objectives: Three-dimensional (3D) printing techniques have been developing rapidly in the past decade. The emergence of affordable, easy-to-use 3D-printing equipment, and user-friendly 3D-design software, have permitted the design and creation of novel devices even by non-experts in the field of computer-aided design. We present a review of the current literature on the applications of 3D-printing in Surgical Pathology, with an analysis of future directions.
Methods: A literature search was performed on the subject, on the databases PubMed, Web of Science and Google Scholar. Several keywords were used, alone or in combination, including "3D-printing", "pathology", "instrument". The final results were summarized.
Results: Several publications on applications of 3D-printing were located, expectedly, mainly in the field of gross examination. In the

setting of prostatectomy specimens, a design of cutting guides to align the sections with magnetic resonance imaging findings exists. The potential for scanning and producing 3D-printed model replicas from excision specimens, to enhance training, has also been explored. Our team created a novel grossing instrument, to aid in metallic staple removal in pulmonary excision specimens, in order to enhance margin evaluation. Further studies exist on other subspecialties of Pathology.
Conclusion: The field of 3D-printing in Surgical Pathology is highly promising, yet currently underexplored. Mainly in surgical specialties, these techniques have been widely utilized for prostheses, instruments and in surgical training. The ease in designing and producing novel instruments and devices can evolve the practice of Pathology.

E-PS-20-034
How important is undergraduate teaching at pathology conferences?
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Background & Objectives: Pathology is a medical specialty and a fundamental subject in medical training. Medical conferences are a way to network with colleagues and learn about new advances. The objective of this study is to identify the role of undergraduate teaching at European pathology conferences.
Methods: Abstracts from the last 10 European conferences published in the journal Virchows Archiv were analysed, searching for the following identifiers: teaching, university, subject, teaching, degree, students. The types of studies were analysed, including oral presentations and posters. The data were analysed using conventional statistics. Teaching papers on medical residents were excluded.
Results: Between 2014 and 2024, a total of 45 oral communications and 12 posters related to teaching or teaching innovation were presented. They were presented by faculty from universities with affiliated university hospitals. Representativeness compared to other subjects averages 2-3%, and there is no teaching topic at the conference. Thirty percent of the papers and posters are related to microscopic visualization and training in the recognition of pathological structures.
Conclusion: European pathology conferences show little interest in teaching pathology in the medical degree program. It doesn't address a specific topic, and the ESP doesn't have a program specifically focused on teaching. The ESP must become involved in generating new teaching and academic vocations to ensure that pathologists and non-related professionals are responsible for teaching pathology to the physicians of the future.

E-PS-20-035
Could pathology laboratory improve accuracy of neuropsychological profiling in early-stage Type 2 Diabetes Mellitus cognitive decline?
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Background & Objectives: The survey of neuropsychological profile in patients with early-stage Type 2 Diabetes Mellitus (T2DM) can mitigate the impacts of cognitive impairment due to disease and this research explores potential connections with early stages of dementia. Interdisciplinary involvement of pathology and neuropsychology, aims to combine psychological evaluations with biochemical analyses, including cytological and chemical examinations of cerebrospinal fluid (CSF), to enhance diagnostic accuracy Additionally, the measurement of biomarkers levels such as Brain-Derived Neurotrophic Factor (BDNF) in blood, influenced by the positive effects of physical exercise, offers a valuable tool to preserve synaptic function, aiding early identification of cognitive decline or confirming a healthy cognitive status.
Methods: A cross sectional study was made to compare participants divided into two groups: 25 with T2DM and 25 without the diagnosis; It was analysed the cognitive profile of patients diagnosed with Type 2 Diabetes Mellitus (T2DM) compared to non-diabetic individuals. Each one was eavaluated using neuropsychological tests such as the MMSE, Rey Auditory Verbal Learning Test, and Rey Complex Figure Test; BDNF leves, glycemic status HbA1c and CSF.
Results: Participants aged between 40 and 70 years old showed that those with T2DM exhibited cognitive deficits in visual memory, visuoconstruction, and working memory, while non-diabetic participants performed better in memory and attention-related tasks. Used biochemical and pathological parametes had some usual presentation without significative differences between groups.
Conclusion: This research contributes to understanding how T2DM influences cognitive processes, advocating for interdisciplinary approaches to improve diagnostic and therapeutic strategies. By addressing cognitive challenges early, patients with T2DM can benefit from personalized care aimed at enhancing their quality of life Insights into neuroinflammation and biochemical changes associated with T2DM are difficult to clear into bias of selection and scarce of participants as control of cases; nowadays It could reinforcing its potential role in the development of cognitive decline or incipient dementia.

E-PS-20-036
Intraoperative communications: pathologist-surgeon communication reexamined
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Background & Objectives: Effective intraoperative communications between pathologists and surgeons is crucial for guiding surgical procedures, particularly during frozen section analysis. Miscommunication in this high-pressure setting can lead to delays, misinterpretations and potential errors that affect outcomes. These challenges often stem from using highly specialized terms and medical jargon, including abbreviations which different specialists can interpret differently. Our study aims to identify common communication patterns and propose strategies to enhance accuracy and efficiency.
Methods: We examined intraoperative communication patterns among surgeons in Georgia's high-impact hospitals, specifically focusing on those working in oncology settings. A mixed-methods approach was utilized, combining both qualitative and quantitative data collection techniques. The data collection process involved distributing a structured questionnaire through the Google Forms platform. The questionnaire contained multiple sections, like: epidemiologic data, case scenarios, open-ended questions and etc.
Results: Our findings suggest that the key challenges include ambiguous terminology, time constraints and lack of standardized phrasing, which contribute to miscommunication. The results also revealed that surgeons with 10+ years of practice were found to have greater misjudgments in understanding pathological terms when faced with case-based scenarios in the survey. Participants with higher scores in the case scenarios tended to consult existing literature more frequently when faced with ambiguous diagnoses, whereas those with lower scores relied more on contacting the same pathologist who issued the report. These findings highlight potential variability in

individual approaches to understanding pathology reports, suggesting that disparities may stem from differences in problem-solving strategies too.
Conclusion: Optimizing intraoperative communication requires a multidisciplinary approach, integrating standardized diagnostic phrasing, closed-loop communication techniques and digital pathology solutions. By refining communication strategies, pathologists and surgeons can enhance the accuracy and efficiency of frozen section analysis, ultimately improving patient outcomes. Future research should focus on evaluating these interventions in clinical practice to establish best practices for intraoperative diagnostics.

E-PS-20-037
A diagnostic trial centre as a key research infrastructure
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Background & Objectives: Pathological assessment has a substantial impact on clinical trials. Trial inclusion, secondary or even primary endpoints or trial-associated research require the expertise of pathologists and thus structural integration of pathologists and histopathological and molecular pathological technology. Guiding trial requests from stakeholders such as the pharmaceutical industry or clinicians and the pathological expertise in a structured manner improves clinical trial outcome, research use and performance of the involved pathology institutions. Therefore, in 2012 we established a diagnostic trial centre in the academic setting at Heidelberg University Hospital as a key translational research infrastructure.
Methods: The diagnostic trial centre operates in a quality-controlled manner according to official standards and especially in GCP conformity.
Results: Performance and key indicators are presented. In the last years the trial centre has contributed to and supported a wide range of trials, e.g. IITs, industry-driven trials, and comparable PPP projects in multi- or single-centre settings. Services of the diagnostic trial centre encompass trial-based case-management, documentation, communication, quality management as well as related administrative issues, such as contractual management, reporting and billing. The diagnostic trial centre closely interacts with diagnostic pathology and other infrastructures, especially tissue biobanking and molecular as well as computational pathology; it is part of the tissue-based research infrastructure platform of the Institute of Pathology.
Conclusion: The demand for histo- and molecular-pathological assessments in clinical trials is increasing as biomarker-driven patient selection, therapy decision making and cooperative translational research projects with industry are increasingly implemented. These approaches result not only in a rising need for pathological expertise, but also in a substantially higher number of samples to be processed highlighting the importance of a coordinating diagnostic infrastructure that acts as a relay between all stakeholders involved. As such a diagnostic trial centre is a key part of the tissue-based research infrastructures.

E-PS-20-038
Vimentin immunohistochemistry as a diagnostic tool to differentiate oligodendrogliomas from astrocytomas in resource-limited settings
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Background & Objectives: Astrocytomas and oligodendrogliomas are common primary brain tumours with distinct histopathological and molecular features. Accurate diagnosis relies on morphology, immunohistochemistry (IHC), and molecular testing. In settings where molecular diagnostics are not readily available, alternative methods are necessary. We aim to assess the diagnostic value of vimentin IHC in distinguishing between these two entities in resource-limited settings.
Methods: This retrospective study included cases of oligodendrogliomas and astrocytic gliomas diagnosed at King Hussein Cancer Centre (KHCC) from 2017 to 2024. The included cases underwent 1p/19q co-deletion FISH and vimentin IHC staining. Diagnostic metrics, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of vimentin IHC, were calculated using FISH results as the reference standard.
Results: 116 cases were included: 65 oligodendrogliomas confirmed by 1p/19q co-deletion and 51 astrocytic gliomas (including pilocytic astrocytoma [n=1], diffuse astrocytoma [n=13], anaplastic astrocytoma [n=11], and glioblastoma [n=26]). Among oligodendrogliomas, 89.3% (n=58) were negative for vimentin, while 10.7% (n=7) were positive. In contrast, 86.3% (n=44) of astrocytic gliomas were vimentin-positive and 13.7% (n=7) were negative. The PPV of negative vimentin IHC in diagnosis of oligodendrogliomas (positive for 1p/19q co-deletion and negative vimentin IHC) is 89.2%. The NPV of positive vimentin staining in the diagnosis of oligodendrogliomas (negative for 1p/19q co-deletion and positive vimentin IHC) is 86.2%. The sensitivity (ability of vimentin IHC to correctly detect oligodendrogliomas) is 89.2%, while the specificity (ability of vimentin to correctly detect astrocytic gliomas) is 86.3%. The accuracy of vimentin IHC in differentiating between the two entities is 87.9%.
Conclusion: Vimentin IHC is a cost-effective and accessible tool for differentiating oligodendrogliomas from astrocytic gliomas in settings lacking molecular diagnostic capabilities. Negative vimentin staining is a strong indicator of oligodendroglioma, while positive staining favours astrocytoma. This approach may aid in accurate diagnosis and treatment planning in resource-limited environments.

Funding: The work was supported by the Intramural Research Grant Program at King Hussein Cancer Centre

E-PS-20-040
High inter-observer agreement and determination of the training effect in the CPS assessment of PD-L1 in different indications
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Background & Objectives: Immunohistochemical testing for programmed cell death-ligand 1 (PD-L1) has proven to be a useful predictive marker for anti-PD-1 therapy. Tumour cells (TC) and/or tumour-associated immune cells (TAIC) are used to determine the level of PD-L1 expression often detected by using the PD-L1 IHC 22C3 pharmDx. samples are either evaluated by the Tumour Proportion Score (TPS: TC PD-L1 staining) or by the Combined Positive Score (CPS: PD-L1 TC and TAIC staining). Depending on the country CPS is used in Gastric Cancer (GC), Oesophageal Cancer (EC) Cervical Cancer (CC) and Urothelial Carcinoma (UC), Head and Neck Squamous Cell Carcinoma (HNSCC) and Triple-Negative Breast Cancer (TNBC). We present data conducted between 2017 and 2024 years for a worldwide, expert-led training in PD-L1 interpretation for the indication name above using CPS.
Methods: All pathologists assessed 20 blinded samples on day 1 and 25 samples on day 2. Latter one only if they participated in the 2-day training. The reproducibility of PD-L1 scoring at the relevant cut points between (inter) and within observer (intra) was assessed.

In 2020, a test was added to measure the training effect by collecting data from the same samples before and after training (n = 5 or 6, respectively for HNSCC).
Results: A total of 2093 participants were trained in 194 sessions. Inter-observer agreement ranged between 88.5% ± 11.8 for TNBC to 93.4 ± 9.6 for UC and intra-observer ranged from 91.3% ± 12.0 for EC to 95.1 ± 17.3 for CC. When looking at the training effect across all indications, around one third showed a higher level of agreement than before the training, and around 50% showed no differences.
Conclusion: The data not only show a high reproducibility of CPS scoring in a variety of indications including challenging cases, but also show the positive impact of standardized training for pathologists in complex biomarker.

Funding: The project was sponsored by MSD. Beyond that is Discovery working with any major pharma and biotechnology companies. I personally are involved in projects as employee paid by AstraZeneca, AbbVie, BMS, Roche, Astellas, Agilent, GSK

E-PS-20-041
Harnessing AI-driven emotional analysis to accelerate change management: a multi-method approach in clinical laboratory settings
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Background & Objectives: Berkshire and Surrey Pathology Services (BSPS), a joint venture of five NHS Trusts, is one of the UK's largest pathology networks processing more than 50 million tests annually. In response to the rapid technological evolution in clinical laboratories, BSPS launched a pilot study to evaluate staff perspectives on organisational transformation, with a particular focus on the role of Artificial Intelligence (AI) - Large Language Models (LLMs). Inspired by AI-led workforce analysis trends in industry, including Microsoft, the study aimed to explore how AI could support staff wellbeing and engagement during change.
Methods: A GPT-o1 model was used to systematically analyse six months of internal communication data, supported by triangulation with interviews, discussions, and workflow observations. The analysis incorporated Lewin's Change Management Model, the Job Demands-Resources (JD-R) Model, and the Linguistic Inquiry and Word Count (LIWC) tool to assess emotional tone, workload balance, and organisational readiness. Insights informed change strategies using Kotter's 8-step model and cognitive-behavioural techniques, such as reframing and behavioural activation.
Results: Findings revealed a strong negative correlation between limited professional development, entrenched practices, and staff morale, driving resistance to technological innovation. High workloads and technological gaps increased frustration and led to cognitive fatigue and avoidance behaviours. LIWC confirmed a negative emotional tone in internal communications, reflecting a focus on general goals over individual recognition, contributing to disengagement.
Conclusion: The study concludes that combining AI-driven text analysis with behavioural frameworks enables the development of responsive, human-centric change strategies. Targeted interventions, such as early engagement, transparent communication, clear role definitions, and accessible training, can enhance receptiveness to change. Integrating BJ Fogg's behaviour model may further support staff motivation, communication, and professional growth. Ultimately, AI-enhanced strategies offer a scalable, evidence-based approach to improving wellbeing, reducing resistance, and fostering sustainable innovation in NHS pathology services, by identifying the drivers.

E-PS-20-042
Transforming an NHS histopathology laboratory through staff engagement and proactive leadership
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Background & Objectives: Berkshire and Surrey Pathology Services (BSPS), a leading pathology network serving over 3.2 million people in the South East, faces rising demand and increasing complexity in histopathology services. In response, BSPS initiated a pilot study to assess staff perspectives on organisational transformation. The objective was to explore how to transition BSPS into a leading, patient-centred care provider by addressing challenges such as low morale, high turnover, lack of training opportunities, and reduced confidence in leadership.
Methods: A structured, multi-method approach, integrating psychological and change leadership theories, was used in this study to evaluate change readiness within a histopathology laboratory setting. Baseline behavioural audits and segmentation were used to assess readiness and resistance, while a behavioural risk matrix, guided by tech adoption personas, helped develop a targeted communication strategy.
Our approach integrated the Awareness, Desire, Knowledge, Ability, and Reinforcement model, BJ Fogg's Behaviour Model, and the Theory of Planned Behaviour. The change strategies effectiveness was reinforced by cognitive-behavioural techniques, reframing, behavioural activation, and exposure.
Results: Analysis revealed three staff segments: one highly engaged and innovation-driven; a second patient-focused but hesitant about new technologies; and a third with minimal engagement and high resistance. Staff perceptions revealed a consistent pattern of disengagement stemming from preconceived notions about AI, particularly concerns around accuracy, complexity, and job relevance. AI-assisted text analysis, mapped to behavioural models, supported the development of targeted interventions. Insights emphasised the need for an open, blame-free culture to build trust. Staff visits to the clinical oncology departments shifted the focus back to the needs of patients.
Conclusion: To understand the NHS's diverse international landscape requires cultural sensitivity, strong leadership, and inclusive communication.
Technology must be integrated with human-centric care, and targeted strategies, such as peer mentoring, early engagement, and clear role structures, are key to enhancing receptiveness and driving sustainable innovation.

E-PS-20-043
The level of collagen type I and type III in connective tissue of umbilical hernia of men and women
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Background & Objectives: The ratio and level of collagen type I and type III determine the strength of connective tissue and scar tissue. The aim of the study was to evaluate the expression level of collagen type I and type III in the connective tissue of umbilical hernia of men and women.

Methods: Seven men and six women with umbilical hernia was included in this study. During surgery a piece of anterior abdominal wall was obtained from umbilical hernia and a piece from the skin of resection edge. The immunohistochemistry antibody collagen type 1A2 (E-AB-10155, 1:400) and collagen type 3A1 (E-AB-22071,1:400) were used. The expression was analysed by the image analysis software Aperio Image Scope [v12.4.6.5003].
Results: The expression of collagen type I was 2.0 (1.0;2.0) %, type III - 5.0 (5.0;6.0) % in the skin of men from resection edge (I:III=1:2.5, p=0.0022). The expression of collagen type I was 17.5 (9.0;28.0) %, type III - 8.0 (3.0;10.0) % in the skin of men under hernia sac (I:III=2.2:1.0, p=0.0091). The expression of collagen type I was 33.5 (18.0;50.0) %, type III - 8.0 (3.0;18.0) % in tissue of hernial sac (I:III=4.2:1.0, p=0.0091). In the skin of women from resection edge the expression of collagen type I was 2.3 (2.0;3.0) %, type III - 8.6 (7.0;10.0) % (I:III=1.0:3.6, p=0.0002) and under hernia sac: the expression of collagen type I - 12.5 (9.0;14.0) %, type III - 17.0 (12.0;19.0) % (I:III=1.0:1.4, p=0.0640). The expression of collagen type I was 22.5 (17.0;34.0) %, type III - 25.5 (19.0;37.0) % in fibrous tissue of the hernial sac of women (I:III=1.0:1.01, p=0.0650).
Conclusion: This study showed a difference in collagen formation in men and women with umbilical hernias: for men was characterized the change in synthesis of collagen type I, but for women - as a type I and type III.

Funding: This study was carried out within the framework of a grant from the Belarusian Foundation for Fundamental Research

E-PS-20-044
New approach to 3D reconstruction of the perineural invasion in prostatic cancer in laboratory mice
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Background & Objectives: Perineural invasion (PNI) is a commonly known process in prostatic cancer, but exact mechanisms are still to be assessed. Our research was to establish a new approach to 3D reconstruction in a lab model of prostatic cancer in mice.
Methods: We analysed tissues obtained from laboratory mice injected with PC3 ML cells to develop prostatic cancer. After scarification the full body was fixated in formalin, decalcified and paraffin embedded. Serial sections were stained with H&E with interval neurofilament staining of every 3rd section. Volumetric scanning of slides was done using Pramana Spectral scanner for 3D reconstruction using dedicated software.
Results: Preliminary results show optimal 3-D reconstruction of PNI at lower magnification with good correlation with MRI. However inter block serial sections pose the challenge with 3-D reconstruction at cellular level, as the same cells cannot be traced in serial sections from subsequent blocks owing to cell size of 10-15 um. To overcome this, we adopted the new approach based on a 5 um serial section from the same FFPE block using the information across the Z stack layers which yielded more accurate results.
Conclusion: The preliminary results let us believe that in the nearest future by such analysis we will be able to understand better processes ongoing in human tissues, like carcinogenesis, development, inflammation and others. Volumetric scanning based 3-D reconstruction may help not only in analysis of malignant invasion, including perineural, but also in non-malignant maladies.

Funding: This publication is a result of a research project No. 2023/07/X/NZ4/01693 financed by the National Science Centre, Poland

E-PS-21 E-Posters Paediatric and Perinatal Pathology

E-PS-21-001
Histopathological features of paediatric Wilson disease in liver biopsies
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Background & Objectives: Wilson Disease (WD) is an autosomal recessive disorder characterized by pathological copper accumulation, primarily affecting the liver and brain. This study aims to investigate the histopathological features of paediatric WD in liver biopsies.
Methods: Liver biopsies from 14 paediatric patients (aged 7–21 years) diagnosed with WD between 2019 and 2025 were analysed. Patients were categorized into three groups based on the mode of diagnosis: neurological, hepatic, and incidental (or family screening).
Results: Histopathological analysis revealed diverse liver pathology, including fibrosis (8 patients), portal inflammation (9 patients), interface hepatitis (7 patients), focal necrosis (5 patients), confluent necrosis (3 patients), copper accumulation (10 patients), and steatosis (6 patients). Biochemical markers showed uniformly low ceruloplasmin levels (0.092–0.195 g/L) and elevated hepatic copper levels (18.5–874 µg/g) in all patients. Urinary copper excretion was significantly increased (70.5 to >3200 µg/24h).
Clinically, hepatic involvement was the most common presentation, followed by neurological symptoms and incidental diagnosis. Among the patients, 5 had a family history of consanguinity, 2 exhibited hepatomegaly, 1 had splenomegaly, and 2 presented with abdominal ascites. Jaundice and Kayser-Fleischer rings were observed in 1 patient each. Cranial MRI findings were consistent with WD in 3 cases.
Conclusion: This study underscores the importance of integrating histopathological, biochemical, and clinical data for diagnosing paediatric WD. The variability in clinical presentation and histopathological features highlights the need for a high index of suspicion, particularly in cases with a family history of consanguinity or unexplained liver disease.

E-PS-21-002
A retrospective evaluation of congenital thoracic malformations
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Background & Objectives: Congenital thoracic malformations (CTM) are a rare group of anomalies, including Congenital pulmonary airway malformation (CPAM), bronchopulmonary sequestrations (BPS), congenital lobar emphysema (CLE), and bronchogenic cysts (BC). Prenatal ultrasound has allowed intrauterine diagnosis of congenital thoracic malformations and managed by a paediatric surgeon from early on.
Methods: This retrospective study examines the diagnosis of CTM and was conducted on 36 patients between March 2019 and March 2025 at Ankara Bilkent City Hospital in Ankara, Türkiye. Patient characteristics, including demographic and clinical data, were gathered through a patient record system. All patients were histopathologically diagnosed with CTM, and their demographic data, including age, sex, cardiac findings, and prenatal diagnosis, were recorded.
Results: In this retrospective study, 36 patients (females and males) diagnosed with CTM were enrolled. The mean age of participants was 2.58 years (ranging from 1 month to 16 years). We reported 23 cases (63.9%) of CPAM (13 cases of CPAM type 1 [36.1%] and 12 cases of CPAM type 2 [33.3%]), 3 cases (8.3%) of bronchogenic cyst, 9 cases (25%) of sequestration (3 cases of extrapulmonary sequestration [8.3%]

and 5 cases of intrapulmonary sequestration [13.9%]), 1 case (2.8%) of lymphangioma, 1 case (2.8%) of bronchial atresia, 2 cases (5.6%) of congenital lobar emphysema, and 1 case (2.8%) of combined vascular malformation. Five cases (13.9%) had overlapping features with CPAM, referred to as hybrid lesions. There were 2 cases of mucinous adenocarcinoma arising in congenital pulmonary airway malformation type 1. Cardiac abnormalities were present in 10 cases (27.8%).
Conclusion: The predominant lung malformation in this study was congenital pulmonary airway malformation. Most of the patients underwent lobectomy. All patients were early symptomatic at the time of diagnostic workup. The most common clinical signs and symptoms were respiratory distress and recurrent pulmonary infections.

E-PS-21-003
A challenging diagnosis: paediatric multifocal Langerhans cell histiocytosis with an unusual phenotype
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Background & Objectives: Langerhans cell histiocytosis (LCH) is a rare disorder characterized by the clonal neoplastic proliferation of Langerhans cells in various tissues. It usually manifests during childhood and it can involve any organ. Most commonly affected sites are the bone and skin.
Methods: A 7-month-old female patient was admitted to the Children's Hospital Iași in 2022 for an erythematous rash involving the face and neck. The clinical diagnosis was chronic dermatitis, with clinicians also considering psoriasis as a differential diagnosis. The patient was admitted again in 2024, with two more suspect lesions on the eyelid and left shoulder. All three lesions were biopsied.
Results: The initial microscopic assessment done in 2022 revealed the presence of histiocyte rich inflammatory infiltrate in the papillary dermis. The histiocytes were immunohistochemically (IHC) positive for CD1a and S100, thus indicating a LCH diagnosis.
The lesion located on the shoulder presented a histologically matching picture with the initial result, the remarkable difference being the addition of multiple giant cells. The histiocyte population was CD1a negative and CD68 positive in IHC, thus raising the suspicion of an independent juvenile xanthogranuloma.
The palpebral lesion presented multiple Touton-like giant cells and negative foci of histiocytes for CD1a in IHC. Examining the clinical and histological data, a synchronous Erdheim-Chester disease diagnosis can be considered.
Conclusion: Whilst the initial histopathological assessment supports the diagnosis of LCH, ruling out Rosai-Dorfman disease and verifying the association with Erdheim-Chester disease calls for additional IHC evaluation, currently being carried out in our case. This type of testing usually involves markers that are infrequent and difficult to access such as Langerin, CyclinD1 and BRAF. Our case is valuable by contributing to a better understanding of the morphological similarities and associations of these rare afflictions, that are scarcely mentioned in medical literature.

E-PS-21-004
Placental chorioangioma and associated pregnancy complications: a retrospective analysis
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Background & Objectives: Placental chorioangioma is a rare pregnancy disorder associated with various maternal and foetal complications. This study retrospectively reviews maternal and foetal outcomes in pregnancies affected by placental chorioangioma and evaluates factors influencing disease prognosis. Histological changes in placentas were analysed using the standardized classification system proposed by the Amsterdam Placental Workshop Group.
Methods: This retrospective study was conducted at Ankara Bilkent City Hospital in Ankara, Türkiye. The study population included all pregnancies with ultrasound-detected chorioangiomas or histologically confirmed chorioangiomas between January 2019 and December 2024.
Results: Placental chorioangioma was diagnosed in 13 patients. Foetal vascular malperfusion was detected in all cases (100%). Maternal vascular malperfusion was observed in 6 cases (46.2%). Ascending intrauterine infection was present in 1 case (7.7%), while chronic villitis was not observed in any case. Regarding pregnancy outcomes, induced abortion or foetal loss occurred in 4 cases (30.8%), preterm birth in 11 cases (84.6%), caesarean delivery in 10 cases (76.9%), preeclampsia in 4 cases (30.8%), and polyhydramnios in 5 cases (38.5%).
Conclusion: Placental chorioangioma is associated with a high risk of adverse pregnancy outcomes, including preterm birth, foetal vascular malperfusion, and maternal complications such as preeclampsia. Early diagnosis and careful monitoring are essential for the effective management of these pregnancies.

E-PS-21-005
Retrospective evaluation of paediatric cholestatic liver diseases
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Background & Objectives: Paediatric cholestatic liver diseases are rare conditions that can result from multiple specific underlying aetiologies, often associated with high morbidity. The aim of this study was to evaluate the etiological spectrum of paediatric cholestatic liver disease.
Methods: Patients diagnosed with cholestasis under the age of 2 years were included in the study. A total of 49 patients (27 girls, 22 boys) with cholestatic liver disease, who were followed up between 2013 and 2024, were retrospectively evaluated. Patients were categorized into intrahepatic and extrahepatic cholestasis groups. Liver biopsies were examined for cholestasis, giant cell change, inflammation, and fibrosis.
Results: The causes of cholestasis included progressive familial intrahepatic cholestasis (n=4, 8.2%), extrahepatic biliary system disorders (n=19, 38.8%), total parenteral nutrition and sepsis-associated cholestasis (n=3, 6.1%), genetic disorders (n=1, 2.0%), metabolic diseases (n=3, 6.1%), syndromic and non syndromic ductopenia (n=8, 16.3%), idiopathic neonatal hepatitis (n=9, 18.4%), and others (n=4, 8.2%). Cholestatic features were found in all cases (100%). Giant cells containing bile were observed in 22 cases (44.9%). Moderate to severe fibrosis was present in 26 cases (53.1%). Varying degrees of portal inflammation were observed in all cases, while lobular inflammation was found in 20 cases (40.8%). Interface hepatitis was identified in 26 cases (53.1%).
Conclusion: This study demonstrated that the most common causes of neonatal cholestasis were biliary atresia and idiopathic neonatal hepatitis. However, a smaller proportion of cases were attributed to genetic or metabolic liver diseases.

E-PS-21-006
Histopathological features and seasonal distribution of chronic histiocytic intervillositis
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Background & Objectives: Chronic histiocytic intervillositis (CHI) is a rare placental lesion with high recurrence rates, characterized by maternal mononuclear cell infiltration in the intervillous space, often accompanied by perivillous fibrin deposition and trophoblast damage.

This study evaluates the clinical course, histopathological findings, and seasonal prevalence of CHI. This is the first study to investigate seasonal variations in CHI.
Methods: We analysed 32 CHI cases, assessing histomorphological findings like maternal vascular malperfusion (MVM), foetal vascular malperfusion (FVM), and inflammatory lesions based on Amsterdam Placental Workshop Group criteria. Seasonal distribution was evaluated by categorizing cases into four seasons. Poisson regression and chi-square tests were used for statistical analysis.
Results: Of the 32 cases, 10 were primiparous and 22 multiparous. Nine cases involved advanced maternal age (>34 years). Intrauterine foetal demise or abortion occurred in 18 cases. Foetal vascular malperfusion was present in 46% of cases, maternal vascular malperfusion in 28%, ascending intrauterine infection in 43%, chronic deciduitis in 46%, and chronic villitis of unknown aetiology in 12%. A higher risk of CHI was observed in fall and winter, though the trend was not statistically significant ($p > 0.05$) due to the small sample size.
Conclusion: CHI is associated with high recurrence rates (70%-100%) and significant foetal morbidity and mortality. While a potential seasonal trend was noted, the small sample size limits definitive conclusions. Larger studies are needed to confirm seasonal variations in CHI.

E-PS-21-007
Trophoblastic inclusions in stillborn placentas from third-trimester pregnancies: correlations with malperfusion and inflammation
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Background & Objectives: Placental abnormalities are among the most common causes of unexplained stillbirth. Trophoblastic inclusions, which result from abnormal infoldings of the trophoblast bilayer, have been associated with poor neurodevelopmental outcomes, including autism. This study investigates histological changes in placentas associated with stillbirth, particularly focusing on trophoblastic inclusions, using the standardized classification system proposed by the Amsterdam Placental Workshop Group.
Methods: This retrospective study analysed 76 placentas from pregnancies between 30 and 40 weeks of gestation, collected over a two-year period. The cases were categorized based on the presence (n=54) or absence (n=22) of trophoblastic inclusions. Clinical and pathological variables, including maternal age, gestational age, placental weight, maternal vascular malperfusion (MVM), foetal vascular malperfusion (FVM), villitis, intervillitis, and ascending infection, were examined. The criteria for MVM included placental hypoplasia, infarction, retroplacental haemorrhage, decidual arteriopathy, and developmental abnormalities such as distal villous hypoplasia and accelerated villous maturation. FVM findings encompassed thrombosis, segmental avascular villi, villous stromal vascular karyorrhexis, intramural fibrin deposition, stem vessel obliteration, and vascular ectasia. The pathologist reviewing the samples was blinded to demographic and clinical data. Descriptive statistics and group comparisons were employed to identify patterns associated with trophoblastic inclusions.
Results: Trophoblastic inclusions were identified in 71.1% of cases (n=54), while 28.9% (n=22) showed no inclusions. Placentas with trophoblastic inclusions had a higher mean weight (456 g) compared to those without inclusions (405 g). MVM was less frequent in the inclusion group (31.5% vs. 40.9%), while FVM was more common (57.4% vs. 31.8%). Villitis was observed in 20.4% of placentas with inclusions, compared to 40.9% in the non-inclusion group. Ascending infections were also more frequent in the inclusion group (20.3% vs. 13.6%).
Conclusion: These findings suggest a correlation between trophoblastic inclusions and specific placental pathologies, underscoring the need for further research to elucidate their clinical implications.

E-PS-21-008
A rare case of an adenomyoma found in a Meckel diverticulum
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Background & Objectives: Adenomyoma of the gastrointestinal tract is a tumour-like condition defined by the presence of glandular structures lined with mucus-producing columnar epithelium, interspersed with smooth muscle bundles. It is most commonly found in the pylorus of the stomach or the duodenum and is rarely observed in the small intestine. In paediatric cases, intussusception is the most frequently reported complication. Here, we present a case of adenomyoma occurring in a Meckel diverticulum.
Methods: A 12-year-old male patient was admitted to the hospital with a 48-hour history of abdominal pain, bilious-vomiting, diarrhoea, fever, and refusal to eat. Abdominal ultrasound revealed ileocolic intussusception, with approximately 10 cm of invaginated bowel loop and significant small bowel distension, indicating possible small bowel obstruction. A segmental enterectomy was performed the day after admission.
Results: A 3.5cm segment of intestine was examined. Upon opening the specimen, an invaginated diverticulum measuring 2.3×1.5×1.2cm was identified. Histological examination revealed an intestinal wall lined with enteric-type mucosa, exhibiting preserved villous architecture and confirming the diverticular lesion observed macroscopically. The lesion contained heterotopic gastric glands and dilated cystic glands surrounded by bundles of smooth muscle.
Immunohistochemical analysis demonstrated smooth muscle actin and focal desmin expression in the smooth muscle bundles, with EMA and focal MUC6 expression present in the cystic glands.
The final pathological diagnosis was adenomyoma arising within a Meckel diverticulum and gastric heterotopia.
Conclusion: We report a case of small intestinal adenomyoma arising in a Meckel's diverticulum. To date, only seven paediatric cases have been documented, with just one involving a Meckel's diverticulum. To our knowledge, this is the first case reported in Portugal. The rarity of this entity in the literature may stem from underreporting or limited recognition by both surgeons and pathologists. Greater awareness and increased vigilance in identifying this lesion may enhance detection and facilitate more frequent diagnosis.

E-PS-21-009
Meconium pseudocyst in a 2-day-old neonate: a case report of a rare congenital entity and possible association with MTHFR and CTFR gene mutations of the mother
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Background & Objectives: Meconium pseudocyst and meconium peritonitis are two rare congenital entities that co-exist in neonates with perforation of gastrointestinal tract leading to meconium leak into the peritoneal cavity.
Methods: A 20-year-old pregnant woman, carrier of mutation in CTFR gene of cystic fibrosis and heterozygous for MTHFR polymorphism (c677t) for thrombophilia presented at our gestational department at 22 weeks of gestation for the appointment of level 2 ultrasound. Ultrasound examination revealed gastrointestinal tract atresia of the neonate and an abdominal, intraperitoneal cystic lesion of maximum diameter

of 10 cm that extended from pelvis to liver. Cesarian section was performed at 37 weeks of gestation and the female infant was admitted to the neonate intense care unit. During the second day of life the neonate was subjected to surgical removal of the cyst and side-to-side small bowel anastomosis.
Results: Microscopic examination of the cyst wall showed a bowel-like layered structure consisting of muscularis propria (circular muscle and longitudinal muscle) and serosa with inflammation. Alongside the internal cystic layer, denuded of the typical intestinal epithelium, calcified, reactive, fibrovascular tissue was observed, which contained macrophages with intracytoplasmic meconium. Consequently, the diagnosis of meconium pseudocyst was established.
Conclusion: Meconium pseudocyst is formed in cases of sterile chemical irritation of the peritoneum (meconium peritonitis) secondary to bowel atresia or ileus. Gastrointestinal tract perforation provokes a fibrous reaction that results in the formation of a fibrous cyst around the leakage. Meconium pseudocyst and meconium peritonitis are associated with cystic fibrosis of the neonate. However, to our knowledge, there is no reported correlation of those entities with mutations in MTHFR gene. Our case report contributes to the literature presenting a rare case of congenital meconium pseudocyst and posing questions regarding the association of this occurrence with CTFR and MTHFR mutations.

E-PS-21-010
Orbital undifferentiated pleomorphic sarcoma in a 4-year-old child – a case that challenged the medical teams of two hospitals
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Background & Objectives: Undifferentiated pleomorphic sarcoma (UPS) is a highly rare and aggressive malignant tumour characterized by an unclear pattern of differentiation. It is most commonly reported in the long tubular bones of older adults, often presenting as a rapidly growing, destructive mass.
Methods: A 4-year-old male patient was admitted to the Neurosurgery Hospital Iași with remarkable unilateral proptosis of the right eye, decreased visual acuity and periocular pain and pressure. A head MRI identified an irregular orbital mass with intracranial extension. Following surgical intervention, tissue samples were collected for histopathological and immunohistochemical examination, conducted in collaboration with pathologists from Children's Hospital in Iași.
Results: The histopathological evaluation revealed a proliferation of atypical cells with numerous multinucleated giant cells (MGCs) and frequent mitosis (5-6/mm²). Immunohistochemical (IHC) analysis showed positivity for CD68 and Ki67 (10-20% of tumour cells) and negativity for Desmin, CD99, p63, and p53. Initially, a giant cell osteolytic and infiltrative bone tumour was suspected. Due to the patient's age, a second opinion was requested. Reevaluation in Children's Hospital identified the tumour proliferation destroying bone tissue, with numerous MGCs. Further IHC tests showed positivity for SMA (50% of tumour cells), CD68, and Ki67 (40%), while Myogenin, MyoD1, CD99, and S100 were negative. Based on these findings, the final diagnosis was orbital undifferentiated pleomorphic sarcoma.
Conclusion: Our patient was diagnosed with undifferentiated pleomorphic sarcoma of the right orbit, an unusual presentation both in terms of location and the patient's age. This case report is significant due to the complex clinical and histological features, which required collaboration between the pathology teams of two hospitals to achieve a thorough understanding and an accurate diagnosis.

E-PS-21-011
Transient abnormal myelopoiesis as a cause of intrauterine death in a foetus with Down Syndrome
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Background & Objectives: Transient abnormal myelopoiesis (TAM) is a hematologic disorder associated with trisomy 21 characterized by abnormal proliferation of cells of myeloid lineage. While TAM typically resolves in 2-3 months postnatally without treatment, some cases can lead to early death, particularly when associated with ascites, hepatomegaly and coagulopathy. TAM typically presents perinatally and is rare in the prenatal period. As such, cases of prenatal manifestation of TAM are particularly relevant as the current available data is still limited.
Methods: We report a case of intrauterine foetal demise (IUFD) of a male foetus with trisomy 21 at 32 weeks and 4 days of gestation. The mother was 45 years old and had two previous gestations resulting in two healthy children.
On prenatal screening at 11 weeks absence of nasal bones was detected leading to a diagnosis of trisomy 21 after amniocentesis, QF-PCR and karyotyping (47, XY, +21), upon which the mother refused termination.
At 32 weeks and 4 days of gestation the mother detected absence of foetal movements which prompted the visit to the ED where, upon confirmation of IUFD, delivery was induced with mifepristone.
Results: On foetal autopsy, besides minor defects associated with Trisomy 21, we detected splenomegaly and hepatomegaly which upon histological examination showed to be due to extensively increased extramedullary myelopoiesis. These findings are consistent with TAM and the cause of death was attributed to hepatic dysfunction secondary to excessive myelopoiesis and congestion.
The available literature highlights hepatosplenomegaly as one of the most common symptoms in cases of IUFD secondary to TAM.
Conclusion: Although typically perinatal, TAM can also present in utero with manifestations ranging from light and self-limiting to severe and fatal. This case is in line with the notion of TAM developing as a gradual process that begins in utero and highlights the need to recognize this diagnosis early.

E-PS-21-012
Placental mesenchymal dysplasia and foetal mesenchymal hamartoma: a case report of this extraordinary clinical presentation
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Background & Objectives: Placental mesenchymal dysplasia (PMD) is an extremely rare entity characterized by excessive mesenchymal proliferation in the chorionic villi, resulting in placentomegaly, multicystic appearance, and vascular abnormalities of the placenta. Only 11 cases of foetal hepatic lesions and PMD are reported in the PubMed database.
Methods: We present the case of a 41-year-old patient whose pregnancy was complicated with foetal growth restriction (FGR) and oligohydramnios. Multiple and focal vascular placental cysts, and a hepatic foetal cyst were detected in ultrasound studies. Genetic analysis of the amniotic fluid was normal. Labor was induced at 30 weeks of

pregnancy due to progressive foetal deterioration. The foetal lesion was surgically removed after birth.
Results: Macroscopic examination of the placenta revealed placentomegaly, and multiple and focal cystic formations arranged in clusters, predominantly on the maternal surface. Histologically, enlarged villi with stromal overgrowth, myxoid stroma, cistern-like spaces, and poor vascularization were observed interspersed with smaller villi containing small peripheral vessels. Immunohistochemical p57 staining showed preserved expression in cytotrophoblast cells but a total loss of expression in villous mesenchymal cells. The hepatic lesion was a solid and cystic mass with primitive mesenchyme and myxoid stroma, consistent with a mesenchymal hamartoma.
Conclusion: The coexistence of a hepatic mesenchymal hamartoma and PMD has been extraordinarily reported. However, the similarities in their histopathological and pathogenetic characteristics suggest a possible common embryonic origin. This origin may be linked to genetic alterations in growth regulation, particularly androgenetic/biparental mosaicism and the genetic methylation of the 11p15.5 locus, which has been implicated in both entities. PMD is associated with FGR, stillbirth, neonatal death, structural malformations and genetic syndromes - specially the Beckwith-Wiedemann syndrome (reported in 20% of the cases). This case highlights the importance of an integrated prenatal approach, including clinical, imaging, genetic and histopathological assessments, to achieve an accurate diagnosis and guide appropriate perinatal care.

E-PS-21-013
Undifferentiated embryonal sarcoma of the liver arising from mesenchymal hamartoma in a paediatric patient: a case report
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Background & Objectives: Undifferentiated embryonal sarcoma (UESL) and mesenchymal hamartoma of the liver (HMH) represent mesenchymal tumours with overlapping clinicopathological characteristics and identical chromosomal abnormalities. The diagnostic challenge arises from their similar presentations, requiring careful histopathological and immunohistochemical examination to distinguish between them.
Methods: We report a challenging UESL case in a 4-year-old male who was admitted to emergency room in critical status due to epileptic seizures. Following extensive assessments, radiological findings revealed a well-defined solitary mass in the left hepatic lobe, with no signs of metastatic disease. Tissue samples were taken and processed for extemporaneous, histopathological, and immunohistochemical examination to confirm the diagnosis.
Results: The extemporaneous examination suggested immature teratoma while haematoxylin-eosin evaluation revealed a proliferative area, displaying a nodular, heterogeneous architecture with hyperplastic and irregular biliary ducts within a myxoid or fibrous stroma. Immunohistochemical analysis showed positivity for CK7 and AE1/AE3 in ductular epithelium, along with focal positivity for S100. Subsequently, foci of spindle cell proliferation with highly pleomorphic cells, with unclear cell borders, large and hyperchromatic nuclei, prominent nucleoli, frequent atypical mitoses and eosinophilic PAS-positive globules disposed in myxoid stroma with necrotic areas were identified. The immunohistochemical profiling showed a focal positive reaction for vimentin and desmin, along with negative expression for myogenin and myoD1. Ki67 was positive in 30% of tumour cells.
Conclusion: The malignant transformation of HMH into UESL is particularly rare, with only a few reported cases in paediatric patients. Our case highlights the critical role of immunohistochemistry in distinguishing HMH from other paediatric tumours, as clinicoradiological features are nonspecific. Additionally, its unusual location and incidental presentation further complicate the diagnosis in our patient. Understanding the oncogenic mechanisms and implementing a targeted diagnostic approach are essential for accurate risk assessment and tailored treatment in such complex cases.

E-PS-21-014
Placenta with multiple chorangiomas: a case report of a rarely documented entity
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Background & Objectives: Placental chorangioma is a benign, nontrophoblastic neoplasm of uncertain aetiology. It has been suggested that hypoxia may induce the overexpression of vascular growth factors, creating a favourable environment for capillary proliferation. Chorangiomas are most often asymptomatic and of little consequence. Nonetheless, large (>4cm) or multiple tumours can affect foetal circulation. Multiple lesions are associated with serious complications, usually leading to intrauterine foetal demise or perinatal death.
Methods: We present the case of a 33-year-old pregnant patient with a long history of iron-deficiency anaemia and a well-controlled vitamin B12 deficiency, positive for anti-parietal cell antibodies. Aside from anaemia (haemoglobin: 8.9g/dL, low ferritin, normal vitamin B12) detected in the third trimester, the pregnancy was otherwise uneventful. Vaginal delivery occurred at 38 weeks, resulting in a live birth (Apgar score: 9/10/10, weight: 3330g)**.** Due to the unusual appearance of the placenta, it was sent to the Department of Pathology for further evaluation.
Results: Gross examination revealed a fragmented placenta with a total weight of 870g (>97th percentile). Focal pale areas and multiple nodular lesions were identified, the latter measuring between 0.5 and 5.5cm and comprising 40-50% of the placental volume. The cut surface of the lesions consisted of haemorrhagic, cystic, necrotic, and solid yellow areas. Histopathological analysis showed multiple chorangiomas of different morphological variants, many of which had areas of necrosis. Focal syncytiotrophoblast hyperplasia, delayed villous maturation, diffuse chorangiosis, and chorangiomatosis were also observed.
Conclusion: Multiple chorangiomas are associated with poor foetal outcomes and a high mortality rate, which contrasts with the result of this case. Our case involved not only multiple lesions but also large ones, along with a newborn delivered without complications and, to date, showing adequate psychomotor development. Maternal anaemia may have contributed to the overall presentation, although the exact aetiology remains unknown.

E-PS-21-015
Autopsy findings in a case of autosomal recessive polycystic kidney disease associated with polydactyly: a case report
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Background & Objectives: Autosomal recessive polycystic kidney disease (ARPKD) is a rare hereditary disorder affecting the kidneys and hepatobiliary system, often leading to perinatal morbidity and mortality. The disease is caused by mutations in the PKHD1 gene. While ARPKD is primarily a renal and hepatobiliary disorder, it's association with limb anomalies such as polydactyly has been reported in rare cases. This report presents a foetal autopsy case diagnosed prenatally with ARPKD and polydactyly at 14 weeks of gestation.
A 24-year-old pregnant woman with a history of consanguinity underwent ultrasonography at 14 weeks and 3 days of gestation. However,

the kidneys appeared hyperechoic and polycystic. At 16 weeks, follow-up ultrasonography showed bilateral multicystic kidneys and oligohydramnios. Based on these findings and the parental decision, the pregnancy was terminated.
Methods: A foetal autopsy was conducted, including macroscopic and routine haematoxylin-eosin histopathological examination.
Results: External examination revealed maceration, low-set ears, micrognathia, and a contracted appearance of the left-hand fingers. The hands had five fingers each, while both feet had six toes. The right upper and lower extremities were contracted. Both kidneys contained multiple cystic masses, the largest measuring 0.5 cm. Histopathological examination confirmed the presence of cystically dilated collecting ducts, characteristic of ARPKD. The renal architecture was distorted, with the replacement of normal parenchyma by multiple cysts. No evidence of hepatic fibrosis was observed in this case. Additionally, the presence of polydactyly suggests a syndromic association, possibly overlapping with ciliopathies.
Conclusion: Detailed ultrasonographic evaluation in early gestation allows for timely diagnosis of ARPKD, facilitating informed decision-making for affected families. The presence of polydactyly in association with ARPKD may suggest an extended ciliopathy spectrum, warranting further genetic and syndromic evaluation. Genetic counselling is crucial, especially in cases with a history of consanguinity, to assess recurrence risks and provide reproductive guidance.

E-PS-21-016
Cornelia de Lange syndrome phenotype in perinatal period: a multi-case pathological analysis
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Background & Objectives: Cornelia de Lange syndrome is a rare genetic disorder characterized by developmental abnormalities, facial dysmorphism, and intellectual disability. Diagnosis is clinically suspected and can be confirmed by genetic testing (cohesin complex). There are few descriptions of foetal phenotype.
Methods: We reviewed our autopsy records from 1967 to 2023, and found five cases of Cornelia de Lange syndrome. All have complete autopsy, radiological study, and placental examination (according to the Amsterdam Consensus classification).
Genetic tests were carried out in the four most recent cases. Our results were compared with previously published studies.
Results: The age of the cases ranged from 17 weeks of gestation to 3 months. In our five cases, we observed a wide range of anatomical abnormalities. Limb deformities and skeletal anomalies were present in all cases, while typical facial features were observed in four cases. Microcephaly and synophrys were each identified in three cases, and hirsutism in two cases. Structural cardiac, renal, and digestive malformations were noted in four cases. As a significant finding, two cases presented with diaphragmatic hernia and umbilical hernia respectively, and two cases had intrauterine growth restriction.
Considering the clinical minor, major, and genetic diagnostic criteria, two cases were diagnosed based on only clinical signs, while the three more recent cases were confirmed through genetic analysis, all of them with a pathogenic variant in the NIPBL gene which belongs to the cohesin complex.
Conclusion: This research enhances our understanding of Cornelia de Lange syndrome phenotype in the foetal period, in terms of the complexity and diversity. This series illustrates that this syndrome can be diagnosed in foetus after induction and in newborns at birth as the phenotype is presents early. Sustained research efforts and a multidisciplinary approach are indispensable for accurate prenatal diagnosis and prognosis of these patients.

E-PS-21-017
Pathological analysis of lesions associated with vein of Galen aneurysm: an autopsy study (1967–2024)
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Background & Objectives: Vein of Galen aneurysmal malformations (VGAM) are congenital vascular anomalies of the cerebral venous system, classified as arteriovenous malformations (AVMs). VGAM represents the most prevalent vascular malformation in foetal and paediatric populations. The clinical-pathological impact varies depending on malformation severity and medical interventions.
This study reviews autopsy cases of VGAM, analysing their epidemiological characteristics and pathological findings.
Methods: A retrospective search of autopsy cases from 1967 to 2024 was conducted at a tertiary hospital to identify VGAM diagnoses. Pathological reports were reviewed to extract clinical-pathological variables.
Results: Nine cases were identified, with a mean gestational age of 37 weeks. One case (11.1%) involved intrauterine death, while the remaining postnatally survived for 6 hours to 21 days. Male predominance was noted (66.7%), and one case (11.1%) involved a twin pregnancy. Aneurysmal rupture with subdural haemorrhage occurred in two cases (22.2%), and thrombosis with subarachnoid haemorrhage in one (11.1%). Acute neuronal necrosis affected seven cases (77.7%), involving multiple CNS regions in three (33.3%). White matter gliosis was observed in four cases (44.4%), diffusely in two (22.2%). Additional findings included basilar AVM (11.1%) and periventricular leukomalacia (11.1%). Regarding the heart involvement, myocardial anomalies were present in five cases (55.6%). Atrial septal defect (22.2%), persistent ductus arteriosus (11.1%), and myocardial infarction (11.1%) were detected. Foetal hydrops was identified in one case (11.1%).
Conclusion: AVMs are characterized by abnormal arterial-to-venous drainage, leading to venous stasis and reduced systemic perfusion due to shunting. VGAM arise from embryological alterations involving multiple arteriovenous shunts in the prosencephalic vein of Markowski, precursor of the vein of Galen.
Cardiomegaly was the most frequent pathological finding, present in over half of the cases. Severe heart failure may lead to foetal hydrops. Neurological complications from vascular compression and shunting contribute significantly to morbidity and mortality, as evidenced by the high incidence of hypoxic-ischemic encephalopathy.

E-PS-21-018
Severe colitis and accelerated adenoma development in an adolescent with a homozygous ITGAV variant
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Background & Objectives: Integrin heterodimers containing an Integrin alpha V subunit (ITGAV) are crucial for development and play significant roles in cell adhesion and signalling. Reduced ITGAV expression/function has been associated with severe embryonic defects, neurodevelopmental disorders, vision impairment, atopy, and inflammatory bowel disease (IBD), with varying

phenotypic manifestations depending on whether the loss of function is complete or incomplete.
Methods: A 15-years-old male patient with a long-standing history of severe colitis, managed with prednisolone, azathioprine and infliximab, associated with growth problems, eye abnormalities, dermatitis, alopecia, and multiple food allergies, was identified as a carrier of a homozygous "ITGAV NM_002210.4: c.1136A>T" variant. In late 2024, he underwent a colonoscopy which revealed multiple polyps, that were not present in a prior examination two years earlier. Histological, these polyps were adenomas with both low- and high-grade dysplasia. In January 2025, a total colectomy surgery was performed.
Results: Examination of the total colectomy specimen identified 10 sessile and pedunculated polyps, with the largest measuring 4.3 cm. Several subcentimeter polyps were also noted. The adenomas predominantly exhibited tubular architecture with low-grade dysplasia; larger adenomas showed pseudo-invasion, with mucus extravasation and focal calcification. Lamina propria of both the polyps and surrounding mucosa was permeated by moderate/severe lymphoplasmacytic infiltrate with eosinophils. No invasive neoplasia was detected.
Conclusion: The described ITGAV variant is associated with severe IBD, but its role in carcinogenesis remains unclear. Although ITGAV expression has been observed in multiple cancers, its specific involvement in digestive system cancer is not well understood. This case represents the first known patient with this variant to reach adolescence, providing novel insights into its potential carcinogenesis effects. The early-onset and rapid development of adenomatous lesions highlights the need for further investigation into ITGAV's contribution to tumour progression.

E-PS-21-019
Testicular adrenal rest tumours in congenital adrenal hyperplasia
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Background & Objectives: Congenital adrenal hyperplasia (CAH) is an inherited disorder that impairs adrenal steroid synthesis. In male CAH patients, testicular adrenal rest tumours (TARTs) are a significant complication, often confused with Leydig cell tumours (LCTs). This case report highlights the diagnostic challenges of TARTs and the importance of long-term monitoring in CAH patients.
Methods: A 15-year-old male with 21-hydroxylase deficiency (CYP21A2 mutation) was referred after scrotal ultrasonography detected a left testicular mass, suggestive of TART. The patient had been diagnosed with CAH during infancy following an episode of diffuse hyperpigmentation and adrenal crisis. In 2024, he underwent surgery for a right testicular mass, which was histopathologically diagnosed as a Leydig cell tumour (LCT) at another medical centre. After the surgery, the patient was treated with hydrocortisone for six months.
Results: During a routine follow-up, scrotal ultrasonography revealed a lesion in the left testicle, consistent with TART. A reevaluation of previous biopsy specimens further supported this diagnosis. The histopathological examination showed sheets, nests, and cords of polygonal cells with abundant eosinophilic cytoplasm. Some cells contained lipochrome pigments, but Reinke's crystals were absent. The cells exhibited mild nuclear pleomorphism without mitotic activity. Immunohistochemical analysis revealed positive staining for inhibin and calretinin in the lesion cells. These findings, along with the absence of Reinke crystals, confirmed the diagnosis of TART and suggested a favourable prognosis.
Conclusion: This case highlights the diagnostic challenges in differentiating between TART and LCT in patients with CAH. The absence of Reinke crystals were critical in distinguishing TART from LCT. This case also emphasizes the necessity of long-term endocrine and radiological follow-up to ensure accurate diagnosis and appropriate management of CAH patients. Early and accurate diagnosis of TART can lead to a more favourable prognosis and better patient outcomes.

E-PS-21-020
Pentalogy of Cantrell: rare and challenging cases
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Background & Objectives: The Pentalogy of Cantrell is a sporadic congenital syndrome characterized by midline defects of the sternum, diaphragm, pericardium, anterior abdominal wall, and heart. The exact aetiology of the syndrome is unknown and has yet to be discovered.
Diagnosis of Pentalogy of Cantrell and its individual manifestations is based primarily on prenatal ultrasound screening. Early prenatal diagnosis helps families make informed decisions regarding pregnancy and, if necessary, determine the extent of the disability for planning subsequent therapeutic strategies. Treatment for Cantrell's pentalogy depends on the defects' presence and extent. This syndrome may be associated with chromosomal aberrations and genetic testing can be a valuable part of the multidisciplinary diagnostic process.
Methods: We selected relevant cases from our laboratory's archive, evaluated them in detail, and categorized them.
Results: We present two cases from the spectrum of the Pentalogy of Cantrell.
Conclusion: The diagnosis of Pentalogy of Cantrell is challenging, especially in foetuses in low gestational weeks. The advantage is a multidisciplinary approach and detailed examinations leading to an assessment of the extent of the defects, determination of the syndrome subtype and determination of possible therapy. For families, it is appropriate to supplement genetic testing, which can influence their informed decision-making about pregnancy.
In the event of termination of pregnancy, it is up to the pathologist to confirm the correctness of the diagnosis or to determine the diagnosis itself through autopsy.

E-PS-21-021
A rare presentation of neurofibromatosis coli in a paediatric patient
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Background & Objectives: In patients with neurofibromatosis type 1 (NF1), gastrointestinal neurofibromas may present as widespread GI involvement or as isolated, sporadic lesions. NF1 is an autosomal dominant condition that affects approximately 1 in 3,000 individuals. Approximately 25% of NF1 patients develop gastrointestinal manifestations, including neurofibromas originating from the myenteric plexus. These tumours can lead to complications such as bleeding, melena, obstruction, and abdominal pain. Neurofibromas may affect various parts of the gastrointestinal tract, including the jejunum, stomach, ileum, duodenum, and colon. While typically solitary, multiple serosal and mucosal polypoid nodules can develop in patients with NF1.
Methods: A 6-year-old female patient presented with chronic diarrhoea and hyperpigmented lesions (café-au-lait spots) that had persisted for

five years. Additionally, the patient had a history of frequent respiratory tract infections.
Results: Physical examination revealed cryptitis in the left tonsil, while the abdominal examination showed no abnormalities. Due to persistent diarrhoea, a colonoscopy was performed, which revealed multiple firm, white polyps measuring 10 to 15 mm in the transverse colon, sigmoid colon, and rectum. Histopathological analysis of colonic biopsies identified neoplastic formations composed of neural cells, Schwann cells, and fibroblasts with spindle shaped morphology and polypoid structures localized within the colonic mucosa. Immunohistochemical studies showed positive staining for S100 and CD34, while DOG-1, CD117, and desmin were negative. Laboratory tests indicated a low naive B cell level (36%), and further investigations for common variable immunodeficiency disease are ongoing.
Conclusion: Histological findings, in correlation with clinical data, support a diagnosis of neurofibromatosis coli (diffuse/submucosal neurofibromatosis). Nutritional supplementation has been arranged to manage diarrhoea, and the patient will be closely monitored due to the potential for recurrent polyps.

E-PS-21-022
Lethal perinatal hypophosphatasia caused by a novel mutation in the ALPL gene
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Background & Objectives: Perinatal hypophosphatasia is a rare genetic disorder caused by mutations in the ALPL gene, leading to decreased tissue-nonspecific alkaline phosphatase (TNAP) activity and impaired bone mineralization. The severe perinatal form is associated with intrauterine complications such as short and curved bones, lack of skeletal mineralization, and pulmonary hypoplasia. This case report presents a diagnosis of perinatal hypophosphatasia at 19 weeks of gestation.
Methods: A 23-year-old mother underwent foetal ultrasound at 19 weeks, revealing micrognathia, short ribs, micromelia, and absent nasal bone. Limb lengths were below the 1st percentile, with hypomineralization observed. The pregnancy was terminated due to severe findings. X-ray imaging and histological examination of the femur were performed. Exome sequencing was conducted on a foetal skin sample to identify ALPL gene mutations.
Results: Imaging showed diffuse osteoporotic bone structure, lack of cranial ossification, thin and deformed ribs, and shortened, bowed femurs and humeri. No ossification was observed in the tibia and fibula. External examination revealed a hypoplastic cranium, epicanthal folds, flattened ears, a thick nasal bridge, and micrognathia. Histological analysis of the femur showed hypercellularity and disorganization. Exome sequencing identified a homozygous pathogenic variant in the ALPL gene.
Conclusion: This case highlights a severe form of perinatal hypophosphatasia caused by a novel ALPL gene mutation, leading to significant bone abnormalities and mineralization defects. Early diagnosis is crucial, and further data on the clinical course of the disease are needed.

E-PS-21-023
Gross and histopathological findings of 111 triplet placentas: a descriptive analysis
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Background & Objectives: Triplet pregnancies have increased over the past few decades due to an increase in assisted reproductive technology (ART). They are considered high-risk pregnancies, and placental evaluation is key for understanding the pregnancy outcomes. Triple placentas pathological findings have not been thoroughly described.
Methods: This is a retrospective observational study that includes all triplet pregnancies followed up in a tertiary referral hospital for multiple pregnancies between January 2000 and December 2024 whose placentas were sent for analysis in a Pathology Department. Gross and pathological placental findings were examined.
Results: A total of 111 triplet pregnancies (333 foetuses) were analysed. Miscarriages or stillbirths occurred in 7.5% of the foetuses. Up to 70.3% of the cases were conceived by ART. The median gestational age at delivery was 32 weeks (P25=30; P75=34). Most cases (50.4%) were trichorionic triamniotic. The mean placental weight was 869±243 g and the median placental size was 22.5 cm (P25=18; P75=30). They presented up to 52.2% of abnormal umbilical cord insertion (marginal or velamentous) and a total of 43.8% of the placental discs showed both central and peripheral intraparenchymatous infarcts (from 0.4 to 3.2 cm). The most frequent histopathological findings were accelerated villous maturation (65.1%), chorangiosis (53.7%), intervillous fibrin deposits (29.4%) and villous oedema (24.3%). The most frequent finding within the inflammatory pattern was chronic villitis of unknown aetiology (9.3%).
Conclusion: Triplet placentas present high rates of gross and pathological abnormalities that may be related to the complications developed in these high-risk pregnancies. Further studies are needed to analyse whether these findings are related to factors such as chorionicity or ART.

E-PS-21-024
Exploring the rare co-occurrence of chronic histiocytic intervillositis and massive subchorionic thrombohematoma: pathological insights into placental dysfunction and foetal loss
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Background & Objectives: The co-occurrence of Chronic Histiocytic Intervillositis (CHI) and a Massive Subchorionic Thrombohematoma (Breus' Mole) in the same placenta is an extremely rare and complex pathological scenario. Both conditions can contribute to adverse pregnancy outcomes, and their simultaneous presence may indicate significant maternal-foetal interactions and placental dysfunction.
The aim of this study is to examine the pathological findings in a case of IUFD at 18 weeks, focusing on the presence of significant placental features including a large subchorionic hematoma, chronic histiocytic intervillositis (CHI), elevated perivillous fibrin deposition. Understanding these features will provide insight into the pathophysiology of IUFD and the role of placental pathology in foetal loss.
Methods: A placental specimen was subjected to histopathologic examination. Standard haematoxylin and eosin (H&E) staining was performed to assess general tissue structure and inflammatory changes. Immunohistochemistry was used for CD68 and CD3 to evaluate the presence and extent of macrophage infiltration (CHI) and T-cell involvement in the villous tissue (VUE). Additionally, the degree of fibrin deposition was assessed to determine placental insufficiency and its potential contribution to foetal demise.
Results: Histopathologic examination revealed a massive bubchorionic thrombohematoma , which likely contributed to uteroplacental insufficiency. Moreover the placenta also demonstrated elevated perivillous fibrin deposition, indicating compromised placental function. Immunostaining for CD68 highlighted moderately sized clusters of macrophages, indicating chronic histiocytic intervillositis (CHI).
Conclusion: This is the first report of these two pathologies co-occurring, raising the possibility of a relationship between chronic histiocytic intervillositis and Breus' Mole.
These findings highlight the complex nature of placental pathology and its crucial role in understanding the mechanisms behind early foetal

loss. Further studies on the interplay of these pathologic features are needed to refine our understanding of their clinical significance and potential impact on pregnancy outcomes.

E-PS-21-025

Underestimated cranial nerve involvement in spinal muscular atrophy type 1: the need for immunohistochemical staining

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Background & Objectives: Spinal muscular atrophy type 1 (SMA1), also called Werdnig-Hoffman disease, is the most severe form of spinal muscular atrophy, characterized by hypotonia from early infancy and difficulties in swallowing and breathing. The histopathological diagnosis of cranial nerve involvement is challenging due to anatomical and embryological complexities, limitations in histopathological characterization, and the availability of specific immunohistochemical markers. Furthermore, the limited experience with cranial nerve pathologies complicates their precise identification. Some authors have proposed the term "brainstem dysgenesis" to describe these abnormalities. The aim is to perform a detailed neuropathological analysis of motor neuron populations in individuals with SMA1.
Methods: We reviewed our records of clinical autopsies foetal (from week 22), perinatal, and infant from 1967 to 2019 and 10 cases of SMA1 were found. These cases were reevaluated and the tissue samples were reprocessed with haematoxylin-eosin and Cresyl violet staining, along with immunohistochemical analysis using choline acetyltransferase (ChAT) and other markers to evaluate motor neuron involvement in the brainstem and spinal cord.
Results: Cranial nerve degeneration and intense gliosis was detected in all cases. Regarding the cranial nerves involved, the hypoglossal nerve (XII) was most frequent (9/9 cases), followed by the facial (VII, 3/9), oculomotor (III, 2/9), abducens (VI, 1/9), and vagus (X, 1/9) nerves. Additionally, the spinal cord exhibited atrophy, gliosis, and/or neuronal degeneration in the anterior horn in five cases. The immunohistochemical analysis with ChAT demonstrated greater cranial nerve involvement compared to initial histopathological evaluation.
Conclusion: Haematoxylin-eosin staining alone may underestimate cranial nerve involvement in SMA1 and other disorders affecting cranial nerves. Incorporating specific immunohistochemical studies is recommended to enhance the identification of motor neurons in suspected cases. We support the term "brainstem dysgenesis" to better characterize histopathologically similar entities, suggesting that SMA1 shares features with other motor brainstem dysgenesis.

E-PS-21-026

A rare foetal case of congenital erythropoietic porphyria: Importance of prenatal and postmortem evaluation

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Background & Objectives: Congenital erythropoietic porphyria (CEP) is a severe autosomical recessive disease due to a uroporphyrinogen III synthase deficiency, leading to uroporphyrinogen I accumulation that cannot be metabolized into haemoglobin. Prenatal manifestations include anaemia, haemolysis and hydrops fetalis.
Methods: We presented a case of legal pregnancy termination diagnosed using fluorescence analysis of amniotic fluid. A complete autopsy study was performed, including postmortem radiography, placental examination and genetic analysis of foetus and parents using Sanger sequencing. Additionally, a review of autopsy records of our centre from 1967 to 2024, identified eight porhyria cases, with this being the only foetal case.
Results: A male foetus at 21 weeks of gestation with appropriate somatometry and development for gestational age was analysed. Notable findings included generalized subcutaneous oedema, pleural and pericardial effusion, severe extramedullary haematopoiesis with diffuse hepatic siderosis, and circulating nucleated red blood cells indicating anaemia. Additionally, the foetus showed facial dysmorphism with closed palpebral fissures, anteverted nares, elongated philtrum, thin upper lip, micrognathia, short nasal bridge, and low-set ears. Pulmonary hypoplasia and a renal cortical cyst with hemosiderosis were observed. Radiological findings showed mildly shortened long bones with coarse trabeculation suggestive of osteopenia. Foetal skin genetic analysis revealed NM_000375.3(UROS): c.217>C (p.Cys73Arg) mutation in homozygosity and parents in heterocygosis.
Conclusion: Our findings present a rare case of CEP, a genetic condition rarely found in autopsy literature. However, the limited cases available exhibit similar anatomical-pathological features. These results highlight the importance of fluorescence analysis in amniotic fluid as an accessible and useful tool for anteantal diagnosis in suspected cases. Furthermore, postmortem studies including placental examination, provide critical insights for planning future pregnancies and recurrence risk assessing.

E-PS-21-027

Diffuse systemic lymphangiectasia, renal cystic dysplasia, and cystic hygroma: a case report from foetal autopsy. What does this indicate to us?

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Background & Objectives: Congenital/foetal generalized lymphangiectasia is a rare condition characterized by the dilation of lymphatic vessels. . Cystic hygroma is a macrocystic lymphatic malformation that typically occurs in the posterior triangle between the neck and axilla in 75% of cases. Renal dysplasia is observed in 2% of paediatric autopsies. The conditions categorized under renal dysplasia include multicystic dysplasia, renal agenesis, hypoplastic dysplasia, segmental dysplasia, and congenital hydronephrosis, both with and without dysplasia. These lesions are primarily of developmental origin, but they may also be part of a syndromic association with a genetic basis.
Methods: We present a case of a 17-week foetal termination performed at the family's request due to prenatal findings.
Results: The moher is a 26-year-old woman with no known complaints or diseases. There is no consanguinity between the parents. Prenatal-ultrasound examination revealed widespread soft tissue oedema, a large cystic hygroma in the neck, atrophic changes in the kidneys, increased echogenicity of the abdominal fluid, and anhydramnios. After termination, foetal autopsy revealed a foetus weighing 223 grams with body measurements consistent with the gestational age of 17-weeks. The autopsy findings showed 4x4 cm cystic lymphangioma in the neck, diffuse systemic lymphangiectasia, and renal cystic dysplasia in the right kidney. Based on these combined findings, a possible chromosomal anomaly was considered a primary concern. Chromosomal analysis performed on the amniotic fluid was completed following the foetal autopsy examination and was reported as consistent with classic Turner syndrome.
Conclusion: Pathological conditions from different spectrums of chromosomal anomalies may be encountered in foetal autopsy

examinations. Although the prenatal imaging and autopsy findings in our case are consistent with Turner syndrome, it is evident that the existing data can suggest a chromosomal anomaly even without the results of chromosomal analysis. We found it valuable to present our case due to the presence of different pathological findings observed together.

E-PS-21-028

Combined vascular malformation of the lung associated with extralobar pulmonary sequestration: a rare neonatal case

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Background & Objectives: Combined vascular malformations (CVMs) are congenital anomalies characterized by the coexistence of two or more types of malformed vascular channels—most commonly venous, lymphatic, capillary, or arterial—within a single lesion. According to the ISSVA classification, CVMs are structural, non-neoplastic lesions that grow proportionally with the individual and may not be clinically apparent at birth. Their recognition is essential for diagnosis, management, and distinguishing them from vascular tumours.
Methods: A term neonate (38w2d, 2907g) born at Akdeniz University Faculty of Medicine was admitted to the NICU for observation due to a prenatal diagnosis of a right-sided thoracic mass. MRI findings revealed a large cystic lesion occupying the right hemithorax, with a vascular pedicle arising from the descending aorta, suggestive of pulmonary sequestration. The patient was discharged after 1 day of non-invasive support and referred to paediatric surgery. At 1 month of age, the sequestered extralobar lung tissue was surgically excised.
Results: Histopathologic examination of the excised lung tissue revealed abnormal, dilated vascular channels located in subpleural, septal, and peribronchial areas. Immunohistochemistry showed CD34 positivity in all malformed structures, with partial CD31 positivity indicating venous features. Absence of epithelial markers Pan-CK and TTF-1 excluded neoplastic or epithelial components. Elastic staining and SMA highlighted elastic lamina and smooth muscle layers, consistent with venous vessel morphology. These findings confirmed a **combined vascular malformation with venous and lymphatic components** in association with extralobar sequestration.
Conclusion: This case highlights the importance of integrating imaging, histopathology, and immunohistochemistry for diagnosing complex vascular malformations in neonates. Combined vascular malformations involving the lung are exceptionally rare and may coexist with other congenital anomalies such as pulmonary sequestration. Awareness of this entity is critical for accurate diagnosis and tailored surgical management.

E-PS-21-029

The bacteriological and virological investigation of stillbirth: further guidance is required to improve diagnosis and standardisation of testing

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Background & Objectives: In the UK stillbirth affects 3.9 per 1000 births[1], of which 10-25% may be caused by an infection[2]. There are no current guidelines detailing optimal specimen type and laboratory testing procedures for different pathogens, and there is variation in practice.
To determine current practices for bacteriological and virological investigation of stillbirth to facilitate development of local guidelines.
Methods: Bacteriological and virological tests performed on post-mortem stillbirth samples received at a regional UK laboratory over a 2-year period (20/4/2021 – 20/4/2023) were reviewed.
Results: Virology: 57 samples were received from 53 stillbirths: 49 liver tissue, 6 lung tissue, 1 splenic tissue, 1 heart swab.
There was considerable variation in test selection, with a selection of 9 PCRs performed: CMV, EBV, adenovirus, HSV-1, HSV-2, VZV, parvovirus, toxoplasma and enterovirus. No specimens were tested for syphilis.
All tests were negative except for 2 positive CMV PCRs (both deemed clinically significant) and 1 weak-positive adenovirus PCR (uncertain clinical significance). Negative PCR results may be useful in providing evidence for lack of infection.
Bacteriology: 72 samples were received for bacterial culture from 39/53 stillbirths. The most common sample types were heart swabs (26), lung swabs (23), and lung tissue (13).
Bacterial growth occurred in 40% of samples, with E.coli, Enterococcus faecium and Pantoea spp most frequently isolated.
Conclusion: There was variability in both specimen types and test selection. In our series the most common specimen types were liver tissue for viral PCRs and heart and lung swabs for bacterial culture. The optimal sample type for investigation of different pathogens is unclear, and interpretation of clinical significance of results can be difficult.
Maternal serological results are often not available alongside foetal samples to assist interpretation of results and guide appropriate test selection.
Development of guidelines would be helpful to improve microbiological investigation of stillbirths and reduce variation in practice.

E-PS-21-030

Immunohistochemical features of the germinal matrix in children with extremely low body weight and intraventricular haemorrhages

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Background & Objectives: The most prevalent complication in infants with extremely low birth weight is intraventricular haemorrhage (IVH). This condition affects the germinal matrix, a specialized tissue composed of numerous thin-walled blood vessels located in the region of the lateral ventricles of the brain. When exposed to a harmful stimulus, such as hypoxia, an apoptotic cascade is triggered, directly inhibiting the proliferation of neural progenitor cells, glial cells, and the intricate vascular network within the brain. The aim of the study was determination the level of CD31 and CD95 expression intensity in the germinal matrix of infants born with extremely low birth weight with IVH.
Methods: The material of the brain tissue of the lateral ventricles of 10 newborns born at 22-25 weeks of gestation with a body weight from 500 to 1000 g, who developed LVH, was studied. The life span ranged from several hours to 11 days after birth. The sections were stained with haematoxylin and eosin, immunohistochemical (IHC) staining with CD95 (inductor of apoptosis) and CD31 (marker of endotheliocytes and indicators of angiogenesis).
Results: During the IHC analysis, notable CD95 immunoreactivity was detected in ependymal cells and CD31 in endotheliocytes of

germinal matrix. The greatest expression of CD95 and CD31 was observed in the area of rupture of the vascular wall of the microcirculatory bed. A negative correlation was observed between marker expression and gestational age.
Conclusion: Increased apoptosis was observed in areas of vascular wall damage and ependymal lining destruction. This may indicate a significant role of apoptosis in the pathogenesis of IVH. The pattern of CD31 expression indicates active angiogenesis, which in turn shows the extreme importance of the morphofunctional state of the germinal matrix. Further studies of the pathogenesis of IVH in premature infants are needed to develop preventive strategies.

E-PS-21-031
A rare case with an unusual location: immature teratoma of tongue in a foetus
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Background & Objectives: Teratomas are the most common congenital tumours. While they predominantly occur in the sacrococcygeal and gonadal regions, head and neck presentations are rare, accounting for approximately 5% of all cases. Within the head and neck, the nasopharynx and cervical regions are the most affected sites. Teratomas of the tongue are exceedingly rare. Here, we present a case of an immature teratoma arising from the tongue in a foetus.
Methods: A 31-year-old woman at 17 weeks and 6 days of gestation, conceived naturally from a consanguineous marriage, underwent prenatal ultrasonography. The examination revealed a mass in the oral cavity. Subsequently, a medical abortion was performed.
Results: Gross examination at autopsy revealed a 5.5×3×1.5 cm exophytic lesion originating from the base of the tongue and protruding from the oral cavity. The lesion had a soft consistency with focal firm areas and a surface covered with papillary projections. Microscopic examination of the tumour demonstrated a heterogeneous lesion composed of varying proportions of bone, cartilage, skin adnexa, and glandular tissue. An immature component was identified, characterized by the presence of neuroepithelial tissue. The immature neuroepithelium exhibited neural tube formation and rosettes structures. Based on these findings, a final pathological diagnosis was immature teratoma.
Conclusion: Tongue teratoma is a rare congenital tumour. In the literature, most reported cases of tongue teratomas are mature teratomas, while immature teratomas are exceedingly rare. Our aim in presenting this case is to raise awareness among pathologists regarding this rare case in an unusual location.

E-PS-21-032
Placental mesenchymal dysplasia: a rare mimicker of molar pregnancy – report of two cases
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Background & Objectives: Placental mesenchymal dysplasia (PMD) is a rare vascular and mesenchymal anomaly that mimics a partial hydatidiform mole, posing diagnostic challenges. Its aetiology remains uncertain, though dysregulation of growth and angiogenic factors have been implicated. The most consistent molecular alteration in PMD is androgenetic-biparental mosaicism. PMD has been associated with adverse pregnancy outcomes, including foetal growth restriction, intrauterine foetal demise, and Beckwith-Wiedemann Syndrome (BWS). This report describes two cases of PMD.
Methods: Case 1: A 36-year-old healthy woman with a previous normal pregnancy was referred for suspected molar placenta on ultrasound. Severe foetal growth restriction prompted an emergency caesarean at 27 weeks. The preterm newborn developed sepsis, anaemia, and thrombocytopenia, passing away at 1 month and 19 days of life.
Case 2: A 37-year-old healthy primigravida underwent amniocentesis at 16 weeks due to a suspected molar placenta. Intrauterine foetal demise occurred at 20 weeks. Karyotype analysis showed a tetraploid placenta, while the foetus had a normal karyotype. However, genetic evaluation was insufficient to rule out BWS.
Results: Both cases showed placentomegaly and grossly visible vesicles. Histopathology revealed villous stromal expansion, eccentric vascular proliferation, thick-walled foetal vessels with thrombi and chorangiosis-like features. Some areas displayed villi with normal maturation, while others showed marked oedema with cistern formation. No atypical trophoblastic proliferation was identified. p57 staining was preserved in trophoblast but was lost in villous stroma of dysmorphic villi. The first case resulted in neonatal death due to intracranial haemorrhage, secondary to a left middle cerebral artery aneurysm. In the second case, placental insufficiency was the cause of death, and the foetus presented with severe hydrops, a hepatic cyst, adrenal cytomegaly and pancreatic neuroendocrine hyperplasia.
Conclusion: PMD is a crucial differential diagnosis due to its clinical implications and potential misinterpretation as a molar pregnancy. Precise identification is essential to ensure appropriate clinical management.

E-PS-21-033
The cause of strongyloidiasis of the newborn
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Background & Objectives: Strongyloidiasis is helminthiasis caused by roundworms which get into bloodstream, migrate into lungs and trachea; there larvae are coughed up, get into intestine and after two moults they lay eggs.
Data on transplacental infection are contradictory, although there are no morphological and physiological obstacles.
Placental villi are washed by maternal blood from spiral arteria, which are expended over 2mm till the end of pregnancy. With strongyloid larvae size up to 0,5-0,6mm placental barrier is passable for them.
Methods: Autopsy
Results: Prematurely baby at 26'th week of gestation was born by Caesarean-section due to premature detachment of a low-lying placenta (body weight/length were 800g/35cm), 4/6 on Apgar scale.
Due to extreme immaturity, respiratory failure, spontaneous left-side pneumothorax after resuscitation measures in operating room one received intensive care.
At the same time, clinical picture of "acute abdomen" with a formation of abdominal infiltrate and intestinal obstruction manifested itself. That is why resection of ileum, double-barreled ileostomy and excision of Meckel's diverticulum was performed. Strongyloidia were founded in operating material.

Baby's condition in postoperative period remained very serious due to multiple organ failure. At the 6th day from operation (29th day from delivery) biological death occurred.
Autopsy shows extreme immature and premature sings. The main disease was disseminating form of strongyloidiasis with of brain, lungs, spleen, small intestine and lymph nodes extensive lesion.
Death occurs due to pulmonary and cerebral oedema. Adult strongylides 2,2-2,5mm length were found subpleural in right lung lower lobe and under spleen capsule.
The abundance of larval forms in intestines allowed us to identify pathogen using light microscopy. Filariform and rhabditiform larvae were identified in the surgical and autopsy material.
Conclusion: Autopsy shows extreme immature and premature sings. The main disease was disseminating form of strongyloidiasis with of brain, lungs, spleen, small intestine and lymph nodes extensive lesion.

E-PS-21-034
Abnormal placental invasion: parental allele specific methylation of the human gene locus INS
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Background & Objectives: An incompetent uterine scar after caesarean sections and placenta previa are considered the main risk factors for placenta accreta spectrum disorders (PAS)/ Until recently, no significant involvement of genetic factors in the development of this pathology was assumed. About 100 placental genes are expressed selectively, depending on the parent from which they are inherited. The insulin gene INS is located next to the paternally expressed IGF2 gene and the maternally expressed H19 gene in an imprinted cluster on human chromosome 11p15.5. In an attempt to elucidate the role of methylation in parental imprinting at the INS gene locus we undertook an allele specific methylation study of the human INS gene in patients with PAS.
Methods: Fifty-four biological samples of the blood and placenta patients with PAS were analysed. TaqMan genotyping wasperformed for the locus *–23HphI* (rs689). *HpaII* and *GlaI*-mediated methylated DNA digestion was performed.
Results: For 24 patients with a heterozygous placental genotype, the parental origin of the alleles of the polymorphic region –23HphI of the INS gene was determined. The paternal "A" allele of the -23HphI SNP was associated with the number of previous caesarean sections and depth of placenta invasion. No signs of methylation of any of the parental alleles were detected in the patients' blood samples. For any of the paternal placental alleles, fluorescence intensity remained unchanged after DNA treatment with GLA1 restriction enzyme (m=447; SD=123). For paternal alleles of the "A" of the -23HphI SNP, after restriction, the number of amplification cycles was delayed by an average of 3.5 cycles (m=3.47; SD=0.82).
Conclusion: Preliminary results of partial methylation of paternal alleles in the 5-untranslated region of the INS gene in patients with PAS were obtained.

Funding: Research within the framework of the State assignment № FGFZ-2025-0005

E-PS-21-035
Foetal vascular malperfusion in chronic deciduitis: an underlying association?
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Background & Objectives: Chronic deciduitis (CD), characterized by lymphocytes and plasma cells in the basal plate of the placenta, has been linked to pregnancy complications. Despite its clinical significance, the underlying mechanisms linking CD to these complications remain poorly understood. Foetal vascular malperfusion (FVM), a condition characterized by impaired blood flow in the foetal placental circulation, has also been implicated in adverse foetal outcomes, including stillbirth and neonatal morbidity. While both CD and FVM are independently recognized as contributors to placental dysfunction, their potential association has not been thoroughly investigated. This study examines the relationship between CD and FVM to determine whether an association exists.
Methods: This retrospective study analysed 176 placentas diagnosed with CD. Clinical and histopathological parameters, including advanced maternal age (40 cases), gestational age, maternal vascular malperfusion (MVM), FVM, villitis, and ascending infection, were evaluated. The study included 57 preterm births (<32 weeks). Statistical analyses included chi-square tests, Fisher's exact test, and logistic regression. Statistically, $p<0.05$ is considered statistically significant.
Results: FVM was observed in 44.3% of CD cases. Chi-square and Fisher's exact tests showed no significant relationship between FVM and MVM ($p = 0.541$), preterm birth ($p = 0.123$), or advanced maternal age ($p = 0.657$). Logistic regression confirmed that these factors were not significant predictors of FVM.
Conclusion: The high prevalence of FVM in CD cases highlights a potential link between these two conditions, although no direct statistical association was established in this study. This raises the possibility that other underlying mechanisms, such as immune dysregulation or vascular pathology, may contribute to the co-occurrence of CD and FVM. Further research with larger cohorts and prospective designs is needed to elucidate the clinical significance of this relationship and to explore the potential interplay between maternal and foetal placental pathologies in adverse pregnancy outcomes.

E-PS-21-036
Exaggerated placental site reaction following an elective interruption of pregnancy: a case report
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Background & Objectives: Gestational trophoblastic diseases are a group of rare pregnancy-related disorders.
They enclose premalignant disorders such as complete and partial hydatidiform mole, exaggerated placental site, and placental-site nodule as well as malignant disorders.
Exaggerated placental site (EPS) reaction is an abnormal process in which intermediate trophoblast cells infiltrate the endometrium and myometrium at the implantation site. Although EPS does not typically lead to adverse pregnancy outcomes, its recognition is essential in pathological evaluations to avoid unnecessary interventions or misdiagnoses.

We report herein a case of an exaggerated placental site subsequent to elective pregnancy termination.
Methods: A 35-year-old patient (G0P1) with a history of surgically treated endometriosis underwent voluntary termination of pregnancy. Approximately two weeks post-procedure, the ultrasonographic examination revealed the presence of hyperechoic, vacuolated, and intensely vascularized material (colour score 4) in the fundic region. Given the documented occurrence of arteriovenous malformation following abortions[7], the differential diagnoses under consideration for gynecologists encompassed both arteriovenous malformation and post-abortion residual effects. An embolization was performed and the neoformation was therefore removed and submitted for histological examination.
Results: Microscopic analysis revealed that the fragments comprised residual placental parenchyma with fibrotic villi and involutive aspects interspersed with fibrin-blood clots. Endometrial flaps, in close proximity to muscular elements, were observed with persistent intermediate trophoblast elements exhibiting modest atypia.
These findings were consistent with those characteristics of an exaggerated placental site.
Conclusion: Gestational trophoblastic diseases are a rare group of diseases that originate from trophoblasts with an incidence ranging from 1.19/1000 to 1.66/1000 pregnancies.
The diagnosis of exaggerated placental site reaction typically occurs during curettage procedures performed to investigate post-gestational vaginal bleeding.
Clinicians should be aware of this possible reaction after an interruption of pregnancy and manage these patients carefully in order to avoid possible complications.

E-PS-21-037

Development of minimally invasive gene therapy for childhood-onset neurodegeneration with cerebellar atrophy (CONDCA) using adeno-associated virus vectors

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Background & Objectives: CONDCA is an autosomal recessive paediatric disorder caused by biallelic mutations in the *ATP/GTP-binding protein 1* (*AGTPBP1*) gene, which encodes a cytosolic carboxypeptidase 1 (CCP1) with deglutamylase activity. CONDCA patients typically exhibit progressive motor and cognitive impairments, often leading to childhood mortality with no effective treatments at present. A previous study using *Agtpbp1* mutant mouse model suggests that replenishing CCP1 with normal function could represent a promising therapeutic strategy for CONDCA.
Our study demonstrates the efficacy of gene therapy using adeno-associated virus (AAV) vectors to deliver a functional mouse Ccp1 mutant in a Ccp1-deficient mouse model of CONDCA.
Methods: 1. Characterization of CONDCA-related CCP1 mutants. Mouse Ccp1 R791C and Q848* (aligns with human CCP1 R799 and Q856, respectively) were expressed in HEK293 cells. Their expression and deglutamylase activity were examined by Western blotting.
2. Generation of CONDCA model mice.Ccp1-deficient mice (*Ccp1-/-*) as a model for CONDCA were generated using the iGONAD method, then histological, behavioural, and biochemical analyses were performed.
3. Generation of an AAV vector expressing functional Ccp1 for gene therapy. A transvenous administration system with a BBB-penetrating AAV vector carrying the PHP.eB capsid and synaptin 1 promoter were employed to express functional Ccp1 in Purkinje cells.
4. Injections of CCP1-AAV (or control AAV) into the orbital venous plexus of Ccp1-deficient neonates at postnatal day 0 and performed histological and behavioural analysis to examine pathology.
Results: Expression of N-terminally truncated form of Ccp1 (Ccp1 Δ1), which retains deglutamylase activity, in neurons of Ccp1-deficient neonates via a blood-brain barrier-penetrating AAV vector strongly prevented Purkinje cell degeneration during postnatal development. Gene therapy with Ccp1Δ1 significantly improved motor function in Ccp1-deficient mice.
Conclusion: This study provides robust preclinical evidence supporting the potential of postnatal AAV gene therapy as a treatment strategy for CONDCA.

E-PS-21-038

Foetal vascular malperfusion in preterm newborns with segmental intestinal dilatation

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Background & Objectives: Foetal vascular malperfusion is a well-known risk factor for neurological impairment in newborns, and few studies report also its importance in necrotizing enterocolitis. Retrospective study of foetal vascular malperfusion in preterm newborns with segmental intestinal dilatation is presented.
Methods: Between years 2007 and 2023, 34 preterm newborns underwent operative treatment for segmental intestinal dilatation (defined as limited bowel dilatation with a three- to fourfold increase of diameter without intra or extraluminal obstruction) at the University hospital in Hradec Králové. Archive slides from the placenta were available for 28 cases. Foetal vascular malperfusion was assessed according to the Amsterdam criteria.
Results: Gestational age ranged from 24+0 to 33+6.
7 cases were from twin placentas (4 dichorionic diamniotic, 2 monochorionic diamniotic, and 1 monochorionic monoamniotic).
Foetal vascular malperfusion was found in 17 cases (61 %), high grade variant in 6 cases (21 %).
Among the dichorionic diamniotic placentas, foetal vascular malperfusion was observed only in the placenta of the affected twin in 3 cases.
Conclusion: The incidence of foetal vascular malperfusion in patients who developed segmental intestinal dilatation is considerably higher than the overall incidence of foetal vascular malperfusion (which, according to literature, reaches a maximum of 25% in the very preterm group). It could be hypothesized that the reparative processes following post-thrombotic changes within the intestinal wall may contribute to architectural impairment of the muscular layers typically seen in segmental intestinal dilatation.

Funding: This work was supported by the project BBMRI-CZ LM2023033

E-PS-21-039

Chorioamnionitis grade and stage and foetal / neonatal outcome - a three-year retrospective study in a tertiary centre

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Background & Objectives: Histologic acute chorioamnionitis (AC) is defined as an acute inflammation involving chorion and amnion,

associated with increased risk of preterm labour and foetal/neonatal mortality. For each case we graduate maternal (MIR) and foetal (FIR) inflammatory response, regarding location (stage) and severity (grade) of inflammation. Usually low-grade inflammation cases are related with uncomplicated deliveries.
Our objective is evaluate the relationship between AC classification in terms of stage and grade and pregnancy outcome.
Methods: We retrospectively reviewed all cases of placentas submitted to histologic evaluation in our institution, in the last 3-years, including only singleton pregnancies with AC and possibility of MIR/FIR evaluation.
Results: From 1537placentas, 218met the inclusion criteria (14.2%). The median gestational-age was 32.5weeks (range 14-41) and the median maternal-age was 32years (range 15-49).
One-hundred and sixty-one new-borns were alive when discharge from hospital. From those, 7 cases had severe MIR and FIR: all were in 3rdtrimester and underwent antibiotic therapy.
The remaining 57cases (26.1%) had an unfavourable outcome, with foetal/neonatal death occurred in relationship with AC in 41cases (71.9%); remaining cases were due to other pathologies. From those 41cases, 11 don't have a FIR despite the presence of MIR, even though, there were 3cases (27.3%) from 3rdtrimester, 2 with an identified microorganism. In the group with severe MIR and FIR we had 10cases, 6 from 2ndtrimester, and 50% showed positive microbiologic studies.
We also observed 3cases with mild MIR and severe FIR (2live newborns; 1stillbirth): none of the new-borns had an identified microorganism, while the stillborn had 2 simultaneous microorganisms.
Conclusion: Our study demonstrate that a higher percentage of high-grade AC is more commonly associated with poor outcome - in accordance with literature. But not all cases with high-grade or discordant AC results in foetal/neonatal death: advanced gestational age, associated microorganisms and early neonatal care play an important role in outcome.

E-PS-21-040
Pattern of childhood cancer in Maputo, Mozambique in 10 years: data from Maputo Central Hospital Cancer Registry
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Background & Objectives: Childhood cancer is a public health problem, with high mortality rates mainly in low- and middle-income countries where it is underdiagnosed and underreported. In sub-Saharan Africa, paediatric cancer is increasing and near 90% of children who are diagnosed with cancers dies. We aimed to describe the patterns of childhood cancer in a tertiary hospital of Mozambique over a 10-year period.
Methods: This was a retrospective descriptive cross-sectional study. Data were retrieved from the cancer registry of the Maputo Central Hospital (MCH) and included all cases in children from 0 to14 years old, registered between June 1, 2014, and May 31, 2024. The topography and morphology were coded according to the International Classification of Oncological Diseases and the International Classification of Childhood Cancer, 3rd edition.
Results: Out of 20842 new cases of cancer diagnosed during the study period in MCH, 1060 cases (5.5%) occurred in children aged 0 - 14 years. From these, 557 (52,5%) were seen in males. Approximately 36% of the cases (n=380) were diagnosed in children aged 0 - 4 years old. The most common cancer in all age groups was leukaemia (197; 18,5%), followed by lymphomas (165; 15,5%), kidney cancer (129; 12,2%), Kaposi Sarcoma (104; 9,8%) and rhabdomyosarcoma (71, 6,6%). Variations were found when considering 5-years age groups. The most common cancer were Nephroblastoma in the group of 0-5 years, leukaemia's in the groups from 5-9 years and lymphomas in the age group of 10-14 years, respectively.
Conclusion: This study provides the data related with childhood cancer pattern in MCH since the implementation of the Cancer registry of the MCH in 2014 and can potentially contributes to select priorities for cancer control care in children including early and adequate diagnosis and treatment in the country.

E-PS-21-041
Complex pathological approach to assessing shaken baby syndrome
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Background & Objectives: Shaken baby syndrome (SBS) is underreported in autopsy literature, particularly regarding pathomorphological correlations between central nervous system (CNS) injury, anatomical vulnerabilities, and meningeal embryogenesis defects. This study analyzes two SBS autopsies to explore these relationships.
Methods: Autopsies of two infants (2 months and 11 months 17 days) included detailed CNS assessment: vertebral artery sections, brain/spinal cord with membranes, cervical spinal nerves. Histochemical staining (haematoxylin-eosin, Kason), immunohistochemistry for neuronal/endothelial markers were performed.
Results: Both children were from young parents, the first pregnancy without complications; were born full-term (Apgar 8/9). They grew and developed according to their age. When collecting additional information, it was established that the parents had used abrupt movements to calm both children down when rocking them in their arms the day before.
- Case 1 (2 months): Subdural hematoma in the cervical spinal cord connected to a vascular "tangle" in the C2-4 pia mater. Histology revealed venous malformation with deformed vessels, smooth muscle defects, and pseudo-connective tissue outgrowths. Endothelial cells showed strong VEGFR2 expression. Spinal cord necrosis and vacuolar nerve fiber degeneration were noted.
- Case 2 (11 months): Massive left hemispheric subdural hematoma, optic nerve haemorrhage, and necrosis in C2-4 spinal cord posterior horns/medulla oblongata. Vertebral artery haemorrhage and spinal cord angiomatosis with weak VEGFR2 expression in venous vessels were observed. Bridging vein abnormalities draining into the sagittal sinus suggested vascular fragility.
Conclusion: Both cases reflect severe impulsive CNS trauma distinct from concussion, exacerbated by congenital vascular malformations. Defective embryogenesis (e.g., venous wall structural abnormalities, dysregulated VEGFR2 signalling) likely predisposed infants to haemorrhage and necrosis under mechanical stress. The findings underscore the interplay of developmental anomalies and trauma in SBS mortality. Comprehensive autopsy protocols, including detailed vascular histology and molecular marker analysis, are critical for diagnosing SBS and elucidating its mechanisms, particularly in infants with embryological CNS vulnerabilities.

E-PS-21-042

Foetuses teratomas. Clustering of cases

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Background & Objectives: Sacrococcygeal teratoma (SCT) is the most common foetal germ cell tumour, usually benign and highly vascularised. The incidence is 1 in 35,000-40,000 newborns.
Prenatal ultrasound currently detects up to 90% of SCTs. A rapidly growing neoplasm with a predominant solid component associated with high vascularisation is the characteristic of a tumour with poor prognosis.
Methods: We present 2 cases:
A 35-year-old, first-time pregnant woman at 21 weeks who was diagnosed with a type I SCT by prenatal ultrasound. At 22 weeks, a voluntary termination of pregnancy (VTP) was performed.
A 32-year-old woman, with a history of a previous pregnancy, who at 20 weeks was diagnosed by prenatal ultrasound as having type 2 SCT. At 22 weeks, a VTP was performed.
Results: Two 22-week foetuses were received:
The first, female, weighed 474 grams with a sacrococcygeal tumour measuring 4.5x4x3cm which was classified as SCT type 1 as ultrasonography identified a predominance of the external component over the internal component with a cul-de-sac anus without continuity with the intestine. On section, the parenchyma was heterogeneous and brownish in appearance, with a friable consistency, with a cystic area reaching the sacrum and adjacent bone structures without infiltration.
The second, male, weighed 670 grams with a sacrococcygeal tumour measuring 8x6x5.5cm, which was classified as SCT type 2. Ultrasonographically there was equality between the external and internal components.
Microscopically
We identified: Vegetative ganglia, pancreatic glandular tissue, bone marrow tissue, cartilage, immature neural tissue with rosette formation, choroid plexus, respiratory epithelium, squamous epithelium and mature glial tissue were identified in both cases.
Conclusion: Malignant teratoma belongs to the group of rare diseases and has serious consequences for the foetus and may lead to the need for abortion. Definitive diagnosis is based on the identification of multiple tissues from different germ lineages (endoderm, mesoderm and ectoderm) within the same tumour.

E-PS-21-043

Screening for gene mutations by targeted RNA-Seq in support of a malignant lymphoid diagnosis from 60 histological abnormal paediatric biopsies revealed spectra of molecular abnormalities, some, but not all are within a specific histopathological subtype

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Background & Objectives: Targeted NGS RNA-Seq molecular analysis by Tru-Sight(Illumina) was used to detect molecular alterations in paediatric biopsies which showed lymphoid abnormalities. The ability to use the findings to diagnose malignancy is discussed.
Methods: Biopsies from 60 paediatric patients (age 1.5 to 17 years) were analysed. Samples included lymph nodes (48), tonsils (3), skin (3), conjunctiva (1), spleen (1), ileum (2), appendix (1) and testicle (1). Histological diagnoses were made in accordance with the 5th ed. WHO classification of tumours, which included IHC, cytogenetic (FISH), B or T cell clonal testing. RNA was extracted from FFPE tissue shavings.
Results: The numbers of positive biopsies and the types of mutations (Mut) /gene fusions reported in the designated categories are: I. Paediatric type follicular lymphoma (2/4 Lymph Nodes Mut+: 1/4 *TNFRSF14*; 1/4 *KMT2D;* 2/2 *TET2* ;1/4 *IDH1*;1/4 *EZH2*, 1/4 *SGK1*); 1/1 conjunctiva: (*IDH1*, *MAR2K1*); 1/1 skin: (*TET2*, *KMT2D,MAP2K1*); 1/1 testicular: (*KMT2D; CREBBP, BCL2, BCL6, BCL10* and *EZH2*, *IRF8*). II. Burkitt: 4/6 Mut+: (*DDx3X, ID3; ID3, KRAS, FOXO1, CREBBP, TP53, Myc, PTEN* and *H1-4,Myc, PTEN, ARID1, ID3, DDX3X*). III. Lymphoplasmacytic: 1/1: (*CYP1B1*). IV. High grade B cell lymphoma with11q aberration: 2/2 Mut+:(*TP53,PIK3C; PTEN*). 4/4 without 11q aberration were Mut+:(*MKRN1::BRAF, TP53, BRCA2, TCF3, GNA13*; *FOXO1, GNA13, MUTYH, PTEN*; *NBN*; *Myc*). V. B cell lymphoma with IRF4 alteration: 1/1 Mut+(*TNFRSF14*). VI. DLBLC: 5/11 Mut+:(*KMT2B; KMT2B, EZH2*; *TP53*; *TP53; KMT2D, HIST1-4, NF2*; *TP53, RHOA*). VII. Mediastinal large B cell lymphoma: 2/2 Mut+:*TP53, SETD2, STAT6*; *TNFA1P*). VIII: Hodgkin's (6/6 negative for Mut). IX. ALCL: 4/8 fusions*: NPM::ALK*; 1/8 *ATIC::ALK*; 1/8 *NFKB::TYK2*). X. T-cell Lymphoblastic: 2/4 Mut+: (*FBXW* ; *NOTCH1,PTEN*); XI. Lymphoid hyperplasia of AICDA immunodeficiency: 1/1 (*TNFA1P3*). XII. Atypical reactive:1/4 Mut+:(*BCL6*). XIII. PTGC: 1/2 Mut+:(*EZH2*).
Conclusion: We observed while some lymphomas showed similar mutations, absence or heterogeneous molecular spectra were encountered. Correlations with histo-immuno-cytogenetic findings are important to make accurate diagnoses.

E-PS-21-044

Desbuquois syndrome: a rare osteochondrodysplasia

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Background & Objectives: Desbuquois Syndrome is a rare osteochondrodysplasia with autosomal recessive inheritance, first described in 1966, with fewer than 50 cases reported. The diagnosis relies on the correlation between physical, radiological and molecular analysis. Type 1 and type 2 are associated with mutations in the CANT1 and XYLT1 genes, respectively.
Methods: This report describes a male newborn of a 28-year-old puerpera from Bangladesh, delivered at 41 weeks and 3 days with Desbuquois Syndrome, who progressed to early neonatal death.
Results: The newborn had a birth weight of 2945g and a total length of 38.1cm. Physical and radiological examinations revealed features of intrauterine growth restriction, such as crown-to-rump length of 31cm and foot and hand lengths of 4.6cm and 4cm, respectively; severe micromelia, joint hyperlaxity, a flattened face with midface hypoplasia, and a long philtrum; narrow and short chest with increased intermamillary distance; herniation of abdominal viscera, pulmonary hypoplasia, and dilation of the right heart cavities; omphalocele; shortened long tubular bones and proximal femur with 'swedish key' appearance. The pathogenic variant *c.100delinsTT* in homozygosity in the *CANT1* gene was identified, rendering the diagnosis.
Desbuquois Syndrome affects skeletal, pulmonary, and cardiac systems. Early detection of the clinical and radiological features is crucial. The differential diagnosis includes Larsen Syndrome, which shares similar characteristics, however, the radiological and molecular findings were key factors confirming the diagnosis. The prognosis is often guarded, with complications associated with pulmonary hypoplasia and cardiac malformations.

Conclusion: Desbuquois Syndrome should be considered in newborns with skeletal dysplasia, with joint hyperlaxity and cardiac and pulmonary anomalies. Genetic confirmation is essential. This case highlights the importance of early diagnosis, clinical monitoring, and genetic counselling due to its poor prognostic.

E-PS-21-045

Kisspeptin dysregulation in early pregnancy complications: linking serum levels with placental expression patterns

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Background & Objectives: Kisspeptin (KISS1) plays a crucial role in trophoblast invasion, placental development, and pregnancy maintenance. Altered kisspeptin levels have been implicated in early pregnancy loss, but the relationship between serum kisspeptin levels and placental KISS1 expression remains limitedly studied. This study aims to evaluate the correlation between serum kisspeptin concentrations and immunohistochemical (IHC) expression of KISS1 in placental tissue from early abortion cases and healthy pregnancies.
Methods: A total of 50 women with early pregnancy loss (≤12 weeks gestation) and 50 women who underwent elective abortion were included, with the latter group serving as controls. Serum kisspeptin levels were measured in all 100 participants using an enzyme-linked immunosorbent assay (ELISA). Placental tissue was collected after abortion for KISS1 immunohistochemistry (IHC).
Results: Women with early pregnancy loss had significantly lower serum kisspeptin levels compared to healthy controls. Immunohistochemistry showed reduced KISS1 expression in placental tissues from miscarriage cases, with a strong correlation between serum kisspeptin levels and placental staining intensity. Higher placental KISS1 staining was associated with higher serum kisspeptin levels, supporting the link between systemic and placental kisspeptin function.
Conclusion: This study demonstrates a direct correlation between serum kisspeptin levels and placental KISS1 expression**,** suggesting that kisspeptin could serve as a biomarker for pregnancy viability. Lower kisspeptin levels in both serum and placental tissue may indicate placental dysfunction contributing to early pregnancy loss. Further research is warranted to explore its clinical applications in predicting and managing pregnancy complications.

Funding: This study is financed by the European Union-NextGenerationEU, through the National Recovery and Resilience Plan of the Republic of Bulgaria, project № BG-RRP-2.004-0007-C03

E-PS-21-046

Angiomatosis of soft tissue: histopathological comparative analysis of three cases

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Background & Objectives: Angiomatosis of soft tissue (AST) is a rare, high-flow vascular anomaly. It affects children and young adults, occurring either sporadically or in association with PTEN hamartoma tumour syndrome (PHTS). The overlap of AST on clinical, radiologic, and histopathologic features with other soft tissue lesions makes diagnosis challenging.
Methods: We retrospectively reviewed the medical records of three children diagnosed with AST in our institution between 2019 and 2025. Clinical, imaging, and histopathological features were reviewed along with sequencing data.
Results: Three children (6 to 11 years) presented with painful soft tissue masses: two 3 cm knee masses and one 15 cm thigh mass. Two children had no predisposition syndrome, and one had Gorlin syndrome. Imaging suggested a haemangioma in two cases and a vascularized soft tissue mass in one case. All underwent upfront surgical excision.
Histopathological examination revealed poorly circumscribed fibro-adipose lesions with a nodular lymphoid component containing thick-walled veins, bulbiform arteries, and honeycomb-like vascular structures composed of dilated, thin-walled, back-to-back veins.
Immunohistochemistry showed SMA-positive abnormal smooth muscle bundles and CD31 and CD34 expression by abnormal vascular endothelial cells in all cases and podoplanin-positive lymphatic channels in two cases.
Recurrence occurred in two children, 1.5 and 2 years post-surgery, emphasizing the need for long-term follow-up and better treatment strategies.
Conclusion: AST occurs in children on the lower limbs close to joints. Key features include malformed veins, bulbiform arteries, pseudoalveolar vessels, and a nodular lymphoid component within a fibro-adipose tissue, which are essential to diagnose AST. PTEN and PIK3CA mutations highlight the relevance of molecular testing for both diagnostic accuracy and treatment planning. While surgical excision remains the primary therapeutic approach, the risk of recurrence underscores the need for long-term follow-up. Incorporating genetic analysis into clinical practice may improve patient management, and further research into targeted therapies could enhance treatment outcomes for this rare condition.

E-PS-21-047

Severe propionic acidemia in newborns: case report

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Background & Objectives: Propionic acidemia is a rare autosomal recessive hereditary metabolic disorder associated with a deficiency of the enzyme propionyl-CoA carboxylase (PCC), whose genes are localized in the 13q22-q34 region of the chromosome. A PCC defect leads to the accumulation of toxic organic acids and the development of systemic lesions. Macro- and microscopically, the disease is manifested by degenerative changes in the liver, brain, and kidneys caused by metabolic intoxication.
Methods: In the presented clinical case, we are talking about a newborn boy who lived only 5 days.
Results: Propionic acidemia was diagnosed shortly after birth, but the child died of pneumonia due to a prolonged clinical course of the disease. A postmortem examination revealed a rare pathological change — widespread vacuolization of the gray matter of the brain, previously described in just one case. In addition, pronounced perivascular and pericellular oedema, necrobiotic changes in the neurons of the cerebral cortex, small-droplet fatty dystrophy of hepatocytes, as well as vacuolar dystrophy of the epithelium of the renal tubules with areas of necrosis were detected, which indicates acidemia. Laboratory tests performed by tandem mass spectrometry revealed an increased level of propionylcarnitine (12.093 mmol/l at a norm of 0.160–6,500), which confirmed the diagnosis.

Conclusion: Thus, the clinical and morphological data combined with the results of laboratory studies suggest that this patient had a pronounced metabolic lesion characteristic of propionic acidemia. The described case highlights the need for early diagnosis of this disease, including neonatal screening using the mass spectrometry method, which can contribute to the timely initiation of therapy and reduce the risk of adverse outcomes.

E-PS-21-048

Morphofunctional characteristics of the placenta in experimental miscarriage associated with preeclampsia

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Background & Objectives: Rodents are often used for in vivo studies of gestational pathology. The aim is to characterize placental changes in a model of experimental miscarriage associated with preeclampsia (PEM).
Methods: Uncomplicated pregnancy (UP) was modeled using a combination of ♀CBA×♂Balb/c mice, PEM was reproduced using a combination of ♀CBA×♂DBA/2 mice and the introduction of 25 μg of muramyl dipeptide intraperitoneally per 1 animal on the 5th and 7th days of pregnancy (DG). The placenta was isolated on GD 14 and examined using light and scanning electron microscopy (SEM); cytokine production in placenta was measured using flow cytofluorimetry.
Results: The placenta in UP consisted of several layers of giant trophoblast cells (GTC), a spongiotrophoblast zone, and a labyrinth with lacunae and vessels uniformly filled with blood. In PEM, the placenta was distinguished by a thin discontinuous GTC layer, suffusion and stagnation of blood in the labyrinth. Excessive proliferation of trophoblas embedded the maternal and foetal labyrinth components. By SEM, it was shown that in UP, the maternal surface of the placenta is smooth, with a large number of uniformly located pinopode-like formations. The trophoblast of the labyrinth was characterized by a moderately fenestrated smooth surface with wide and deep vascular passages. The placenta on PEM was with flattened and chaotic pinopode-like formations on the maternal surface. Thrombotic deposits were observed, as in the labyrinth, making it difficult to visualize fenestrae and narrowed vessels. Pathological pregnancy was accompanied by a significant increase in IL-1 concentration, as well as a decrease in the level of IL-4, -6 and-10.
Conclusion: We identified in experimental miscarriage associated with preeclampsia signs of placental insufficiency. Our results showed that this model is suitable for modelling preeclampsia.

Funding: FGFZ-2025-0005

E-PS-21-049

The uteroplacental region is an alternative system for regulating arterial pressure

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Background & Objectives: It is known that BNP (brain natriuretic peptide) and its precursor ProBNP are markers of cardiovascular pathology and are synthesized in the atria. It is an angiotensin antagonist, has a protective effect on the cardiovascular system. Preeclampsia is characterized by an increase in blood pressure over 140/90 mm Hg, and in severe cases over 160/110 mmHg. The aim of the study: to assess whether the placental structures and the uterine wall can be a source of BNP and ProBNP.
Methods: A total of 20 placentas from women with severe PE, aged 25-43 years(34-38 weeks of gestation), were examined. The level of BNP and ProBNP staining(Hytest, RU) in the placental and myometrium structures was assessed using hematoxilin and immunohistochemistry. Staining is measured in units of optical density by ImageM programm.
Results: Histological examination with haematoxylin and eosin staining revealed that severe PE had dissociated, randomly located fibrotic villi, the syncytiotrophoblast was significantly exfoliated, the villi were exposed, and signs of placental insufficiency were noted. In the comparison group, the villous tree corresponded to the gestational age. Weak ProBNP staining was found in the comparison group in the villous(35(24-36) and extravillous trophoblast decidual cells, and vascular endothelium. In severe PE, on the contrary, a decrease in staining espessially in damaged villi 21(4-42). Although the preserved villi were characterized by increased staining. Placental ProBNP is a resource for entering the mother's bloodstream in hypertensive disorders. ProBNP was also moderately expressed in the cytoplasm of smooth muscle cells of the inner third of the myometrium ($p<0,05$).BNP expression was represented by no staining in both groups and was not significant.
Conclusion: Decreased ProBNP expression in placental tissue in severe PE. A decrease in ProBNP, which has protective properties in hypertensive disorders, in placental structures indicates depletion of compensatory mechanisms in severe PE and a breakdown of regulatory mechanisms.

Funding: FGFZ-2025-0005

E-PS-21-050

Epidemiological and histopathological profile of renal tumours in children

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Background & Objectives: Renal tumours comprise 7 to 8% of all tumours in children. Nephroblastoma is by far the most common (90%), followed by renal cell carcinomas RCC (4%), clear cell sarcoma of kidney CCSK (3%), and the rhabdoid tumour of the kidney (2%).
The objective of this study was to assess the histopathological spectrum of lesions in tumour nephrectomy specimens of children.
Methods: We present a retrospective study conducted in the Department of Pathology EHS DAKSI Constantine Algeria, including nephrectomy specimens of paediatric patients received over a period of three years (August 1st, 2021 to July 31, 2024). A total of 23 cases were studied.
Results: Patients were aged from 3 months to 14 years (mean 3.86 y). 60.90% of children (n=14) were males (1.6 M/1F). Tumours measured 3.3 cm to 15 cm (mean 8.5 cm). Histological analysis found a nephroblastoma in 20 patients (86.96%), a RCC in 2 patients (8.70%) and CCSK in one patient (4.34%). The SIOP classification concerned nephroblastoma and CCSK (21 patients): 71.43% were intermediate risk tumours n=15, 19.05% were low risk tumours n=4 and 9.52% were high risk tumours n=2. 82.60% of our patients had a complete surgical

resection (n=19). The COG staging was also performed for nephroblastoma and CCSK: 52.38% of our tumours were a COG I (n=11), 28.57% were of COG II (n=6) and 19.05% were of COG III (n=4). The RCCs were respectively pT1aNx and pT2a tumours.
Conclusion: Renal tumours occur in children essentially under the age of 5. Histologically, they are largely dominated by nephroblastma (90%). The treatment advocates pre-operative therapy followed by surgical resection. Prognosis is determined by histopathological type, stage at presentation (COG or TNM) and evenly response of prior therapy.

E-PS-21-051
Fatal congenital toxoplasmosis: contribution of autopsy and histopathology to diagnosis
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Background & Objectives: Congenital toxoplasmosis is a parasitic infection transmitted in utero, often asymptomatic or mild. However, severe cases can lead to neurological damage and, in rare instances, be fatal. This case highlights the crucial role of histopathological examination in confirming the diagnosis.
Methods: A forensic autopsy was conducted on a 40-day-old male infant born by caesarean section four days before term due to acute foetal distress. The newborn exhibited feeding refusal and general deterioration before being found deceased. Macroscopic examination and histopathological analysis were performed to identify the underlying cause of death, focusing on neurological and systemic findings indicative of congenital toxoplasmosis.
Results: The external examination revealed a pale, hypotrophic infant (47 cm, 2140 g, 33.5 cm head circumference) with purpuric lesions on the ankles. Autopsy findings included multivisceral congestion, pulmonary oedema, and supraventricular yellowish-tan brain lesions. Histopathological analysis identified cerebral haemorrhagic foci surrounded by inflammatory infiltration, periventricular reactive gliosis, and toxoplasmic trophozoite cysts, confirming congenital toxoplasmosis. These findings correlated with severe systemic involvement, suggesting a fulminant progression of the infection. The absence of prior diagnosis or treatment highlights the silent yet potentially fatal nature of this condition in neonates.
Conclusion: This case underscores the importance of autopsy and histopathological analysis in diagnosing congenital toxoplasmosis, particularly in fatal cases. These methods are complementary, with macroscopic findings suggesting the disease and histopathology confirming it. The study highlights the necessity of prenatal toxoplasmosis screening, serological monitoring in pregnant women, and early therapeutic intervention to improve neonatal prognosis and prevent severe outcomes.

E-PS-21-052
Paediatric sacrococcygeal ependymoma: a rare extraneural localization with diagnostic challenges - case report
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Background & Objectives: This study presents a rare paediatric case of extracranial and extraspinal myxopapillary ependymoma with sacrococcygeal localization. While these tumours typically arise in the distal spinal cord and carry a favourable prognosis, this case demonstrated anaplastic features, that may indicate increased risk of aggressive behaviour. This case highlights the importance of considering uncommon locations.
Methods: An 8-year-old male presented with an 8 cm sacral mass initially radiologically suspected to be a pilonidal sinus. Complete surgical resection was performed, revealing a 3.5 × 3.5 cm solid, whitish mass with haemorrhagic areas on sectioning.
Results: Microscopic examination showed dermal and subcutaneous tumour infiltration with moderate-to-high cellularity displaying papillary, solid, and cord-like architectural patterns. Tumour cells featured round nuclei with granular chromatin, radially arranged around vascular structures forming papillae with numerous pseudorosettes and occasional true ependymal rosettes, embedded in Alcian blue-positive myxoid matrix. Notable absence of necrosis or microvascular proliferation was observed. Immunohistochemical profiling demonstrated strong GFAP and S-100 positivity. The proliferation index reached 30% by Ki-67 staining with mitotic activity up to 7/mm².
Conclusion: Extracranial ependymomas represent exceptionally rare neoplasms, showing slight female predominance, with presacral/sacrococcygeal localization being the most frequent extracranial site, which is hypothesized to originate from coccygeal medullary vestiges. The myxopapillary variant predominates in reported cases. The observed histological features - including high cellularity, reduced myxoid component, elevated mitotic count and proliferation index, support the anaplastic features. This case underscores: 1) the necessity for multidisciplinary management, and 2) the unresolved question regarding adjuvant therapy for sacral region presentations. Our patient remains recurrence-free during follow-up, though local radiotherapy is being considered due to metastatic potential.

E-PS-21-053
Foetal neoplasms: a study in foetal autopsy perspective
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Background & Objectives: Foetal neoplasms are neoplasms that have increased in frequency in recent years due to technological advances in foetal imaging techniques and increased awareness, but are still extremely rare. They are found in approximately 0.01% of all live births, 0.5% of all stillbirths and 1.2% of foetuses with birth defects.
The aim of this retrospective study was to review our 18-year foetal autopsy series and to examine the clinicopathologic features of the cases with neoplasia in the perspective of the literature.
Methods: Clinical records and pathology reports of foetal autopsies performed in our centre between 2007 and 2025 were reviewed and cases diagnosed with foetal neoplasia were identified. In the screening performed without differentiation between benign and malignant neoplasia, 16 cases diagnosed with foetal neoplasia were identified.
Results: Of the 16 foetal autopsies, 8 (50%) were female and 8 (50%) were male. The mean gestational week was 23.6+5.2 weeks, the minimum gestational week was 16 weeks and the maximum gestational week was 34 weeks. Maternal age ranged between 18 and 36 years with a mean of 27+6.5 years.
Histopathological evaluation revealed vascular neoplasia in 8 (50%), teratoma in 5 (31.3%), cardiac myxoma in 1 (6.3%), cardiac rhabdomyoma in 1 (6.3%) and high-grade diffuse glial tumour in 1 (6.3%) of 16 foetuses. Among the vascular neoplasms, 5 were haemangioma, 2 were lymphangioma and 1 was arteriovenous malformation. Among the 5 cases with teratoma, 1 was an immature teratoma and the others were mature teratomas.
Conclusion: The rare foetal neoplasms comprise a heterogeneous group of neoplasms. The basic steps of patient management in foetal neoplasms include evaluation of the cases by experienced physicians using the right imaging techniques, proper parental counselling,

planning of foetal surgical intervention if necessary and termination of pregnancy under mandatory conditions.

E-PS-21-054

Histopathological findings in placenta delivered from SARS-CoV-2 infected mothers. A single centre experience from South Africa

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Background & Objectives: There is a paucity of data describing the effects of the coronavirus disease 2019 on placental pathology from South Africa. The consequences of SARS-CoV-2 on the human placenta and the newborn are still not clearly understood, yet there have been reports of stillbirth and preterm birth. Chronic histiocytic intervillositis and massive perivillous fibrin deposition have been described as the common features associated with SARS-CoV-2 infection in the placenta. The objective of this study was to describe the histopathological features of the placenta in women affected by SARS-CoV-2 in our centre.
Methods: This was a retrospective study which assessed histopathological features of placenta delivered from women infected with SARS-CoV-2 in the Department of Anatomical Pathology, Ga-Rankuwa, South Africa, from 01/03/2020 to 31/12/2023. The clinicopathological data was retrieved from the National Health Laboratory Service's laboratory information system. The placenta was assessed according to the Amsterdam consensus. Data was analysed using a statistical software package.
Results: A total of 64 placenta were delivered from SARS-CoV-2 infected mothers with an average age of 28 years old (range 14 – 42). According to Amsterdam consensus, maternal vascular perfusion (45%, n=29) was the commonest finding, followed by foetal vascular perfusion (25%, n=16), chronic villitis (22%, n=14) and acute chorioamnionitis (8%, n=5).

Conclusion: This study is the first of its kind in South Africa. These findings corroborate that the placenta that has been infected with SARS-CoV-2 primarily exhibits characteristics of maternal foetal perfusion. Although no pathognomonic features were identified, it is crucial for obstetricians to anticipate the potential adverse pregnancy outcome in these cases.

Funding: National Research Fund (NRF). South African Medical Research Council (SAMRC)

E-PS-21-056

Early infantile form of globoid cell leukodystrophy (Krabbe disease): the histopathological description of an interesting case

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Background & Objectives: Globoid cell leukodystrophy (GCL) is a rare and severe disorder caused by a mutation in the GALC gene, leading to galactocerebroside accumulation and white matter degradation. This study aims to highlight the histopathological characteristics of GCL in a case report.
Methods: We present the case of a one-year-old boy who was diagnosed with GCL at four months of age, based on symptoms of irritability, developmental delay, and motor deterioration, confirmed by genetic testing. His sister had the same condition and passed away at one year and six months. The child died at home, and an autopsy was performed.
Results: An autopsy was carried out at the Institute of Forensic Medicine in Targu Mures. Macroscopic examination revealed moderate brain atrophy with widened sulci and weight reduction. On sectioning, the white matter showed a greyish appearance and increased consistency. The subcortical white matter appeared unaffected. Histologically, the white matter contained numerous macrophages, multinucleated globoid cells around blood vessels, and intense gliosis. Additionally, areas of dystrophic calcifications were noted. Respiratory failure due to bronchopneumonia was determined as the cause of death.
Conclusion: This case underscores the importance of considering GCL in the differential diagnosis of neurodegenerative disorders in infants. The characteristic histopathological features are vital for diagnosis and understanding the disease pathology. Early recognition is essential for both clinical management and genetic counselling, given the severe and progressive nature of the disease.

E-PS-21-057

Foetal intracranial haemorrhage, porencephaly and an occipital soft tissue malformation associated with collagen 4a1 mutation

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Background & Objectives: Foetal intracranial haemorrhage complicates up to 1‰ of pregnancies and may deeply influence the perinatal course affecting neonatal morbidity and mortality. In many cases the cause may not be identifiable. Risk factors include infectious disease, alloimmune thrombocytopenia, maternal drug exposure, maternal trauma, coagulation disorders and twin-to-twin transfusion syndrome. Genetic disorders associated with an increased risk for cerebral arteriopathy, have been reported in a few foetal cases. Of those, COL4A1 gene mutations are responsible for a hereditary autosomal dominant cerebrovascular disease, characterized by a wide phenotypical spectrum, including the development of perinatal intracranial haemorrhage, as well as porencephaly / schizencephaly. Herein, we describe a case of a foetus with microvascular haemorrhagic encephalopathy, porencephaly and a COL4A1 pathogenic variant.
Methods: Termination of pregnancy at 22 weeks-gestation was carried out due to pathological prenatal ultrasonographic and MRI brain findings. Foetal autopsy was performed and followed by whole exome sequencing (WES) in foetal genomic DNA.
Results: At autopsy the foetus showed increased growth (100^{th} centile), bilobed lungs and a small atrial septal defect. There was a soft-tissue stalk connecting the scalp with the posterior fontanelle, without an underlying encephalocele. Histology of the brain showed scattered parenchymal petechial microhemorrhages, siderophages consistent with older haemorrhage, encephaloclastic lesions, porencephaly, and areas of decreased density of the white matter. In the placenta small villous vessels were seen to be dilated and haemorrhagic. WES identified a heterozygous missense variant in the COL4A1 gene: c.3104G>T (p.Gly1035Val) (rs1555302922), classified as pathogenic in the ClinVar database [ID 440782]. Maternal serology for TORCH infection and PCR testing on foetal tissues for cytomegalovirus and herpesviruses was negative, while there was no other evidence suggestive of congenital infection.
Conclusion: Foetal intracranial haemorrhage and disruptive lesions considered idiopathic may have underlying genetic causes, which should be accounted for and investigated.

E-PS-22 E-Posters Pathology in Favour of Developing Countries

E-PS-22-001

Pathology in Cambodia: the past, present, and future

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Background & Objectives: Pathology in Cambodia has a complex history, shaped by periods of progress and setbacks. The first known pathologists, trained in France and played a key role in the field's early development before their tragic disappearance during the Khmer Rouge era. The systematic eradication of intellectuals led to the total collapse of pathology services, leaving the country without specialists for over a decade. It was not until the late 1980s that pathology was revived, demanding extreme efforts to restore diagnostic services with limited resources.
Methods: Over the next two decades, Cambodia saw only a handful of new pathologists trained abroad, and diagnostic capabilities remained basic, relying primarily on conventional histology and cytology. A significant milestone was reached in 2015 with the establishment of the country's first pathology residency program. Despite its success in training 10 pathologists to date, the program struggles with low recruitment and continues to depend on international collaborations, particularly from Asia and Europe.
Results: Currently, only 10 pathologists serve in eight laboratories across Phnom Penh, offering routine histology, and a few special stains. Among them, only the laboratory at Calmette Hospital is equipped to perform frozen sections, a broader range of more than 10 special stains, and limited immunohistochemistry. However, molecular diagnostics remain unavailable in pathology labs, limiting the ability to implement modern classification systems and precision medicine. Emerging technologies, including digital pathology and artificial intelligence, further highlight the urgent need for infrastructure development and workforce expansion.
Conclusion: Future efforts must focus on strengthening local training, increasing mentorship, and expanding laboratory capabilities. Establishing molecular diagnostics, such as FISH and PCR for targeted genetic testing, is a critical step forward. International partnerships will remain essential in bridging these gaps and ensuring sustainable progress in Cambodia's pathology services.

E-PS-22-002

Leveraging social media for professional growth: empowering pathology residents in low-resource settings

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Background & Objectives: Social media's impact has extended beyond traditional domains, notably in the medical profession, including specialized fields like pathology. Social media platforms such as LinkedIn and Twitter have become essential for professional interactions, knowledge sharing, and career advancement. This study examines the role of virtual social networks in shaping the professional development of pathology residents in low-resource settings in West Africa.
Methods: A cross-sectional, multi-institutional survey was conducted in the Pathology Departments of Korle Bu Teaching Hospital and Komfo Anokye Teaching Hospital from July to August 2024. An online questionnaire was distributed via WhatsApp to pathology residents. Data analysis was performed using STATA 14 to assess the influence of virtual media on professional development and career progression.
Results: A total of 34 pathology residents participated. The majority (83%) were aged 30 and above, with 53% identifying as female. Anatomic Pathology residents made up the largest group (47%). Of the respondents, 77% regularly used social media for professional development, with YouTube being the most frequently used platform cited by 83.9% of respondents . Regarding social media's utility for learning, 56% rated it as somewhat useful, and 23% as very useful.
The majority of residents found social media beneficial for professional development. For increasing understanding of the profession, 79% found it useful. In problem-solving, 79% rated it somewhat or very useful. For critical thinking, 85% found it useful, and 94% found it helpful for clinical decision-making. In enhancing clinical expertise, 85% rated it useful.
Conclusion: Social media plays a significant role in the professional development of pathology residents in low-resource settings. The high perceived usefulness of these tools highlights their importance in advancing clinical skills and knowledge. While most residents appreciate these resources, addressing the concerns of those who find them less useful could improve engagement and optimize their impact.

E-PS-22-003

Delphi's echo: interim findings on a cross-continental biobanking effort

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Background & Objectives: Despite ongoing globalization, a profound North-South gap persists across various scientific disciplines, including medical research and biobanking. From this perspective, we developed a collaborative network between Mali and Germany to facilitate integrative research, establish the base for a robust biobank system in Mali and ultimately reduce global inequalities.
Methods: To facilitate our collaborative efforts, we conduct a Delphi process, a structured communication technique to achieve consensus among a panel of experts from diverse backgrounds. Our expert panel includes 11 members: five from Germany, five from Mali, and one neutral, mediative expert from France. This methodology emphasizes the anonymity of responses to ensure unbiased input, iterative rounds, and controlled feedback after each round. The process started with an initial round of open questions to explore broad perspectives in the collaboration regarding biobanking and precision medicine.
Results: The Delphi process focused on the central question: "How can we efficiently design future collaborative projects?" Key expectations included agreement on the need to establish common educational programs, foster international exchanges of scientific experience, and initiate collaborative projects in biobanking and precision medicine. However, several challenges have been identified. Resource and infrastructure limitations include funding, facility availability, equipment access, and connectivity between medical information systems. Research coordination faces the absence of standardized protocols and varying scientific frameworks. Geographic and systemic obstacles include differing legal frameworks, distance, language barriers, and diverse system knowledge. Effective collaboration also requires improved sharing of experiences and partnership development.
Conclusion: After a successful first round, our network will shortly continue with the second and third rounds that will feature more specific, closed questions to solidify consensus on discussed issues, such as a harmonized minimal dataset. In general, the Delphi process

provides a powerful tool in times of global uncertainties and disrupted discourse. It facilitates debates, discussions, and the development of effective joint solutions.

E-PS-23 E-Posters Pulmonary Pathology

E-PS-23-001

Synchronous and metachronous malignancies in a heavy smoker: a case of metastatic lung carcinoma, neuroendocrine tumour and follicular thyroid carcinoma

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Background & Objectives: A 69-year-old male smoker with a 100 pack-years history presented in April 2023 with a three-month history of left hip. Scintigraphy findings raised suspicion of sarcoma; however, an iliac bone biopsy revealed metastasis of adenocarcinoma of unknown origin (CK7, CK19 positive and TTF-1, CK20, CDX2, PAX8 negative).
Methods: Colonoscopy and gastroscopy were unremarkable. Thoracic MSCT demonstrated a 1.7x1.6x1.2 cm peribronchial lesion in the right middle lobe with central necrosis. No evidence of dissemination was observed on abdominal MSCT. Cytological and pathological analysis of bronchoscopic samples confirmed a poorly differentiated carcinoma (TTF1, p40 negative) with 70% PD-L1 expression. Molecular analysis showed no mutations in EGFR, ALK, ROS1, RET or MET genes. Chemoimmunotherapy was initiated, and follow-up MSCT showed regression of the primary lung lesion.
Results: In May 2024, the patient sought medical attention for swallowing difficulties and throat pain. Fiberendoscopy and MSCT revealed a 2.9x2.1x1.3 cm epiglottic mass. Two biopsys confirmed a malignant epithelial tumour with neuroendocrine differentiation. Surgery was performed and histopathological examination established a diagnosis of grade 2 neuroendocrine tumour with bilateral lymph node metastasis. Additionally, a 1.5 cm angioinvasive follicular carcinoma was detected in the left thyroid lobe.
Adjuvant radiotherapy was recommended, but the patient declined further treatment. He remains under regular oncologic surveillance and continues to receive immunotherapy as part of his treatment regimen. Follow-up assessments indicate stable disease with no evidence of progression.
Conclusion: This case underscores the challenges of diagnosing and managing malignancies in heavy smokers, emphasizing the need for a multidisciplinary approach in oncologic care. The occurrence of synchronous and metachronous tumours suggests a potential underlying genetic and/or environmental predisposition. Although molecular testing ruled out common driver mutations, potentially broader genomic analysis could provide valuable insights to refine future treatment strategies.

E-PS-23-002

Pulmonary nodular hyperplasia presenting as tumour like mass suspected for malignancy in patient with rheumatoid arthritis and positive Quantiferon test: a case report

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Background & Objectives: Pulmonary nodular lymphoid hyperplasia (PNLH) is a rare benign lymphoproliferative interstitial lung disease which is radiologicaly difficult to differentiate from malignant tumours. It is assosiated with autoimune diseases such as rheumoatoid arthritis and lung infections such as tuberculosis.
Methods: We report a case of a 59-year-old woman without pulmonary simptomatology with recently diagnosed rheumatoid arthritis (RA) who has been administred to pulmologist because of a positive Quantiferon test. A multi sliced computed tomography thorax scan showed a tumour like mass with differential diagnosis of lung infiltrat in the lower right lung lobe.
Patient medical history including evidence of rheumatoid artritis, microbiology Quantiferon test and bacterial culture tests were assesed throught hospital electronic system for medical records.
Results: Percutaneous transthoracic needle biopsy was perfomed but histopathologic findings were nonspecific and undiagnostic. Subsequently, atipical right lower lobe resection was perfomed. PNHL was confirmed throught light mycroscopy morphology and imunohistocemical examination of postoperative speciment. Histopathologic evidence of lung tuberculosis was not found.
Conclusion: PNLH is most often presenting as unilocular tumour like mass and in some cases as multilocular mass mimicing malignancy. It has been documented in various autoimmune diseases including RA but case reports searched throught pub med database which establish a definitive connection between PNLH and RA are limited and rather include assosiations with a more general group of interstitial lung diseases.

E-PS-23-003

Bronchial fibroepithelial polyp: a case report on a rarely encountered malignancy mimic

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Background & Objectives: Bronchial fibroepithelial polyps are rare lesions that appear to be underreported. Since they have not been extensively studied, there is still debate over whether they are neoplastic (similar to skin tags) or hyperplastic (similar to anal tags). These polyps have male predominance and can present with haemoptysis, cough, fever or as asymptomatic lesions. Previous case reports have shown that they mostly mimic malignancy, although they can also resemble pneumonia. Recurrence may occur if incompletely resected, but the prognosis is favourable.
Methods: We report a case of a 59-year-old male who presented with right-sided chest pain that persisted for four months, without other symptoms. He had personal history of smoking, schizophrenia and dyslipidemia, as well as a family history of breast cancer. The CT scan showed an irregular nodule measuring 28 mm in the apical region of the right lung, as well as a 14 mm nodule in the superior lobe of the left lung. These findings were consistent with PET scan results. However, bronchoscopy and endobronchial ultrasound revealed a previously undiagnosed vegetative lesion with 1 cm in long axis located in the basal pyramid of the right lung, prompting a biopsy.
Results: The biopsy of the vegetative lesion revealed a lobulated lesion with a squamous and respiratory mucosa lining, and a fibrovascular stroma core with a sparse mononucleate inflammatory infiltrate. Immunohistochemistry showed epithelial immunoreactivity for CK7 and p63, as well as stromal immunoreactivity for vimentin and CD34/SMA (capillaries). Desmin was not immunorreactive. Transthoracic biopsies of the other lesions previously described in the imaging exams confirmed lung adenocarcinoma.
Conclusion: The patient underwent chemoradiotherapy and is currently receiving immunotherapy. No follow-up bronchoscopy has been performed. This case highlights a rare but underdiagnosed entity that may be encountered. Furthermore, bronchial fibroepithelial polyps may resemble malignant lesions, often leading to misinterpretation during bronchoscopy or imaging exams.

E-PS-23-004

Peritoneal mesothelioma: review of cases in a Portuguese tertiary centre

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Background & Objectives: Mesothelioma is a malignant proliferation of mesothelial cells lining the serosal surfaces, with peritoneal mesothelioma (PM) accounting for 6-10% of cases. We retrospectively reviewed all PM cases managed at our institution, focusing on clinical, histopathologic, and immunohistochemical features, as well as treatment outcomes.
Methods: Between 1999 and 2025, we identified 11 confirmed cases of PM, based on histopathological examination and immunohistochemical profiling. Clinical data, including age, sex, occupational history, and treatment regimens, were collected from medical records.
Results: The cohort was predominantly male (9/11; 82%) with a median age of 60 years. Only two patients had known asbestos exposure (2/11; 18%). The majority were diagnosed with diffuse malignant mesothelioma (10/11; 91%), with one case of well-differentiated papillary mesothelial tumour (1/11; 9%). Most of the diffuse malignant mesotheliomas were of the epithelioid subtype (9/10; 90%), with one biphasic case (1/10; 10%). Immunohistochemistry showed positivity for mesothelial markers: calretinin (82%), WT1 (73%), podoplanin (55%), and CK5 (64%). The loss of BAP-1 was also analysed. Regarding treatment, 27% (3/11) of patients underwent hyperthermic intraperitoneal chemotherapy (HIPEC), and 64% (7/11) received adjuvant/palliative chemotherapy. The patient with a well-differentiated papillary mesothelial tumour remains recurrence-free after 63 months of follow-up. Of the patients with diffuse malignant mesothelioma, two were lost to follow-up, two are alive with disease, and six died of the disease, with a median survival of 21.6 months.
Conclusion: Our findings align with the literature, showing peritoneal mesothelioma as a rare, poor-prognosis disease. Unlike pleural mesothelioma, few patients had asbestos exposure, suggesting other etiologic factors may play a role. Histopathological and immunohistochemical analysis are critical in distinguishing PM from peritoneal carcinomatosis.

E-PS-23-005

Rare pulmonary neoplasms: a multimodal diagnostic approach

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Background & Objectives: Rare pulmonary neoplasms pose a significant diagnostic challenge due to their low incidence and histological diversity. Accurate classification is essential for appropriate clinical management but often requires a comprehensive diagnostic strategy integrating histopathology and molecular profiling. In this study, we present two exceptionally rare pulmonary tumours, underscoring the critical role of multimodal diagnostics.
Methods: Immunohistochemical staining was performed as part of routine laboratory protocols. Molecular profiling was conducted using the Oncomine Comprehensive Assay Plus panel, and ZytoLight SPEC KRAS/CEN 17 Dual Color FISH analysis was performed.
Results: The first case involved a 1.5-year-old child with a cystic pulmonary lesion. Histopathological analysis identified rhabdomyoblasts in small foci via desmin and myogenin staining. Molecular analysis reveal a DICER mutation at low allele frequency.
The second case concerned a 74-year-old male with a lung tumour. Detailed immunohistochemical findings raised multiple differential diagnoses, including metastatic hepatoid/yolk sac-like adenocarcinoma of the stomach, metastatic germ cell tumour, and high-grade foetal adenocarcinoma. Notably, molecular analysis identified a 12p isochromosome, strongly suggesting a germ cell tumour. Imaging and other clinical studies failed to reveal an extrathoracic primary tumour.
Conclusion: In the first case, histopathological and molecular findings confirmed a type I pleuropulmonary blastoma arising in the context of type IV congenital pulmonary adenomatoid malformation.
In the second case, given the presence of a 12p isochromosome and the clinical context, the most probable diagnosis was a primary pulmonary germ cell tumour, or an occult metastatic germ cell tumour, both extraordinarily rare entities in this age group.
These cases highlight the diagnostic complexity of rare pulmonary neoplasms and the essential role of molecular pathology in achieving diagnostic precision. Our findings contribute to the limited literature on these tumour types and may aid in refining diagnostic and therapeutic strategies.

E-PS-23-006

A rare case of granulomatous reaction to diffuse idiopathic neuroendocrine cell hyperplasia (DIPNECH) radiologically mimicking rapidly progressive malignancy

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Background & Objectives: A 53-year-old female non-smoker presented with an 18-month history of persistent cough. Initial CT scan demonstrated an 11mm right upper lobe nodule as well as numerous small nodules throughout both upper and middle lobes. Only the larger upper lobe lesion was FDG avid on PET scan and biopsy demonstrated this was a carcinoid tumour.
Methods: Interval CT scan showed significant increase in size of the middle lobe lesions with features concerning for rapid progression of malignancy. A middle lobe wedge excision with intraoperative frozen section was performed to determine the histogenesis of the rapidly growing nodule prior to decision regarding resection/management of the upper lobe nodule. Histological examination showed a 22mm nodule of confluent, necrotising granulomatous inflammation with no evidence of malignancy. An upper lobe anterior segmentectomy was therefore undertaken to excise the carcinoid tumour.
Results: Following formalin fixation, tissue analysis confirmed necrotising granulomatous inflammation containing occasional neuroendocrine tumourlets, and foci of neuroendocrine hyperplasia that were not present in the sections used for frozen section. No mycobacteria or other pathogens were identified. The right upper lobe contained two separate carcinoid tumours, multiple carcinoid tumourlets and foci of neuroendocrine cell hyperplasia.
Conclusion: Overall, the features were those of a rarely described florid granulomatous inflammatory reaction to diffuse idiopathic pulmonary neuroendocrine hyperplasia (DIPNECH) which can mimic rapidly progressive malignancy on imaging. This case underscores the importance clinical, pathological and radiological correlation, as well as the value of intra-operative frozen sections in guiding surgical decision making particularly when dealing with complex and unusual presentations of disease.

E-PS-23-007

A case report of NTRK translocations in a patient's lesion of the left lung's lower lobe

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Background & Objectives: Translocations of NTRK genes are significant oncogenic drivers in various tumours, both in children and adults. Herein we report a case of pleomorphic undifferentiated NTRK1-positive sarcoma with the lower lobe of the left lung involvement.
Methods: The medical history, laboratory and instrumental data of the clinical case were analysed. Histological slides of the lung's tissue samples were stained with haematoxylin & eosin, then studied according to a standard protocol. Immunohistochemical study (IHC) was performed using monoclonal mouse antibodies to SMA, BRG1, CD34, Chromogranin A, Synaptophysin, Desmin, S100, EMA, AE1/AE3, HMB45, Melan A, SALL4, SOX10, STAT6, TLE1, WT1, TTF1, PAX8, NTRK, Ki-67, PDL1 (22C3). Next-generation sequencing (NGS) was also used.
Results: A study of the medical data revealed that the patient had a cough and general weakness after COVID infection in May, 2023. Multi-slice computed tomography detected a large solid neoplasm of irregular shape and approximate size 171*103*123 mm in the left half of the thoracic cavity. Histological examination has shown the tumour tissue built from epithelial and spindle-shaped cells that formed solid clusters of intertwining bundles located in a loose stroma. The tumour positively expressed: BRG1, WT-1, STAT-6, NTRK, Ki-67 – 87%. Tumour cells were immune negative to: SMA, CD34, Chromogranin A, Synaptophysin, Desmin, S100, EMA, AE1/AE3, HMB45, Melan A, SALL4, SOX10, TLE1, WT1, TTF1, PAX8. Analysis of PDL-1 positive 15% of tumour and 3% of immune cells (CPS=18). A genetic study has confirmed NTRK1-KHDRBS1 fusion.
Conclusion: The accumulation of data about the clinical and morphological profile of patients with rare oncogenic mutations makes it possible for pathologists to gain knowledge about the diagnostics algorithm of rare tumours. The results of the study are discussed in terms of the necessary comprehensive genetic, immunohistochemical and pathomorphological studies for further successful targeted therapy.

E-PS-23-008

Histopathological changes in a mouse model exposed to fine particulate matter collected from Korean air

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Background & Objectives: PM2.5 exposure is widely studied for its association with lung cancer risk. However, most prior studies have relied on standardized commercial PM2.5 samples, which may not fully reflect real-world exposure conditions. To address this, we investigated the potential effects of PM2.5 collected directly from ambient air in South Korea on lung tissue alterations in a murine model. This study aimed to assess how regionally collected PM2.5 influences lung histopathology, focusing on neoplastic changes, inflammation, and fibrosis.
Methods: Male A/J mice (7 weeks old) were assigned to four experimental groups: saline control, urethane, PM, and urethane + PM. Following urethane injection (250 mg/kg intraperitoneally), PM2.5 (35 μL) or saline was intranasally administered twice per week for five weeks. PM2.5 samples were collected from ambient air in South Korea using a high-capacity air sampler, then processed and purified for experimental use. Lung tissues were harvested at 40 weeks and evaluated histologically for hyperplasia, adenoma, carcinoma, fibrosis, and inflammation severity. Statistical significance was determined using Kruskal-Wallis and Mann-Whitney tests ($p < 0.05$).
Results: Mice exposed to PM2.5, either alone or in combination with urethane, exhibited a greater tendency for adenoma formation compared to controls. The mean maximum adenoma diameter was larger in both the urethane + PM and PM groups than in the saline group, with the urethane + PM group showing the most pronounced increase. While these findings indicate a possible relationship between PM2.5 exposure and lung tissue alterations, additional studies are necessary to further explore these effects.
Conclusion: Our study highlights the potential impact of real-world PM2.5 exposure on lung tissue changes in a murine model. While the observed trends suggest a role for PM2.5 in early neoplastic processes, further validation with expanded sample sizes and mechanistic analyses will be essential for a more comprehensive understanding of its biological effects.

E-PS-23-009

Tumourlets in surgical lung specimens: an incidental finding with an unclear significance

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Background & Objectives: Pulmonary tumourlets are benign neuroendocrine (NE) proliferations measuring ≤5 mm, often discovered incidentally in patients with various chronic lung diseases. This study aims to examine the histopathological features of tumourlets and their associated disorders.
Methods: A retrospective review of six cases collected over nine years (2016–2024) was conducted. Clinico- radiological, histopathological, and data for NE markers were analysed.
Results: The study included six patients (sex ratio F/M = 2) with a median age of 69 years (range: 55–85). One patient presented with massive haemoptysis. Three had a cystic lesion (left lower lobe, lingula). Two patients had a culmen mass, with ground-glass nodules observed in one of them. The last patient, with colorectal adenocarcinoma, had lung nodules on follow-up imaging. Tumourlets, discovered incidentally, measured between 2 mm and 5 mm. The associated lung conditions included bronchiectasis with secondary inflammatory or haemorrhagic changes (3 patients), emphysematous changes with pleural fibrosis (1 patient), pulmonary aspergillosis (1 patient), and colorectal adenocarcinoma with emphysematous changes (1 patient). In all cases, tumourlets appeared as small nests of NE cells expressing chromogranin A and synaptophysin.
Conclusion: This case series, in line with the literature, highlights the common association of pulmonary tumourlets with chronic lung damage, such as fibrosis, bronchiectasis, emphysema, and subacute or chronic inflammation. In most instances, tumourlets are considered a secondary tissue reaction to cellular hypoxia, although some studies suggest that multiple lesions may play a role in the pathogenesis of chronic obstructive pulmonary disease. It has been suggested that NE cells in tumourlets secrete VEGF, potentially contributing to lung tissue scarring, particularly fibrosis.

E-PS-23-010

Comprehensive analysis of PD-L1, ALK, and EGFR biomarker testing in lung carcinoma: insights from a five-year study at single centre

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Background & Objectives: Lung carcinoma is a leading cause of cancer-related mortality worldwide. Biomarker testing for PD-L1, ALK, and EGFR is essential for guiding targeted therapies and improving

patient outcomes. This study evaluates the prevalence and distribution of these biomarkers over a five-year period at the Institute of Pathology, Faculty of Medicine, University of Belgrade, a tertiary referral centre that handles consultation cases from secondary institutions across Serbia.
Methods: A retrospective analysis of lung carcinoma patients who underwent testing for PD-L1, ALK, and EGFR between 2020 and 2024. Patient demographics, histological subtypes, smoking status, clinical staging, and biomarker expression levels were collected and analysed. All results are cumulative over the five-year period.
Results: The cohort comprised 3,470 patients, with 2,222 males (64%) and 1,248 females (36%), aged between 19 and 90 years (mean age: 66.11 years). Histological subtypes included adenocarcinoma (64.2%), squamous cell carcinoma (23.3%), NSCLC-NOS (9.7%), and other types (2.8%). PD-L1 expression was <1% in 35.2% of patients, 1–49% in 30.7%, ≥50% in 29.1%, with 5% untested. ALK testing was positive in 1.6% of patients. EGFR mutations were detected in 8% of patients. Regarding smoking status, 2,739 patients (78.9%) were smokers, 276 (8%) were non-smokers, and 455 (13.1%) had unknown smoking status. Clinical staging indicated that most patients were in stage IV (2,768; 79.8%), followed by stage III (18.3%), stage II (1%), and stage I (0.9%).
Conclusion: The observed histological subtypes and biomarker prevalence align with international data. The lower-than-expected EGFR mutation rate may be due to reduced testing during the COVID-19 pandemic in 2020. The high smoking rates and late-stage diagnoses in Serbia underscore the need for comprehensive tobacco control and enhanced early detection programs. The initiation of a lung cancer screening program at the University Clinical Centre of Serbia in late 2024 is a promising step toward improving patient outcomes.

E-PS-23-011
Evaluation of prognostic clinicopathological parameters in non-small cell lung cancer: insights from a single-centre study
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Background & Objectives: Non-small cell lung cancer (NSCLC) is one of the most common malignancies with high mortality rate. Aim of this study was to evaluate prognostic clinicopathological features in NSCLC patients.
Methods: 136 cases diagnosed with NSCLC from resection materials between 2017-2024 were retrospectively analysed for age, gender, tumour localisation, tumour size, histological type, grade, spread through airspaces (STAS), pleural invasion, lymphovascular invasion, perineural invasion, lymph node metastasis and PD-L1 status.
Results: Out of 136 cases, 74 were lung adenocarcinoma(LUAD), 60 were squamous cell carcinoma(SCC) and 2 were adenosquamous carcinoma. 105(77.20%) of the patients were male, 31(22.80%) were female. Mean age was 64.08(40-86) years. Mean tumour size was 3cm(0.5-10cm). Pleural invasion was present in 39(28.67%), LVI in 63(46.32%), PNI in 18(13.23%), lymph node metastasis in 32(24.24%) cases. Among LUAD cases, 68(91.89%) were non-mucinous, 3(4.05%) were mucinous and 3(4.05%) were mixed invasive mucinous non-mucinous adenocarcinoma. While 55.88% of non-mucinous adenocarcinoma cases were grade 3, most common dominant pattern was acinar (47.05%). STAS was observed in 63.5% of adenocarcinoma cases. Of the 60 SCC cases, 33(55%) were non-keratinizing, 23(38.33%) were keratinizing, 3(5%) were basaloid, 1(1.67%) was lymphoepithelial type. Furthermore, PNI was six times more frequent in SCC cases compared to LUAD cases. 38(27.94%) of the cases have died. 14 of these cases were adenocarcinoma and 24 were SCC. The calculated 1-year, 3-year, 5-year overall survival rates were 86.48%, 76.27%, and 67.85% respectively. PD-L1 immunohistochemistry was performed in 24 cases and 7 (LUAD=6, SCC=1) had a tumour proportion score (TPS) above 50%. While 2 PD-L1 positive cases died, all seven cases with a TPS>50% remained alive.
Conclusion: Lung cancer is one of the most lethal malignancies worldwide. Prognostic clinicopathological features play crucial role in patient survival. In addition, the higher survival rates of patients with high PD-L1 expression highlight the prognostic and therapeutic importance of immunotherapy.

E-PS-23-012
PD-L1 expression in non-small cell lung cancer: clinicopathological and theranostic implications study of 69 cases
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Background & Objectives: Lung cancer is the leading cause of cancer death worldwide. Non-small cell lung cancer (NSCLC) accounts for most cases, with adenocarcinoma and squamous cell carcinoma being the main types. About 30% of cases are diagnosed at stage III, and the prognosis remains poor despite various treatments. Immunotherapy is an interesting new option for treating advanced NSCLC.
The objective of this study is to investigate the expression of PDL1 in NSLCC and to assess its clinic-pathological significance.
Methods: The present retrospective study examined 69NSLCC cases, assessing PDL1 expression through immunohistochemistry using the clones CAL10 and 22c3. The tumour proportion score (TPS) was used for quantitative analysis, with two positivity thresholds (TPS<1%, TPS1≥%). Expression was also investigated in lymph node metastasis in 7cases. The results of the two clones were compared. A statistical study of PDL1 expression and clinicopathological factors was performed.
Results: Most patients were between 55 and 65 (43.5%) and mostly male (91.3%). The main histological type was adenocarcinoma, with 33.3% classified as IASLC grade3. Surgical margins were clear in 94.3%, stage IIIB was reported in 21.2%, and 2patients had a cerebral metastasis.
Overall, 36.2% of tumours had TPS levels <1%, while 63.8% had PDL1 expression in at least 1% of cells. Of these, 14.5% had strong PDL1 expression (TPS ≥50%). The results of the PDL1 expression analysis remained consistent across the two clones, with TPS ranging from below 1% to ≥50%. PD-L1 expression remained stable between primary tumours and their lymph node metastasis. However, differences were observed in brain metastasis (case1: primary tumour TPS=10% versus brain metastasis TPS=90%; case2: primary tumour TPS=25% versus brain metastasis TPS=10%). A significant correlation was observed between PD-L1 expression and surgical margins (p=0.031).
Conclusion: The present study revealed variability in PD-L1 expression in NSCLC, with a significant proportion of tumours potentially eligible for PD-1/PD-L1 inhibitor therapies.

E-PS-23-013
Pulmonary dirofilariasis: diagnostic challenges in the presence of pulmonary tuberculosis and a history of colorectal cancer
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Background & Objectives: Pulmonary dirofilariasis, a rare parasitic infection caused by the filarial nematode Dirofilaria typically affects dogs but can incidentally infect humans as aberrant hosts. Pulmonary dirofilariasis is an uncommon condition that primarily involves the lungs, where it manifests as solitary pulmonary nodules or masses, often leading to diagnostic confusion due to its clinical similarity to malignancy or infectious diseases.
Methods: We report the only two cases of pulmonary dirofilariasis diagnosed at the Marius Nasta Institute of Pneumophthisiology, Bucharest, Romania between 2000 and 2025. All data was extracted from the digital archive of the Institute.
Results: **Case 1:** A 58-year-old male, with history of right hemicolectomy for colorectal cancer, presents for further investigations of a pulmonary nodule detected on chest radiograph. An atypical pulmonary resection was performed. On gross examination the specimen presented a well-defined nodule of 12mm diameter which microscopically revealed granulomatous inflammation and the presence of characteristic Dirofilaria larvae. 55
Case 2: A 36-year-old female presented with dry cough, dyspnea and weight loss. Chest radiograph showed multiple, bilateral pulmonary nodules. The laboratory received an atypical pulmonary resection specimen which, on gross examination, presented multiple grey-white nodules between 1 and 7mm diameter. Microscopic examination revealed a necrotizing granulomatous inflammation suggestive of pulmonary tuberculosis further confirmed by a Ziehl-Neelsen stain. One of the examined slides revealed the presence of Dirofilaria larvae inside one necrotizing granuloma.
Conclusion: Both cases demonstrate the importance of considering pulmonary dirofilariasis in patients presenting with solitary pulmonary nodules. Additionally, the co-occurrence of other pulmonary or systemic conditions, such as tuberculosis or a history of cancer, requires clinicians to maintain a broad differential diagnosis and avoid prematurely attributing pulmonary findings solely to the underlying disease. A careful and thorough workup, including biopsy or resection specimen and histopathological examination, is essential in providing an accurate diagnosis and ensuring appropriate management.

E-PS-23-014

Calcifying fibrous tumour of the pleura: a case report of an uncommon entity in an unusual location

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Background & Objectives: Calcifying fibrous tumour (CFT) is an uncommon, benign entity primarily associated with the gastrointestinal tract. It is an extremely rare finding in a pleural location, with only 42 cases reported in the literature.
Methods: We here present a case of a 42-year-old woman undergoing follow-up consultations after being diagnosed with hyperplastic intraductal papilloma of the breast. MRI revealed, as an incidental finding, an 18mm oval nodule in the left cardiophrenic field. The patient had no symptoms. The possibility of a solitary fibrous tumour was considered and a biopsy was performed. The histological findings of the specimen were consistent with the diagnosis of calcifying fibrous tumour of the pleura.
Results: The specimen was a 15mm filiform fragment, and the histological analysis revealed a paucicellular lesion composed of spindle-shaped cells without evident atypia, embedded in a collagenized stroma, accompanied by psammomatous calcifications and minor chronic inflammation. Immunohistochemical analysis revealed positivity for CD34 and negativity for STAT6.
Conclusion: Calcifying fibrous tumour of the pleura is an extremely rare presentation of a benign soft tissue lesion and, as seen in our case, it usually is an incidental finding. Biopsy specimens can impose a challenge when diagnosing CTF as the lack of specific genetic and immunohistochemical markers makes it mostly a morphological diagnosis and, in a limited biopsy sampling, it may mimic other entities with a higher risk of aggressiveness, such as the solitary fibrous tumour. Recognizing this entity can ultimately avoid overtreating patients, as it is a completely benign lesion.

E-PS-23-015

Giant solitary fibrous tumour of the thorax: an unusual presentation on a known thoracic neoplasm of uncertain malignant potential

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Background & Objectives: Solitary Fibrous Tumour (SFT) can occur in almost any part of the body, however, the thoracic region is among the most common locations. SFTs often have indolent growth, with larger tumours normally causing symptoms of cough, dyspnea or chest pain. Around 10% to 20% display an aggressive behaviour. In several cases, SFTs are asymptomatic and only discovered incidentally.
Methods: We report the case of a 77-year-old woman who had asthenia following a viral upper respiratory infection. The ensuing computed tomography (CT) study revealed a 17x16x15 cm right hemithorax mass. A biopsy was then performed and the presence of a neoplasm displaying SFT features was suggested. After surgical excision we received a 20x18x13,5cm tumour weighing 2538g. The external surface was smooth and, upon sectioning, there was a whitish, well-defined, vaguely multinodular neoplasm.
Results: The histological analysis revealed a mesenchymal neoplasm with mostly well-defined limits, made up of spindle-shaped to ovoid cells, with poorly defined cytoplasmic borders, scarce to slight eosinophilic cytoplasm and small to medium-sized hyperchromatic nuclei, sometimes with obvious nucleoli. The cells were slightly to moderately pleomorphic, mostly distributed in a disorganized manner around a rich vascular network and sometimes intertwined bundles could be seen. Occasional staghorn vessels could be observed. There were >2 mitotic figures/mm^2. Necrosis was absent. Images of vascular invasion or perineural invasion were not identified. Immunohistochemistry showed diffuse positivity for CD34 and STAT6. Based on the WHO critera, the metastatic risk was predicted to be elevated.
Conclusion: This case highlights the uncommon presentation of a 20 cm thoracic SFT, which was successfully treated with surgical resection. Larger SFTs are more likely to be malignant and are therefore associated with worse prognosis. Nearly 5 months have elapsed after surgery and the patient remains well, under a thorough CT scan surveillance scheme, without signs of disease relapse.

E-PS-23-016

SMARCA4-deficient thoracic undifferentiated tumour: the case report of a rapidly progressive malignancy at risk of diagnostic oversight

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Background & Objectives: SMARCA4-deficient thoracic undifferentiated tumour is a rare and aggressive malignancy associated with biallelic inactivation of the *SMARCA4* gene. It typically presents as a rapidly growing thoracic mass, often with metastases at the time of diagnosis, carrying a poor prognosis.
Methods: We report the case of an 81-year-old man who presented with recent significant weight loss, dyspnea, and right-sided hemiparesis. Imaging studies revealed a 10 × 8 cm nodule in the upper lobe of the right lung, along with brain metastases. A transthoracic biopsy of the pulmonary nodule was performed. The patient was provided with the best supportive care, dying one week after the diagnosis was established.
Results: Microscopic examination revealed a predominance of large ovoid cells with vesicular nuclei, prominent nucleoli, and abundant basophilic cytoplasm, apart from rare dispersed rhabdoid cells. The tumour exhibited extensive necrosis and a mitotic rate of 36 mitoses per 10 high-power fields. Immunophenotypically, the tumour was negative for CKAE1/AE3, Cam5.2, CK20, p40, TTF-1, synaptophysin, chromogranin A, INSM1, SOX10, CD20, CD3, ERG, calretinin and WT1, with loss of SMARCA-4 expression.
Conclusion: SMARCA4-deficient thoracic undifferentiated tumour represents a rare and aggressive malignancy with a poor prognosis. Its diagnosis remains challenging due to histological overlapping features with other undifferentiated neoplasms.
This rare entity should be considered in the differential diagnosis of high-grade thoracic neoplasms, particularly in cases with challenging immunohistochemical characterization.

E-PS-23-017

Challenges in diagnosing pulmonary salivary gland-type tumours: a case study

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Background & Objectives: Salivary gland-type tumours (SGTs) of the lung are rare neoplasms arising from the submucosal glands of the tracheobronchial tree. While the majority of SGTs show specific morphological and genomic features, a subset of currently unclassifiable tumours are recognised, presenting diagnostic particularly in small biopsy setting. We present a case of unclassifiable SGT of the lung with likely pathogenic *BCOR* mutation and *APC* deletion.
Methods: This is a case report of resected pulmonary tumour at a tertiary thoracic centre. DNA next generation sequencing (NGS) was performed using a customised 200-gene panel, and RNA NGS was performed using Illumina Pancancer RNA fusion panel.
Results: The patient was a 70-year old male presenting with an incidental right middle lobe lesion with low grade FDG-avidity (SUVmax 2.7), together with right hilar and subcarinal nodal activity. A total of four biopsies were attempted, neither of which achieved a definitive pre-operative diagnosis with diagnostic opinions including SGT, bronchiolar adenoma, primary lung cancer and an inflammatory lesion. Right middle lobectomy reveals a low-grade biphasic neoplasm composed of epithelial and myoepithelial components within a fibromyxoid stroma. Immunohistochemistry (IHC) demonstrated AE1/3 and CK7 positivity in epithelial cells, while myoepithelial cells showed strong SMA, SOX10, multifocal S100, and focal p40 positivity, with largely negative TTF-1 expression. Definitive features of recognised SGT entities are not present. The tumour was classified as a low grade salivary gland-type neoplasm at this stage.
NGS revealed likely pathogenic *BCOR* p.H358fs* (c.1072del) mutation and *APC* deletion, without specific re-arrangements of SGTs. The consensus diagnosis was a salivary gland-type neoplasm without discernible features of atypia. The patient is currently under clinical follow-up.
Conclusion: This case underscores the diagnostic complexity of currently unclassifiable SGTs, representing an unmet clinical need in tumour classification. Our case could represent either a novel SGT entity, or an existing tumour subtype with non-canonical genomic profile.

E-PS-23-018

Histopathologic analysis of H69PR *in ovo* culture treated with *Carmona retusa* leaf extract: bridging basic sciences and clinical practice

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Background & Objectives: Lung cancer is the second-most common cause of mortality in the Philippines. There have been instances that lung cancer developed resistance to chemotherapeutic agents, and one of the reasons is the overexpression of signalling molecules involved in angiogenesis. This study investigated the effects of an antiangiogenic leaf extract to H69PR *in ovo* culture.
Methods: H69PR was inoculated in the chorioallantoic membrane of duck embryos. These cultures were treated with 5 mg/mL and 10 mg/mL of *Carmona retusa* leaf extract. Isotretinoin (10 mg) was used as positive control. Tumour invasion, necrosis, and mitosis were assessed using haematoxylin & eosin staining. Microvascular density was determined using desmin immunohistochemical staining.
Results: Analysis of the H&E sections showed squamous cell carcinoma instead of small cell carcinoma (H69PR). Tumour invasion was absent in the culture treated with 10 mg/mL concentration of leaf extract. Necrosis was present in all set-ups except positive control. This may be attributed to apoptosis triggered by retinoic acid response elements. Mitosis (5 per high-power field) was only observed in the negative control. One-way ANOVA of the microvascular density showed significant difference among the groups with a 0.03 p-value suggesting inhibition of angiogenesis in the treated groups.
Conclusion: The metaplastic change of H69PR was an unexpected but interesting finding in this study, which emphasizes the importance of pathology in validating the cell line thus bridging basic sciences with clinical practice. *Carmona retusa* leaf extract was just as effective as isotretinoin in inhibiting angiogenesis. At higher concentration, *Carmona retusa* may possibly prevent tumour invasion warranting further investigation.

E-PS-23-019

Negative prognostic significance of primary cilia and cytoplasmic β-catenin expression in non-small cell lung cancer

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Background & Objectives: The aim of this study was to investigate the prognostic significance of the frequency of primary cilia (PC) and cytoplasmic β-catenin expression in non-small cell lung cancer (NSCLC) (pts).
Methods: Ninety-three pts with histologically verified squamous cell carcinoma and 218 pts with adenocarcinoma of the lung were retrospectively studied. The frequency of PC and cytoplasmic β-catenin expression were immunohistochemically and immunoflourescence evaluated.
Results: In the whole group of 218 pts with NSCLC, overall survival (OS) was significantly inferior among pts with present PC than without PC (p=0.024) and with higher cytoplasmic β-catenin expression (25-75%) than with lower cytoplasmic β-catenin expression (<25%) (p=0.008). In the univariate Cox proportional hazard model, the hazard ratio was 1.653 in pts with present PC (p=0.026) and 1.851 in pts with higher cytoplasmic β-catenin (25-75%) (p=0.009). Multivariate testing of the whole group of 218 pts with NSCLC showed that the presence of PC was associated with a worse prognosis (p=0.018). In the subgroup of 125 pts with adenocarcinoma, OS was significantly improved in pts with higher membranous β-catenin expression (≥50%) than in pts with lower expression (<50%) (p=0.0300) and OS was significantly inferior in pts with higher cytoplasmic β-catenin expression (25-75%) than in pts with lower expression (<25%) (p=0.0004). Multivariate testing of the subgroup of pts with adenocarcinoma showed that cytoplasmic β-catenin (p<0.001) and pleural invasion (p=0.017) were associated with worse prognosis.
Conclusion: The present results indicate a negative prognostic significance of PC and cytoplasmic β-catenin expression in NSCLC and a negative prognostic significance of cytoplasmic β-catenin expression in adenocarcinoma.

Funding: This study was supported by the Ministry of Health, Czech Republic (AZV NU22-03–00130), the Ministry of Health, Czech Republic - conceptual development of research organization (Thomayer University Hospital - TUH, 00064190), the Charles University, Prague, Czech Republic (project Cooperatio Medical Diagnostics), Ministry of Defence of the Czech Republic "Long Term Organization Development Plan 1011" - Healthcare Challenges of WMD II of the Military Faculty of Medicine Hradec Kralove, University of Defence, Czech Republic (Project No: DZRO-FVZ22-ZHN II) and the project National Institute for Cancer Research (Programme EXCELES, ID Project No. LX22NPO5102) – Funded by the European Union - Next Generation EU

E-PS-23-021
Bilateral lung transplantation in a patient with Clinically Amyopathic Dermatomyositis associated with rapidly progressive interstitial lung disease: a case report
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Background & Objectives: Clinically amyopathic dermatomyositis (CADM) is a rare type of auto-immune disease within the dermatomyositis spectrum with cutaneous manifestations, which lack the typical muscle weakness. It has a high risk of developing interstitial lung disease (ILD), malignancy and other fatal complications. ILD associated with CADM is often refractory and rapidly progressive. In these patients, MDA-5 antibodies are associated with worse prognosis.
Methods: A 55-year-old man presented with fatigue, digital ulcers secondary to Raynaud's phenomenon, productive cough, shortness of breath, nailfold erythema and shawl sign with skin rash of back and neck. Chest CT showed bilateral ground-glass and cystic changes with lower lobe predominance. The diagnosis of CADM was made based on clinical assessment and immunological findings of PM-Scl, Anti-Ro and Anti-La autoantibodies. The MDA5 antibody was negative. The follow up wedge biopsy showed histological features suggestive of lymphoid interstitial pneumonia (LIP) pattern. Due to worsening of his symptoms and lack of response to immunosuppression, he underwent bilateral lung transplantation.
Results: Microscopically explanted lungs showed extensive areas of diffuse moderate interstitial fibrosis, chronic remodelling of small airways, patchy mild chronic interstitial inflammation, focal cystic parenchymal changes and old fibrous pleural adhesions, consistent with systemic connective tissue disease associated with CADM involving the lungs. Additionally, marked chronic pulmonary arteriopathy was also identified, consistent with his history of pulmonary hypertension, and likely representing a secondary complication of connective tissue disease. After transplant, the patient developed multiple respiratory infections and ultimately died 11 months post-transplant from acute respiratory failure.
Conclusion: CADM has been associated with progressive ILD. Due to the severity and low survival rate, accurate diagnosis is of utmost importance. Early detection, with early and aggressive combined immunosuppression, is key to better survival. Early screening for malignancy as well as presence of MDA-5 antibodies, which is associated with adverse prognosis and progressive ILD, is essential.

E-PS-23-022
Mediastinal Inflammatory Myofibroblastic Tumour mimicking a mediastinal cyst: a rare case
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Background & Objectives: Inflammatory myofibroblastic tumours (IMT) are rare mesenchymal neoplasm. It is common in children and young adults. It has been reported in many anatomical locations such as lung, liver, spleen, head and neck. The mediastinal IMT has been rarely documented. IMT has different morphological features ranging from benign to malignant. It is associated with ALK gene rearrangements as well as fusions of some kinase genes including ROS1, RET, etc. in ALK negative IMT.
Methods: We report a case of non-smoker 66-year-old male who presented for atrial fibrillation and found to have an incidental 7.4 cm middle mediastinal thin-walled cyst on chest CT scan. On chest CT angiogram, the cystic mass had partial effacement of the oesophagus and left atrium without any evidence of invasive or complex components.
Results: The patient underwent complete surgical excision of the mass. Morphology revealed bland spindle shaped cell proliferation devoid of atypia or mitotic activity admixed with inflammatory infiltrates including plasma cells and myxoid appearing background. Immunohistochemical stains showed positivity for S100, CD34, calretinin, SOX10. The ki-67 proliferation index was less than 3%. The ALK gene rearrangement by FISH analysis was detected, confirming the diagnosis.
Conclusion: IMT is a rare tumour and the mediastinal location has been reported very infrequent. The radiologic features are very nonspecific and variable, hence the diagnosis is solely based on tissue diagnosis and molecular studies. It should be considered in the differential diagnosis of mediastinal neoplasms. Complete surgical excision with close follow up after surgery is the definitive treatment. Overall IMT has an indolent behaviour.

E-PS-23-023
Endobronchial hamartoma, an extremely rare benign tumour involving the respiratory tract
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Background & Objectives: Hamartoma is the most common benign neoplasm involving the lung. Most hamartomas are located peripherally in the lung parenchyma and endobronchial hamartoma is a rare lesion. Their clinical presentation mimics obstructive lung diseases such as asthma and chronic obstructive pulmonary disease, or malignancy because of their obstructive character, leading to a delay in diagnosis and errors in treatment. Therefore, making precise diagnosis may be challenging.
To better understand this entity, we reviewed clinicopathological data of patients with endobronchial hamartoma.
Methods: We report a retrospective study of 18 cases of endobronchial hamartoma, diagnosed at our department of pathology and treated at our institution, with a hindsight of 30 years, from 1995 to 2024.
Results: There were 15 male and 3 female patients, aged between 3 and 68 years with a mean of 52,88 years. Chest pain and cough were the most commonly reported symptom. Bronchoscopy revealed well-defined submucosal endobronchial lesions (n=12) and the clinical impression was that of a benign neoplasm. Computed tomography of the chest showed an endobronchial lesions in all cases. Histologic diagnosis was obtained by endobronchial biopsy in 4 cases and surgical resection (lobectomy, pnemonectomy, bilobectomy, wedge) in 14 cases. All lesions showed similar morphology: showed the presence of nodules of hyaline cartilage admixed with variable amounts of fibrous adipose tissue, spindle cells, hypertrophic seromucous gland and myxoid stroma without signs of specificity or malignancy. The diagnosis of endobronchial hamartoma was established. No recurrence was observed after a follow-up period of 12 months.
Conclusion: Endobronchial hamartoma is an extremely rare benign lesion of the respiratory tract which may lead to obstructive complications if unresected. It should be distinguished from malignancy lesion. All endobronchial HC tumours in the present series behaved in a benign manner.

E-PS-23-024
A rare case of pulmonary alveolar adenoma mimicking metastatic breast carcinoma: radiologic, pathologic and molecular characterisation
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Background & Objectives: Alveolar adenomas are exceedingly rare benign epithelial lung neoplasms, accounting for <1% of all lung tumours. They usually present as incidental radiologic findings in asymptomatic patients. We present a case of alveolar adenoma that clinically and radiologically mimicked a metastatic breast carcinoma and describe its histologic, immunohistochemical, and molecular profiles.
Methods: Clinical, radiologic, and pathologic data were reviewed. Immunohistochemical and molecular investigations (Myriapod NGS 50 genes) were carried out. This case report adheres to the Declaration of Helsinki.
Results: A 55-year-old female with left breast carcinoma underwent a chest computed tomography (CT) for radiologic staging, which evidenced a 13mm hypodense solitary nodule in the left lower lobe (LLL) base. Following left breast quadrantectomy and adjuvant chemo-radiotherapy, 3-monthly radiologic surveillance of the solitary lung nodule was performed. The nodule showed no radioisotope avidity on positron emission tomography (PET)-CT, but increased 5mm in size within one year and a half. Thus, the patient underwent LLL segmentectomy and mediastinal lymphadenectomy. Histologically, this was a well-circumscribed, cystic and solid neoplasm. The cystic spaces contained abundant eosinophilic granular material and were lined by cuboidal to hobnailed cells resembling type II pneumocytes. The intervening solid areas comprised spindle cells admixed with lymphocytes, plasma cells, and conspicuous eosinophils. No nuclear pleomorphism, mitoses, necrosis, or lymph node metastases were present. On immunohistochemistry, the cyst-lining cells strongly expressed CK MNF116, EMA, and TTF-1 and did not express GATA3, ER or PR. The stromal spindle cells showed vimentin and CD34 expression only. Immunohistochemistry was crucial for distinction from differential diagnosis such as metastatic breast carcinoma and primary lung tumour mimickers (sclerosing pneumocytoma, bronchiolar adenoma, lymphangioma, adenocarcinoma). NGS did not reveal any gene alteration.
Conclusion: We report this case because of its rarity, good prognosis and to avoid misdiagnosis. Histological examination, including immunohistochemistry, is mandatory for precise diagnosis.

E-PS-23-025
Can murine influenza A-induced pneumonia serve to study human post-viral lung disease?
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Background & Objectives: Influenza viruses are one of the most common pathogens causing respiratory infections in humans, with a wide spectrum of clinical symptoms and even mortality. The study aimed to characterize the alveolar repair response occurring in a murine model of sublethal pneumonia induced by the influenza A (PR/8/34) virus.
Methods: BALB/c female mice were intranasally infected with a sublethal dose of influenza A virus (PR/8/34). Lung tissue was collected at designated time-points from day 3 until day 31 post-infection (p.i.), formalin-fixed paraffin-embedded and stained by haematoxylin-eosin and immunohistochemistry (primary antibodies against surfactant protein C (SFTPC), cytokeratin 5 (KRT5), doublecortin-like kinase 1 (DCLK1) and collagen type I alpha1 (COL1A1). Slides were scanned using the AxioScan scanner (Zeiss).
Results: Intranasal infection with a sublethal dose of influenza A virus induced severe damage of alveolar epithelium, characterized by multifocal dropout of alveolar epithelial cells type II (SFTPC+ cells) that were replaced by clusters of KRT5+ stem cells, i.e., pods. Pods were observed from day 12 p.i. onwards and were still present on day 21 p.i. In addition, within KRT5+ regions in lung parenchyma, a differentiation into tuft cells occurred, which was recognized by the DCLK1 expression. Interstitial fibrosis was detected from day 12 p.i., and persisted until the end of the study on day 31 p.i.
Conclusion: Alveolar epithelial injury and repair process was studied in a murine model of post-viral lung remodelling induced by influenza A virus. At sites of severe alveolar epithelium injury, islands of KRT5+ pods were formed with ectopic tuft cell differentiation. By the end of the observation period, interstitial fibrosis developed. The lung repair process described in this model has been documented in human post-viral lung disease, among others post-SARS-CoV-2 infection. This opens the possibility for wider use of this murine model in translational respiratory research.

E-PS-23-026
Inflammatory myofibroblastic tumour of the lung: a diagnostic challenge in an asymptomatic adolescent
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Background & Objectives: Inflammatory myofibroblastic tumour (IMT) of the lung is a rare lesion within the inflammatory pseudotumor spectrum, primarily affecting children and young adults. This

report details a case of pulmonary inflammatory myofibroblastic tumour (IMT) in an 18-year-old male. A 3 cm mass was incidentally detected on thoracic CT at 11 years of age, with no subsequent medical follow-up. The patient re-presented in 2024 for a pre-employment evaluation, where repeat thoracic CT revealed progression of the lesion. This case is presented to underscore the diagnostic challenges and clinicopathological correlations inherent to IMT.
Methods: Following detection of a left upper lobe mass (55×43 mm, lobulated, peripherally located with central calcification) on contrast-enhanced CT, a lobectomy specimen (299,5 g, 16,4 × 12,3 × 5,2 cm) was subjected to histopathological analysis.
Results: Gross examination revealed a well-circumscribed lesion (5,2×4,6×3,3 cm) adjacent to pleura with central calcification and peripheral solid components. Microscopy demonstrated alveoli entrapped within haphazardly distributed spindle-shaped fibroblasts and inflammatory cells rich in plasma cells. These alveolar cells exhibited hyperplasia, and focal calcifications were observed in scattered areas. No cytological atypia, mitotic activity, or necrosis was identified. Immunohistochemistry confirmed diffuse ALK positivity (ALK-1/D5F3+), polyclonal light chains, and a low Ki-67 index (1-2%), while excluding mimics (STAT6−, CD34−, p40−, TTF-1−). Surgical margins were tumour-free.
Conclusion: This case underscores the diagnostic complexity of IMT, requiring correlation of histomorphological features with immunohistochemical markers (particularly ALK positivity) to exclude malignancy and distinguish it from benign mimics, such as sclerosing pneumocytoma. Despite its benign classification, complete surgical excision is imperative to mitigate recurrence or local invasiveness. In the context of a well-circumscribed, incidentally detected pulmonary lesion, inflammatory myofibroblastic tumour (IMT) merits inclusion in the differential diagnosis.

E-PS-23-028
Autoimmune Pulmonary Alveolar Proteinosis and mantle cell lymphoma
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Background & Objectives: Pulmonary alveolar proteinosis (PAP) is a rare lung disease with an incidence of 0.2 cases per million. It is characterized by the accumulation of lipoproteinaceous material within the alveoli due to impaired clearance by alveolar macrophages. PAP can be classified as congenital, secondary, or autoimmune. The objective of this abstract is to present an extremely rare case of autoimmune alveolar proteinosis occurring simultaneously with CD5(+) B-cell lymphoma.
Methods: An 80-year-old female smoker with a recent hospitalization in a pulmonary clinic due to bilateral lung infiltrates underwent a lung biopsy. Two lung specimens were excised and analysed using haematoxylin-eosin (H&E) staining, immunohistochemistry, and periodic acid–Schiff (PAS) histochemical staining. Following the pathology report, a serum sample was tested for anti-GM-CSF antibodies, and the patient was thoroughly evaluated for a possible hematologic malignancy.
Results: Microscopically, an amorphous, eosinophilic material was observed within the alveoli, which was PAS-positive, along with macrophages/histiocytes. The interstitial space showed a small number of lymphocytes and areas of mild fibrosis. Additionally, in other lung tissue sections, a neuroendocrine nodule (tumourlet) measuring 0.1 cm in diameter was identified near a terminal bronchiole, with the following immunohistochemical profile: CK8/18 (+), Chromogranin A (focal+), OTP (+), and TTF-1 (+). Furthermore, anti-GM-CSF antibodies were positive, and the bone marrow biopsy confirmed the presence of mantle cell lymphoma.
Conclusion: Although PAP is a rare entity, it should be considered in the differential diagnosis by pathologists, as its clinical course can range from complete resolution to respiratory failure and increased susceptibility to opportunistic infections. Additionally, thorough histological examination and comprehensive clinical and laboratory evaluation are crucial, as PAP may coexist with other pathological conditions.

E-PS-23-029
Confusion in the diagnosis of endobronchial tumours: not so obvious or are we too late?
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Background & Objectives: Primary endobronchial tree tumours can be either malignant or benign. Benign tumours of the lung constitute a small minority of all lung tumours but they can cause clinical roentgenographic changes similar to those seen in malignant neoplasms. Most benign tumours are located peripherally in the lung parenchyma and endobronchial location a is an unusual lesion.
In this study, we aimed to present our experience with the diagnosis of endobronchial benign tumours in our clinic
Methods: We report a retrospective study of 36 cases of endobronchial tumour, diagnosed at our department of pathology and treated at our institution, with a hindsight of 30 years, from 1995 to 2024.
Results: There were 30 male and 6 female patients, aged between 3 and 80 years with a mean of 46,44 years. Chest pain and cough were the most commonly reported symptom. Bronchoscopy revealed well-defined submucosal endobronchial lesions (n=30) and the clinical impression was that of a suspected neoplasm in 11 cases. Additionally, the procedure led to the complete excision of the tumour in 7 cases. Computed tomography of the chest showed an endobronchial lesions in all cases. The diagnosis was obtained by endobronchial biopsy in 16 cases and surgical resection (lobectomy, pnemonectomy, bilobectomy, wedge) in 20 cases. Histologically, 50% of tumours were hamartomas (n=18), followed by papillomas in 30,55% (n=11), lipomas in 16,6% (n=6) and pleomorphic adenoma in 2,85% (n=1). No recurrence was observed after a follow-up period of 12 months.
Conclusion: Benign endobronchial tumours are uncommon location lesions. The course of the disease is unpredictable. It may regress spontaneously, but in other instances it may lead to serious complications ranging from airway obstruction up to malignant transformation.

E-PS-23-030
Case report: primary pulmonary extraskeletal osteosarcoma – a rare diagnostic challenge in thoracic tumours
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Background & Objectives: Primary pulmonary extraskeletal osteosarcoma (ESOS) is an exceptionally rare and aggressive malignant mesenchymal tumour characterized by the production of osteoid matrix by tumour cells in the absence of skeletal involvement. In contrast to metastatic osteosarcoma, this tumour originates from the lung parenchyma, mimicking other high-grade thoracic sarcomas. The objective of this report is to underscore the hallmark features aiding accurate diagnosis and differentiate this entity from other tumours with sarcomatoid features.
Methods: Formalin-fixed, paraffin-embedded sections were stained with haematoxylin and eosin, and immunohistochemistry was performed with an antibody panel including Pancytokeratin (AE1/AE3), EMA, S100, Desmin, SMA, Myogenin, MyoD1, TLE1, SATB2, and

CD99. A literature review was conducted to compare this case to previously reported cases.
Results: A 73-year-old male presented with pleuritic chest pain. Imaging showed 10.9×8.5 cm heterogeneous mass with cystic areas in the left upper lobe. The specimens included left upper lobectomy, 2nd to 4th rib resection, regional lymphadenectomy, and separately submitted tumour tissue. Histology revealed a high-grade sarcoma with hyperchromatic nuclei, prominent nucleoli, occasional osteoblast-like cytoplasm, multinucleated giant cells, frequent mitoses, cytologic atypia, and necrosis. Malignant osteoid appeared as thin, lace-like or irregular trabecular deposits closely associated with tumour cells. The tumour was diffusely positive for CD99 and negative for all other tested markers. Although it extended into adjacent soft tissue, the resected ribs were uninvolved, confirming a primary pulmonary origin.
Conclusion: Primary pulmonary ESOS is a rare and aggressive neoplasm that requires a thorough histopathological assessment to distinguish it from other high-grade sarcomas and metastatic lesions. In this case, the diagnosis was established by identifying malignant osteoid and excluding mimickers through immunohistochemistry, while the absence of rib involvement further supported a pulmonary origin. This case adds to the current knowledge of pulmonary ESOS and serves as a reminder to include it in the differential diagnosis of thoracic sarcomas.

E-PS-23-031
Pulmonary oxalosis associated with Aspergillus niger infection: case report
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Background & Objectives: *Aspergillus niger* is an opportunistic fungal pathogen that can cause invasive and non-invasive aspergillosis, particularly in patients with underlying lung disease or immunosuppression. Pulmonary oxalosis, characterized by calcium oxalate crystal deposition within lung tissue, is a rare but significant complication of *Aspergillus* infections, contributing to tissue destruction and disease progression.
Methods: We report a case of a 62-year-old male, a former heavy smoker with a 20-year history of chronic obstructive pulmonary disease (COPD), who underwent left lower lobectomy for moderately differentiated non-keratinizing squamous cell carcinoma (pT2aN1). Postoperatively, he developed a persistent dry cough, recurrent fever, and worsening respiratory symptoms. Bronchoscopy revealed a bronchopleural fistula, and microbiological cultures identified *Acinetobacter spp.*, *Corynebacterium spp.*, and *Escherichia coli*, leading to broad-spectrum antibiotic therapy. Despite treatment, he developed empyema and progressive respiratory failure, necessitating completion pneumonectomy.
Results: Histopathological examination of the pneumonectomy specimen revealed a necrotic cavitary lesion with extensive suppurative inflammation. Brown-black pigmented fungal hyphae and conidia, consistent with *Aspergillus niger*, were identified, along with birefringent calcium oxalate crystal deposition within necrotic lung tissue. Background changes included emphysematous lung parenchyma, fibrosis, anthracosis, and chronic inflammation. Fluconazole therapy was initiated postoperatively; however, the patient's condition deteriorated, and he succumbed to sepsis and multiple cardiac arrests on postoperative day 11.
Conclusion: Pulmonary oxalosis is an uncommon but serious manifestation of *Aspergillus niger* infection, resulting from fungal production of oxalic acid, which reacts with tissue calcium to form calcium oxalate crystals. This process exacerbates local tissue damage and may contribute to poor clinical outcomes. While *Aspergillus fumigatus* is the most common species in pulmonary aspergillosis, *Aspergillus niger* should also be considered, particularly in patients with persistent respiratory decline postoperatively. Recognition of calcium oxalate crystal deposition in lung tissue should raise suspicion for invasive fungal infection, emphasizing the need for early diagnosis and prompt antifungal treatment to improve outcomes.

E-PS-23-032
Clinicopathological analysis of EGFR mutation subtypes in lung adenocarcinoma
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Background & Objectives: EGFR mutations are the most common driver alterations in lung adenocarcinoma. Although their general clinical and pathological features are documented, the specific characteristics and outcomes of different EGFR mutation subtypes remain unclear.
Methods: We analysed retrospectively 60 lung adenocarcinoma cases with confirmed EGFR mutations at our centre between 2013 and 2023. Tumours were evaluated for histological pattern, grade, lymphovascular invasion (LVI), pleural invasion (PLI), lymph node metastasis (LNM), spread through air spaces (STAS), and survival outcomes. EGFR mutations were detected using the EGFR Pyro Kit.They were classified as typical (exon 19 deletions, exon 21 L858R), atypical (exon 18 G719, exon 21 L861), or compound. Overall survival(OS) and recurrence-free survival(RFS) were analysed using the Kaplan-Meier method.
Results: The cohort included 40 females (67%) and 20 males (33%), with a mean age of 60.8 years.The most common predominant morphological pattern was acinar, observed in 66.7% of cases, followed by lepidic in 21.7%, with papillary, micropapillary, and solid patterns each found in 3.3% of cases. STAS, PLI, LVI, and LNM were observed in 38%, 57%, 28%, and 23% of cases, respectively. Typical mutations were found in 78.3% of patients, atypical in 15%, and compound in 6.6%. The cases with predominant lepidic pattern were seen only in typical mutations, and 84.3% of these cases showed exon19 deletions.However, differences in histological patterns between mutation subtypes were not statistically significant (p=0.2).
Mean OS was 72.5 months, and mean RFS was 51.6 months. Although no statistically significant differences were found between mutation type and OS (p=0,093), patients with atypical mutations had 33.9% 5-year survival rate while those with typical mutations and compound mutations showed 68.5% and 66.7%, respectively.
Conclusion: Atypical EGFR mutations may show different pathological features and outcomes, but our findings are not sufficient to confirm this. Further studies are warranted to clarify the differences between EGFR mutation subtypes.

E-PS-23-033
Generation-age structured modelling of neuroendocrine lung tumours: a biopsy-calibrated approach to understanding small cell lung cancer dynamics
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Background & Objectives: Small Cell Lung Cancer (SCLC), an aggressive neuroendocrine tumour of the lung, is characterized by rapid proliferation, early metastasis, and resistance to therapy. Despite advances in molecular profiling, its clinical management remains largely empirical. In this talk, we present a novel generation-age structured mathematical model that extends the Iwata framework of metastatic progression to account for clonal proliferation and generational age in primary and metastatic lesions.
Methods: The central innovation of our approach lies in modelling tumour growth as a process driven by successive generations of proliferating cells, where each generation carries distinct phenotypic characteristics and metastatic potentials—linking tumour "age" to aggressiveness and therapeutic response.
Results: A key aspect of our work is the direct calibration of the model using patient-derived tumour biopsies. By integrating histopathological data—such as Ki-67 proliferation indices, neuroendocrine marker expression, spatial distribution of clones—we aim to extract generational fingerprints that inform the distribution of cell division rates and clonal hierarchies. This biopsy-calibrated approach enables us to simulate patient-specific tumour evolution and predict the burden of occult micrometastases.
Conclusion: To our knowledge, this is the first effort to quantitatively link tumour age structure with real-world biopsy data in the context of neuroendocrine lung cancer. The model not only offers mechanistic insights into SCLC progression but also lays the foundation for computational tools that can stratify patients based on generational dynamics and forecast response to treatment.

E-PS-23-034
Serum protein - Omics of non-small cell lung cancer patients in Greece
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Background & Objectives: Lung cancer remains the leading cause of cancer-related mortality worldwide, demanding for revolutionary approaches to enhance accurate diagnosis and treatment. The study aimed to investigate proteins of serum samples from patients with lung cancer across various stages of the disease to identify prognostic biomarkers as well as elucidate molecular mechanisms underlying disease pathophysiology and progression.
Methods: Patients diagnosed with Non-Small Cell Lung Cancer (NSCLC) were prospectively recruited at the Oncology Unit of the 3rd Department of Internal Medicine, "Sotiria" University Hospital. Serum samples were obtained from Stage II, III, and IV patients, whilst their clinical and demographic data were also recorded. Serum from all patients was analysed by in-depth liquid chromatography–tandem mass spectrometry based on in-house developed protocols followed by rigorous statistical evaluation.
Results: Two proteins, haptoglobin (HP) and vitronectin (VTN), were found to be increasingly expressed in NSCLC advanced-stage patients compared to those of lower-grade disease. These biochemical alterations were pinpointed in parallel with marked disease progression. Overexpression of VTN and HP in cancer patients, is traditionally associated with increased tumour aggressiveness, a higher likelihood of metastasis, and overall poor clinical outcomes.
Conclusion: Serum protein -omics remains crucial in advancing precision medicine for lung cancer by facilitating earlier prognosis and tailored therapeutic approaches.

E-PS-23-035
Multinodular epithelioid haemangioendothelioma with intermediate grade of malignancy (G2) in combination with tuberculoma in the same lung lobe
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Background & Objectives: Epithelioid haemangioendothelioma (EHE) of the lung is a rare low- to intermediate-grade vascular tumour composed of solid nests and short cords of epithelioid endothelial cells in a myxohyaline stroma. In 60% of the cases it presents as a multinodular mass, rarely diagnosed radiographically, clinically presented with chest pain or haemoptysis.
We present a clinical case of a 50-year-old man with recurrent haemoptysis for several months, with computer tomographic data for a nodular formation in the left upper lobe, in whom a lobectomy of the left upper lobe revealed a multinodular EHE and a tuberculoma in the same lobe.
Methods: Surgical resection material from left upper lobectomy was examined histologically by haematoxylin-eosin, and immunohistochemical markers - CD34, ERG, Vimentin, CK7.
Results: Macroscopically: encapsulated subpleural, nodular lesion measuring 16/21 mm, with an inhomogeneous yellow-whitish cut surface, friable.
Microscopically: nodular structure containing caseous necrosis, surrounded by expanded connective tissue, in places with hyalinization, in the periphery histiocytes with anthracotic pigment, lymphocytes, corresponding to tuberculoma. In the vicinity - multifocal proliferations of atypical endothelial cells with intracytoplasmic capillary lumens (pseudo signet-ring cells) with angiocentric location - in vascular walls of blood vessel lumens, perivascularly, along alveolar septa; intraalveolar spaces with nodular structures of atypical endothelial cells; myxoid stroma; irregularly shaped vascular channels filled with blood; remodelling of the lung parenchyma by tumour proliferations; blood in alveolar spaces, bronchiolar, bronchial lumens. Immunohistochemically, the atypical cells express CD34, ERG, Vimentin and focally CK7.
Conclusion: We present a rare neoplasm of the lung, and in a combination with tuberculosis in the same lung lobe. The lobectomy was performed for persistent haemoptysis and a nodular mass that proved to be a tuberculoma. The described case demonstrates that persistent haemoptysis can be due to EHE, which should be taken into consideration in clinical practice.

E-PS-23-036
The changing landscape of lung cancer diagnosis with emphasis on unusual histologies
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Background & Objectives: Advances in lung cancer biology have led to the development of targeted therapies. The need for accurate histological classification and guided molecular characterization highlights the continued role of the surgical pathologist in the multidisciplinary team. The emphasis has shifted towards diagnosis on endoscopic biopsies rather than resections. Preserving tissue for molecular studies is crucial. Minimal material may be sufficient to distinguish non-small cell lung cancer (NSCLC) from small cell lung cancer, however, additional tissue is needed to perform immunohistochemistry (IHC) for subtyping of NSCLC. Lack of accurate NSCLC subclassification could expose patients to unnecessary risks or deny them effective treatment. A diagnostic strategy for small biopsies lacking differentiation criteria relies on IHC markers, TTF1 and P63. These IHC markers lead to a specific diagnosis in over 80% of biopsies.

When there is no clear morphological or immunohistochemical evidence of lineage differentiation, it becomes imperative to classify the tumour as NSCLC-NOS. Pathologists are discouraged from using excessive IHC stains and should focus on saving tissue for molecular analysis. Searching for relevant mutations will direct the choice of targeted therapy. These new paradigms emphasize close communication between pathologists and clinical colleagues to ensure tissue adequacy and optimal triage for appropriate diagnostic studies.
Methods: All the lung cancer cases confirmed histologically between January 2023 and March 2025 were retrieved from the hospital information system. Demographic data, morphology, IHC and the molecular studies were collated for these cases.
Results: Of the 484 histologically confirmed cases, 13.4% were identified as small cell lung cancer, 37.2% as adenocarcinoma, 17.8% as squamous cell carcinoma, while 6.8% remained unclassified as NSCLC, NOS. The diverse morphology observed in NSCLC, NOS cases often necessitates multidisciplinary discussions to determine the optimal utilization of tissue.
Conclusion: Our study emphasizes the importance of preserving tissue for molecular studies to improve the diagnosis and treatment protocols.

E-PS-23-038
How does tumour spread through air spaces survive (STAS)? – An approach to the microenvironment of STAS and the role of extracellular matrix in airborne metastases
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Background & Objectives: It is hypothesized that a novel form of airborne metastasis may be observed, involving the dissemination of tumours through air spaces. This phenomenon has been observed at the periphery of some pulmonary adenocarcinoma cases. The objective of the present study was to achieve a more profound comprehension of the survival mechanisms of STAS, with particular reference to the impact of hypoxia and extracellular matrix on progress, as well as PDL1-expression in STAS in comparison with the primary tumour.
Methods: The present study identified STAS using haematoxylin and eosin (HE) and immunohistochemistry (IHC). MALDI-TOF imaging was utilized for the analysis of the extracellular matrix. The NanoString GeoMx platform was used to perform high-plex profiling at the RNA level, thereby facilitating a comprehensive assessment of the microenvironment associated with STAS. Furthermore, the expression levels of PDL1 in the primary tumour and STAS were examined, as well as the levels of MUC-1 and MUC-5AC.
Results: It has been demonstrated that STAS exhibits heterogeneity with respect to spatial distribution and quantity, thereby demonstrating aberrant functional gene expression in tumours and inflammatory pathways.
Conclusion: Changes in the extracellular matrix and mucin levels appear to be significant in the development of STAS. Further investigation is required to characterize the various entities involved and to evaluate therapeutic options.

E-PS-23-040
Spontaneous haemothorax revealing a malignant solitary fibrous tumour in the postpartum period
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Background & Objectives: Malignant Solitary Fibrous Tumours (SFTs) are rare tumours that develop from mesenchymal cells of the pleura. Their occurrence within the lung tissue itself is even more uncommon. By this case, we want to explore the differential diagnoses of malignant SFTs and highlight the importance of immunohistochemistry in confirming the diagnosis.
Methods: We report the case of a 33-year-old woman in her third trimester of pregnancy who underwent a caesarean section due to acute foetal distress. Shortly after delivery, she developed a spontaneous haemothorax. Thoracic imaging revealed a highly vascularized tumour located in the left lung apex.
Results: The macroscopic examination showed a firm tumour and whitish, measuring 8×7×5 cm, with areas of necrosis and haemorrhage. Microscopically, it showed a mix of cellular and fibrous regions interspersed with hyaline and necrotic areas. The low-cellularity regions contained hemangiopericytoma-like blood vessels, while the denser areas consisted of spindle-shaped cells with moderate nuclear atypia and a mitotic rate of 9 mitoses per 10 high-power fields. Immunohistochemical analysis showed positivity for CD99, CD34, and STAT6. While BCL2 and ERG were negative. These findings confirmed the diagnosis of a malignant solitary fibrous tumour of the lung.
Conclusion: Intrapulmonary SFTs are extremely rare and present a variable clinical and radiological picture that can resemble other intrathoracic lesions. These tumours are generally slow-growing but can exhibit malignant behaviour in 10–30% of cases. Histopathological examination, along with immunohistochemistry, is crucial to distinguish SFTs from other tumours such as monophasic synovial sarcoma, fibrosarcoma, or high-grade vascular tumours like angiosarcoma.

E-PS-23-041
Bronchopulmonary carcinoma: unusual subtypes A study of 11 cases
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Background & Objectives: Primary malignant tumours of the pulmonary salivary gland type (PMTSG) are rare, accounting for 1% of all bronchopulmonary malignancies. They present distinctly, so it's crucial to distinguish them from other bronchopulmonary tumours to ensure optimal management.
This work describes the clinico-pathological features of 11cases of PMTSG.
Methods: This retrospective study reviewed 11cases of PMTSG over 29years, including seven mucoepidermoid carcinoma (MEC) and four adenoid cystic carcinoma (ACC) cases.
Results: Mean age was 47.4years and sex ratio was 1:0. Most common symptom included cough and thoracic pain. Diagnosis was made after 7.45months from symptom onset. Chest X-rays showed opacities in all cases. Chest CTscans were performed in 10patients showing proximal mass in all cases, involving stem bronchus in 4cases, lobar bronchus

in 4others, and the hilar region in two. The mean tumour size was 3.6cm. Tumour invasion of middle mediastinum was noted, as well as vascular structure invasion in one and lower lobe collapse in two. Hilar and mediastinal adenopathies were noted in 3cases. Extension assessment included abdominal CTscan, performed in all cases, showing adrenal metastasis in 1case of MEC. Histological examination of bronchial biopsies revealed 3cases of ACC, 2cases of MEC, and 3 negative cases that subsequently were found to be MECs. Eight patients had localized stage, 2 had locally advanced stages and 1 had metastatic stage. Eight patients underwent surgery. Two of them received adjuvant radiotherapy. Neoadjuvant and palliative chemotherapy were prescribed in 1case each. Radiotherapy was the only indicated treatment in 1case. One patient had locoregional relapse and two had metastatic relapse (ACC). Mean overall survival was 37.8months. One patient died after 24months. Seven patients are alive and progression free at 24-72months, two have relapsed. One patient is lost to progression.
Conclusion: PMTSGs have a more favourable prognosis than other bronchopulmonary carcinomas, but recurrence and metastasis are common, requiring long-term monitoring.

E-PS-23-042
Pulmonary adenoid cystic carcinoma in patient with history of breast cancer
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Background & Objectives: Pulmonary adenoid cystic carcinoma (PACC) is one of the rarest (0.04–0.2%) and unexplored presentations of lung cancer. It is considered a slow-growing tumour with a low-grade malignancy. Diagnosis is typically confirmed through histological examination. This report aimed to highlight the importance of being aware of this pathology and reducing the risk of misdiagnosis.
Methods: A 68-year-old woman with a history of breast cancer twelve years ago, presented non-specific respiratory symptoms. A CT scan highlighted a bilateral pulmonary nodule. The patient underwent a right medial segmental lobectomy with mediastinal lymphadenectomy and biopsy. Histopathological examination showed two solid lesions, measuring 2.2 x 1.4 x 1.2 cm and 1 x 1 x 0.7 cm, respectively. Both exhibited lung parenchyma compromised by a malignant tumour lesion composed of intermediate-sized cells exhibiting little euchromic cytoplasm, nuclei slightly pleomorphic, some with prominent nucleoli, and low mitotic activity. These cells were arranged predominantly in solid nests interspersed with cribriform areas exhibiting intraluminal myxoid secretion. Immunohistochemical analysis revealed reactivity for Cytokeratin-AE1/AE3, Cytokeratin-7, CD117, and focal S100, and negativity for Cytokeratin-20, TTF1, GATA3 and GCDFP15.
Results: The morphologic features of PACC are not very distinctive to give a confirmed diagnosis in routine H&E stains. To improve diagnosis, the immunohistochemistry study is highly recommended, the expression of myoepithelial markers, such as Cytokeratin 7, Cytokeratin AE1/AE3, CD117, and S-100 protein, is a strong argument for PACC. In this case, the immunophenotypic findings were compatible with a diagnosis of PACC and the histological features were consistent with PACC grade III (solid-type mass).
Conclusion: Pulmonary adenoid cystic carcinoma (PAAC) represents a malignant neoplasm wherein diagnosis can be challenging both clinically and histologically. Hence, PACC should be well recognized by pathologist to avoid misdiagnosis. The microscopic characteristics may deceptively suggest a benign lesion; accordingly, techniques including immunohistochemical analysis remain imperative for establishing malignant differentiation.

E-PS-23-043
MicroRNA 21 (miR-21) expression in non-small cell lung carcinoma (NSCLC) among Filipinos
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Background & Objectives: In the Philippines, lung cancer is the top cause of cancer-related deaths. This is worsened by the continuous incidence of resistance to *EGFR* tyrosine kinase inhibitors (TKIs). MicroRNA-21 (miR-21), because of its role in invasion, metastasis, and chemoresistance, is a good candidate for targeted therapy. This study seeks to determine the expression of miR-21 in non-small cell lung carcinoma (NSCLC) among Filipinos.
Methods: Five (5) formalin-fixed, paraffin-embedded (FFPE) primary lung tumour tissue samples and 5 FFPE non-neoplastic lung tissue samples were retrieved from Tondo Medical Centre's Department of Pathology and Laboratory. RNA was isolated and purified, which was then subjected to reverse transcription. The resulting complementary DNA (cDNA) was analysed through quantitative PCR using miR-21 primers. Expression of miR-21 between NSCLC and non-neoplastic lung tissues were compared.
Results: All non-neoplastic lung tissues were diagnosed with chronic granulomatous inflammation. Two of five non-neoplastic lung tissues expressed miR-21, which both had extensive fibrosis. Age ranges from 15 to 48 years with female predominance. Two of five NSCLC tissues similarly expressed miR-21, one of which demonstrated squamous cell carcinoma with vascular invasion. This also had the lowest C_T value (suggesting highest expression) across all non-neoplastic and NSCLC tissues. The other one was diagnosed as invasive adenocacinoma. Upon microscopic review, the remaining three without miR-21 expression had very minute foci of tumour cells that may have contributed to this qRT-PCR outcome. Age ranges of patients with NSCLC were 64 to 72 years with male predominance. Student t-test (p value = 0.9646) showed no significant difference in the miR-21 expression between non-neoplastic lung and NSCLC tissues.
Conclusion: The high expression of miR-21 in the squamous cell carcinoma with vascular invasion is consistent with the association of miR-21 to tumour aggressiveness. The results, however, were not statistically significant. A prospective study with larger cohort is warranted.

E-PS-23-044
High-grade adenoid cystic carcinoma: a case report
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Background & Objectives: Adenoid cystic carcinoma (AdCC) is a rare malignant neoplasm that primarily affects the salivary glands but can also occur in other areas such as the respiratory tract, lacrimal glands and breast. When occurring in the lung it makes up less than 0.2% of all primary lung neoplasms. High-grade transformation of AdCC is a rare, progressive transformation associated with to poorer prognosis and aggressive behaviour.
Methods: We report the case of a patient diagnosed with high-grade AdCC of the lung which presented at the Marius Nasta Institute of Pneumophthisiology, Bucharest, Romania in 2024. All data was extracted from the digital archive of the Institute.

Results: A 17-year-old male presented with progressive shortness of breath over the course of several months. During initial examination a chest CT was performed which revealed a 50mm diameter mediastinal mass invading the trachea and cervical oesophagus raising suspicion for a malignant tumour. A second mass was identified in the right pulmonary hilum. During bronchoscopy multiple fragments were resected and sent for histopathological examination. The laboratory received multiple fragments with sizes varying between 2 and 4cm which were completely processed. Histopathologic examination led to the diagnosis of high-grade AdCC which was further confirmed by immunohistochemistry.
Conclusion: There are several challenges when diagnosing high-grade AdCC. Considering that AdCC mainly affects patients in their sixth decade, a potential challenge occurs when the diagnosis is made in paediatric populations given its rarity and nonspecific clinical presentation. Another challenge is the slow growing yet insidious progression with propensity for local recurrence and distant metastasis which underscore the importance of early recognition and a thorough workup particularly in young individuals where rare malignancies can be overlooked. High-grade transformation AdCC diagnosis is based on sufficient material for microscopic examination, a high index of suspicion and appropriate immunohistochemical studies.

E-PS-23-045
EGFR-driven nuclear retention of the proteasome in NSCLC, mediated via p38-MAPK signalling
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Background & Objectives: The proteasome, a central effector of protein degradation, exhibits dynamic subcellular localization that responds to cellular stress. Beyond its well-established role in proteostasis, proteasome localization has recently emerged as a marker of tumour biology, with evidence suggesting that proteasome dynamics, largely regulated by anabolic and catabolic stimuli, play a key role in cancer cell survival. Insights from animal tumour models further position proteasome dynamics not only as a functional mechanism, but also as a potential marker of tumour aggressiveness. In this study, we observed an unexpected pattern in non-small cell lung carcinoma (NSCLC), where many tumours displayed predominant nuclear proteasome localization. Given the frequent presence of activating mutations in the EGFR-KRAS pathway in NSCLC, we hypothesized that oncogenic signalling may modulate proteasome distribution.
Methods: Using immunohistochemistry, proteasome localization was evaluated in FFPE samples of NSCLC, stratified by EGFR molecular status. In vitro, cultured cells were treated with EGF to assess the pathway effects on proteasome localization under both basal and amino acid-starved conditions. Key components of the MAPK pathway were perturbed to identify downstream mediators of EGFR-dependent proteasome control.
Results: Tumours lacking driver mutations showed predominantly cytosolic proteasomes, similar to other malignancies. In contrast, EGFR-mutant NSCLC exhibited strong nuclear proteasome localization ($OR = 76.0$, $p = 2.2 \times 10^{-6}$). EGF stimulation in culture induced nuclear retention of the proteasome, even during nutrient stress. Further, p38-MAPK was identified as a critical mediator linking EGFR activation to proteasome translocation.
Conclusion: These findings uncover a mechanistic connection between EGFR signalling and proteasome localization in NSCLC, mediated by p38-MAPK. Results from perturbation studies strongly suggest a causative mechanistic relation between EGFR signalling and proteasome localization. This pathway may contribute to altered stress responses and tumour behaviour, and this work prompts an investigation into potential clinical and prognostic implications of proteasome localization in EGFR-driven lung cancers.

E-PS-23-046
Peribronchiolar metaplasia mimicking pulmonary masses: a case series about a worrisome differential diagnosis
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Background & Objectives: This abstract aims to present three cases of peribronchiolar metaplasia (PBM), also known as Lambertosis, that clinically manifested as pulmonary masses. Peribronchiolar metaplasia is an uncommon lesion characterized by fibrosis and bronchiolar epithelial cell proliferation, typically in response to bronchiolar and peribronchiolar injuries. It usually appears as ground-glass nodules or sub-solid nodules on computed tomography (CT).
Methods: We describe three patients with PBM. The first patient, an 83-year-old male, presented with multiple pulmonary masses suspected of metastases from a previously diagnosed clear cell carcinoma of the kidney. One of the masses, measuring 11 mm, exhibited a spiculated appearance on CT. The second patient, a 79-year-old male, was found to have two basal nodules, with the larger nodule measuring 12 mm. The third patient, a 64-year-old female, showed an sub-solid area of ground-glass opacity in the middle lobe of the right lung, with a maximum diameter of approximately 30 mm. They were all submited to transthoracic fine needle biopsy.
Results: Histologically, all cases showed growth of ciliated columnar epithelium replacing alveolar epithelium in the bronchioloalveolar wall. Lesions sometimes exhibited a bronchioloalveolar growth pattern, associated with dilated bronchioles. The epithelium ranged from cuboidal to columnar, often ciliated, without atypia.
Conclusion: PBM is a nonspecific reaction to bronchiolar and peribronchiolar injury. It is characterized by fibrosis and proliferation of bronchiolar epithelium along the peribronchiolar alveolar walls. While PBM typically presents as ground-glass opacity lesions on CT, it can uncommonly manifest as solitary solid nodules or sub-solid nodules, posing diagnostic challenges. Recognizing the variable clinical and radiological presentations of PBM is essential for accurate diagnosis and differentiation from primary lung cancer and metastatic lung tumours.

E-PS-23-047
Lymphangitic breast cancer spread in explanted lungs with fibrosing interstitial lung disease: an unexpected finding
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Background & Objectives: Breast metastases in explanted lungs and hilar lymphnodes are an exceedingly rare event, with lymphangitic spread previously virtually unreported. We present a very rare case of lymphangitic carcinomatosis from a previously undiagnosed breast carcinoma, identified only through systematic examination of explanted lungs in a patient undergoing bilateral lung transplantation for unclassifiable lung fibrosis. This case underscores the importance of standardized sampling protocols and multidisciplinary evaluation in transplant pathology.
Methods: A 60-year-old woman with progressive unclassifiable lung fibrosis underwent bilateral lung transplantation. Explanted lungs and hilar lymph nodes were sampled according to our institutional protocol, which includes multiple tissue blocks from all lobes (at least 3 per

lobe), vascular and bronchial margins, and complete hilar node dissection. Histological evaluation was supported by a immunohistochemical stainings. Clinical and radiological data were retrospectively reviewed in a multidisciplinary discussion.
Results: Gross examination of the explanted lungs and lymph nodes was unremarkable. Histology revealed metastatic involvement of multiple hilar lymph nodes and extensive architectural fibrotic remodelling with widespread lymphangitic infiltration of interlobular septa and peribronchial spaces by malignant epithelial cells. Immunohistochemistry (CK AE1/AE3+, GATA3+, ER+, PR+, HER2 2+) confirmed breast origin. Retrospective review of prior mammography revealed a previously uninvestigated suspicious lesion. The patient was subsequently diagnosed with metastatic breast cancer and treated with hormone therapy. Despite all efforts, the disease progressed, and she died 12 months post-transplantation.
Conclusion: This is the first reported case of bilateral lymphangitic breast cancer discovered incidentally in explant lungs. Neoplastic infiltration can be easily masked by pre-existing architectural distortion in end-stage fibrotic interstitial lung disease. Therefore, we highlight the critical role of a generous sampling and a thorough, standardized pathological evaluation in lung explants as well as a multidisciplinary discussion. Establishing shared protocols across transplant centres could improve early cancer detection and optimize long-term outcomes.

E-PS-23-048

A lung adenocarcinoma "collision tumour": two distinct driver mutations in histologically divergent regions

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Background & Objectives: In 2024, 13% of cancers diagnosed in Canada and 23% of cancer-related deaths were due to lung cancers. There is a strong association with smoking and pulmonary carcinogenesis, and multiple oncogene mutations have been identified in lung cancers. In some cases, drugs can target specific oncogene mutations to improve patient outcomes or predict prognosis. The two main oncogenes mutated in lung cancers at our site in 2024 were EGFR (14%) and KRAS (41%). We report a case of a lung adenocarcinoma biopsy with two histologically distinct morphologies that also each showed unique oncogene mutations.
Methods: We used histology, immunohistochemistry, and Next-Generation Sequencing to diagnose and identify the mutations.
Results: The patient is a 67-year-old female with a 35-pack-year smoking history. A core biopsy of her right upper lobe tumour showed a lung adenocarcinoma with lepidic and invasive distinct components. Next-generation sequencing (NGS) identified two clinically significant mutations, including a EGFR exon 19 deletion and a KRAS G12C mutation. Repeat NGS of each individual component isolated the EGFR mutation to the lepidic region and the KRAS mutation to the invasive region. The copy number profiles of the two components were strikingly similar, suggesting a clonal relationship between the two components. These results therefore indicate a single tumour with two molecularly and histologically distinct clones arising from the same progenitor.
Conclusion: The molecular findings in this case are unique given there is a single tumour composed of two separate clones from the same progenitor. Activating KRAS and EGFR mutations are thought to be mutually exclusive due to synthetic lethality. The most likely explanation for their co-occurrence in this case is that the original tumour clone separately acquired KRAS and EGFR variants in distinct cell populations. The patient recently had a lobectomy, which may help shed additional light on the tumour's evolution.

E-PS-23-049

EGFR p.Glu709Lys mutation in lung adenocarcinoma – case report

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Background & Objectives: Classic activating mutations (exon 19 deletion and exon 21 L858R) make up the vast majority of *EGFR* mutations and are well defined as strong predictors of good clinical response. However, low-frequency mutations still raise questions, because despite the increased use of more sensitive detection methods to identify rare *EGFR* mutations in patients, our understanding of the biology of these rare *EGFR* mutations is poor compared to classic mutations.
Methods: We present a case of a 72-year-old woman with an adenocarcinoma with acinar, lepidic, papillary and micropapillary patterns from the right upper and middle lobes. It were detected TP53 c.833C>A;p.(Pro278His); *EGFR* c.2573T>G;p.(Leu858Arg) and c.2125G>A;p.(Glu709Lys) known to be oncogenic in NSCLC. It was performed mutation research by next-generation sequencing (Genexus, Oncomine Precision Assay Panel, Thermo Fisher Platform). Manual macrodissection was performed and nucleic acid extraction was carried out with the MagMAX FFPE DNA/RNA Ultra Kit.
Results: The *EGFR* exon 18 E709K mutation occurs in the *EGFR* tyrosine kinase domain. This mutation has been found in patients with non-small cell lung cancer. Cell line experiments demonstrate that is an activating and transforming mutation, sensitizing to *EGFR* tyrosine kinase inhibitors (TKIs), gefitinib and erlotinib, with superior sensitivity to second-generation inhibitors such as afatinib and neratinib. Studies shown that patients with NSCLC harbouring the *EGFR* E709K mutation in combination with other TKI-sensitizing mutations derived clinical benefit from treatment with erlotinib or gefitinib.
Conclusion: Patients with *EGFR* E709K mutant non-small cell lung cancer (NSCLC) have tumours that typically carry a coincident *EGFR*-tyrosine kinase inhibitor (TKI)-sensitizing mutation such as L858R *or* G719X. The EGFR TKIs erlotinib, afatinib, and gefitinib are FDA and EMA approved for the treatment of patients with NSCLC harbouring specified EGFR sensitizing mutations including L858R and exon 19 deletions.

E-PS-23-050

Cytological diagnosis of paracoccidioidomycosis in pleural fluid

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Background & Objectives: Paracoccidioides brasiliensis is a dimorphic fungus and the causative agent of paracoccidioidomycosis, an infectious disease also known as South American blastomycosis. This report highlights its diagnosis in pleural fluid cytology.
Methods: A 60-year-old female patient presented to the emergency department reporting chest pain. For two weeks, she had been experiencing flu-like symptoms, which progressed to a persistent dry cough, ventilatory-dependent pain in the left costal region, and dyspnea. She reported a fever lasting approximately three days and denied purulent expectoration, but reported decreased urine output (oliguria).

Results: The hospitalized patient initially received treatment with Koide D and Dipyrone. However, the patient's condition did not improve, and she began to experience pain in the left hemithorax. Subsequently, Amoxicillin and Clavulanate were prescribed. After seeking care at another hospital, Clarithromycin, Atrovent inhalations, and another course of corticosteroids were added to her treatment regimen. Despite these interventions, there was no improvement, and she returned to the hospital in Brazil, where she was hospitalized. A chest CT scan revealed consolidation with left-sided hydrothorax. Pleural aspiration was performed. Cytological analysis of the pleural fluid revealed blood components with frequent neutrophils, lymphocytes, and histiocytes, some of which were multinucleated. Round structures with birefringent membranes, consistent with Paracoccidioides brasiliensis, were also observed, along with mesothelial cells with homogeneous nuclei and cytoplasm.
Conclusion: Diagnosing paracoccidioidomycosis through pleural fluid cytology presents a significant challenge due to the rarity and complexity of identifying Paracoccidioides brasiliensis. This case underscores the importance of meticulous cytological evaluation, particularly in patients who do not respond to conventional treatments for respiratory symptoms. Accurate identification of the fungus is crucial for effective clinical management, highlighting the value of cytology as a vital, though sometimes underutilized, diagnostic tool in complex clinical scenarios.

E-PS-23-051
Regulators of actin cytoskeleton LIMK1 and SSH1 are implcated in human lung adenocarcinoma
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Background & Objectives: Cofilin phospho-regulation, which is mediated by LIM kinases (LIMKs) and Slingshot phosphatases (SSH), is important for actin filament turnover, cancer cell invasion and metastasis. However, little is known regarding the role of actin cytoskeleton regulators in human lung adenocarcinoma (LUADC). In this study, we aimed to assess expression and significance of LIMK1 and SSH1 in human LUADC.
Methods: Expression of LIMK1 and SSH1 was evaluated by immunohistochemistry in 105 human LUADC samples in relation to clinicopathologic parameters (grade, pTNM, lymph node metastasis). Correlation with epithelial-mesenchymal transition (EMT) markers E-cadherin and ZEB (data available from previous studies in the same cohort) was also assessed. In addition, cell proliferation of human lung cancer cell lines was examined by MTT assay upon pharmacologic inhibition of SSH1.
Results: We here show that LIMK1 and SSH1 are expressed in 95/97 (98%) and 105/105 (100%) cases of human LUADC. Immunostaining for LIMK1 and SSH1 in lung cancer cells is mainly cytoplasmic with mean H-scores 111.9±6.6 and 156.6 ±6.5 respectively. Statistical analysis showed no significant association with tumour progression parameters although there is a trend towards significant correlation of SSH1 with lymph node metastasis ($p=0.06$). Expression of SSH1 is also significantly correlated with EMT marker ZEB ($r=0.445$, $p<0.001$). Inhibition of SSH1 by sennoside inhibits A549 lung cancer cell proliferation.
Conclusion: Our results suggest that overexpression of F-actin regulator SSH1 is implicated in the pathogenesis of lung adenocarcinoma representing a promising tumour biomarker and therapeutic target in the disease.

E-PS-23-055
Pulmonary squamous cell carcinoma with a predominant lepidic growth pattern mimicking metastasis: a case report and review of the literature
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Background & Objectives: Lepidic growth is classically associated with lung adenocarcinoma and is exceedingly rare in squamous cell carcinoma (SCC). To date, only **12 cases** of pulmonary SCC with a lepidic growth pattern have been reported in the literature. This unusual morphology can lead to diagnostic confusion, particularly in patients with a history of malignancy. We present a rare case of pulmonary SCC with a predominant lepidic growth pattern initially suspected to be metastatic urothelial carcinoma.
Methods: A 77-year-old male with a prior diagnosis of T2 high-grade urothelial carcinoma underwent PET imaging during follow-up, which revealed a 1.5 cm hypermetabolic nodule in the left lower lobe of the lung. Wedge resection was performed for diagnosis and treatment. Histopathologic and immunohistochemical analysis was conducted to determine the origin and nature of the tumour.
Results: Histologic evaluation showed a tumour with an 85% lepidic growth pattern and a 15% poorly differentiated invasive squamous component. Tumour cells were positive for p63, p40, and CK 5/6 and negative for CK-7, TTF-1, Napsin-A, and Uroplakin II. No lymphovascular or perineural invasion was identified. Based on morphology and immunoprofile, a diagnosis of primary pulmonary SCC with a lepidic growth pattern was made. The tumour was staged as pT1b. The patient was alive and free of disease at 6-month follow-up.
Conclusion: Pulmonary SCC with a lepidic growth pattern is an **extremely rare variant**, with only 12 reported cases in the literature. It may closely mimic adenocarcinoma or metastatic disease, especially in patients with known malignancies. Accurate recognition and classification of this pattern are crucial to avoid diagnostic errors and to guide appropriate management. Our case supports the inclusion of lepidic components in the pathological staging system for pulmonary SCC, similar to adenocarcinoma.

E-PS-24 E-Posters Soft Tissue and Bone Pathology

E-PS-24-001
Axillary presentation of CIC-rearranged sarcoma: a diagnostic conundrum in soft tissue pathology
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Background & Objectives: CIC-rearranged sarcoma (CIC-DUX4 fusion-positive sarcoma) is a rare, aggressive undifferentiated round cell tumour mimicking Ewing sarcoma. It typically occurs in young adults in deep soft tissue; lymph node or unusual site involvement is uncommon. We report a case of a healthy 57-year-old woman with an axillary mass, highlighting the diagnostic challenges of this tumour.
Methods: Clinical examination and imaging studies (MRI, Mammography and PET scan) were performed, followed by biopsies of the breast and axilla. Histopathological evaluation with H&E staining and an immunohistochemical panel was undertaken. FISH assessed SS18 and EWSR1 rearrangements, while targeted NGS detected gene fusions, confirming the diagnosis.

Results: Mammography revealed enlarged left axillary nodes (up to 6.5 cm) suggesting breast malignancy. Biopsy of a contralateral BIRADS3 breast lesion was benign, while core biopsy of the axillary mass showed an undifferentiated malignant small round cell neoplasm. The tumour was highly cellular with scant stroma, delicate "chicken-wire" vasculature, focal necrosis, and brisk mitotic activity (17/1.73 mm², including atypical mitoses). Differential diagnoses included lymphoma and perivascular epithelioid cell tumour (PEComa). However, the immunoprofile (WT1, BCL-2, cyclin D1, CD99, vimentin, TLE1 positive; negative for epithelial, melanocytic, and myogenic markers) supported a non-epithelial malignancy. FISH excluded SS18 and EWSR1 rearrangements, ruling out synovial and Ewing sarcoma; NGS detected a CIC-DUX4 fusion, establishing the diagnosis.
Conclusion: This case underscores the need to consider CIC-rearranged sarcoma in axillary masses with undifferentiated round cell morphology. Its unusual topography adds diagnostic challenge, as seen in similar reports. Molecular techniques, especially FISH and NGS, are essential for confirmation. Early, accurate identification is crucial to guide appropriate therapy in this aggressive malignancy.

E-PS-24-002
PEComa of the gastrointestinal tract: a case report in this exceedingly rare location
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Background & Objectives: Perivascular epithelioid cell tumours (PEComas) are a family of mesenchymal tumours with a wide morphological variety that exhibit melanocytic and smooth muscle differentiation. They present a broad differential diagnosis. They can anise in any location, but less than 60 cases of gastrointestinal tract (GIT) have been reported.
Methods: A 52-year-old female patient with a prior history of low-grade uterine leiomyosarcoma surgically treated in 2012 was admitted at the hospital due to intestinal obstruction. A 9 cm mass occupying up to 70% of the ileum lumen was described in radiological studies. A surgical resection was performed.
Results: The tumour was composed of a densely cellular proliferation with a multinodular growth pattern. It was originated form the muscularis propria. The cells were large, with ample, clear and granular cytoplasm, round nuclei, and occasionally prominent nucleoli. The cells showed no significant atypia or pleomorphism. Seven mitoses were seen in 50 high-power fields. No evidence of lymphovascular or perineural invasion was found. No lymph node metastases were detected. The cells were positive for desmin, smooth muscle actin, calponin, caldesmon, HMB45, S100 protein and hormonal receptors. Cytokeratins, CD34, DOG1, MDM-2, MelanA and myogenin were negative. Ki-67 was 5%. Molecular studies (next generation sequencing) were negative.
Conclusion: PEComas exceptionally arise in GIT. The most frequent location within the GIT is the colon, and they usually present epithelioid morphology. The biological risk of GIT PEComas is assessed using the criteria established by Doyle et al. in 2013. They may develop an indolent or an aggressive course. Considering its morphological and immunohistochemical wide spectrum, this entity should be included in the differential diagnosis of mesenchymal tumours in the GIT.

E-PS-24-003
Histopathological and clinical evaluation of pleomorphic soft tissue sarcomas: a case series
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Background & Objectives: Pleomorphic soft tissue sarcomas are highly malignant mesenchymal tumours with heterogeneous histogenesis, characterized by marked cellular pleomorphism, atypia, and high mitotic activity. Pleomorphism refers to significant variations in tumour cell size, shape, and nuclear morphology, which are associated with aggressive biological behaviour.
Methods: This study retrospectively analysed 47 patients (23 females, 24 males) diagnosed between 2016 and 2025, with a mean age of 50–61 years. The aim was to assess the histopathological features of the most common pleomorphic soft tissue sarcoma subtypes and correlate them with clinical findings.
Results: The cases included 14 undifferentiated pleomorphic sarcomas (UPS), 22 dedifferentiated liposarcomas (DDLPS), 5 malignant peripheral nerve sheath tumours (MPNST), 3 pleomorphic liposarcomas (PLPS), and 3 pleomorphic leiomyosarcomas (PLMS). Mean tumour sizes were 12.5 cm (UPS), 21 cm (DDLPS), 6 cm (MPNST), 13 cm (PLPS), and 10 cm (PLMS). The mean mitotic rate was 12/mm² in UPS, 6/mm² in MPNST and PLPS, and 31/mm² in PLMS. The mean necrosis rate was 20–25% in UPS, <50% in MPNST and PLPS, and 30% in PLMS. The Ki-67 proliferation index was 60% in UPS, 55% in PLMS, 25% in DDLPS, and 30% in PLPS. In 19 cases of dedifferentiated liposarcoma, the mean mitotic count was determined to be 4–5/mm². Necrosis was present in 13 cases, while it was absent in 6 cases. All cases were high-grade. One DDLPS case exhibited rhabdomyoblastic differentiation. Twenty one additional cases displayed undifferentiated non-lipogenic pleomorphic sarcoma morphology. Pleomorphic liposarcomas featured pleomorphic lipoblasts, while PLMS exhibited pleomorphic spindle cells in fascicular arrangements.
Conclusion: Pleomorphic soft tissue sarcomas constitute a heterogeneous group of high-grade tumours that can reach large sizes, exhibit high mitotic activity, and display diverse morphological features.

E-PS-24-004
Osteofibrous dysplasia, osteofibrous dysplasia like adamantinoma and adamantinoma: a small case series including tumours with late recurrences
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Background & Objectives: Osteofibrous dysplasia (OFD) is a benign fibro-osseous tumour of the anterior cortex of the tibia and/or fibula. OFD-like adamantinoma (AD), contains small nests of epithelial cells with fibroosseous stroma. AD is a locally aggressive or malignant tumour that has epithelial cells within the osteofibrous component. In recent years, the clinical course of OFD and OFD-like AD has been debated for their similarities.
Methods: We evaluated 4 cases of OFD-like AD, 2 cases of AD, and 1 case of OFD diagnosed in our laboratory between 2015 and 2025, in terms of histopathological, immunohistochemical and clinical findings.
Results: The median age was 26 years (range: 8–68). The most common gender was female, and the most frequent location was the diaphysis of the left tibia. Recurrence was observed in 2 patients, after 8 and 9 years, respectively. One of these was OFD-like AD, the other AD. The core biopsy of the recurrent OFD-like AD showed only OFD areas. The number of nested epithelial cells stained with keratin in OFD-like AD ranged from 1 to 10. All tumours were treated by wide resection. Additionally, in one patient with AD and one with OFD-like AD, cement was also used. Recurrence occurred in

the OFD-like AD patient. In three patients with OFD-like AD, liquid nitrogen application and bone recycling were performed. One patient with classic AD treated by resection alone had recurrence. This tumour exhibited an Ewing-like pattern but did not contain EWSR1 rearrangement.
Conclusion: OFD, OFD- like AD and AD are tumours showing similar morphological findings and a predilection to cortex of the tibia. Although they do not show an aggressive clinical behaviour we have observed late recurrences in AD patients.

E-PS-24-005
A rare case of sinonasal primary aneurysmal bone cyst in a paediatric patient
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Background & Objectives: Aneurysmal bone cysts (ABCs) are benign lesions characterized by multiloculated blood-filled cystic spaces, fluid-fluid levels and well defined, lytic, expansile lesions on imaging. It has a broad skeletal distribution but primarily it is seen in metaphysis of long bones and vertebrae. Occurrence in the head and neck region, particularly in the paranasal sinuses, is exceedingly rare.
Methods: We present a case of an 8-year-old female with a history of Burkitt lymphoma diagnosed in 2020, with the maxillary sinus as the primary site of involvement. After her treatment, she presented with nasal congestion, snoring, and sleeping with her mouth open in December 2024, 4 years after initial diagnosis.
Results: CT scan revealed an expansile mass in the sinonasal cavity, which shows fluid-fluid levels and causes destruction in lamina papyracea. FESS was performed. Histopathological analysis revealed a giant cell-rich mesenchymal lesion containing cystic and solid areas with spindle cells in storiform fashion and blue-bone formation.
Conclusion: FISH study demonstrated USP6 gene rearrangement and confirmed the diagnosis of primary ABC. This case underscores the importance of considering ABC in the differential diagnosis of paediatric patients presenting with sinonasal masses, especially those with a history of malignancy, to ensure timely and appropriate management.

E-PS-24-006
Aggressive angiomyxoma of the vulva: a case report
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Background & Objectives: Aggressive Angiomyxoma of the vulva is a rare, locally invasive mesenchymal tumour that has a strong predominance amongst middle-aged women. Majority of the cases of this neoplasm are only discovered through case reports due to its rarity. Due to its propensity to increasingly grow in size, it may cause the patient and clinicians to be alarmed of its potential threat to the patient's quality of life. This is a case of a 50 year old female who came in with a 10 year history of gradually-enlarging vulvar mass. On physical examination, there is a noted fleshy, foul-smelling, nodulo-cystic mass hanging at the right labia approximately measuring 22 x 14 x 12 cm. The objective of this study is to understand the histopathologic nature of the identified mass.
Methods: Microsections of the mass show a myxoid, hypocellular stroma with spindle to stellate shaped cells with fine cytoplasmic processes, very mild nuclear atypia, numerous varisized vessels and extravasated red blood cells. To further support the diagnosis of aggressive angiomyxoma, immunohistochemistry studies were recommended.
Results: Further testing revealed a strong, diffuse positivity for SMA and desmin. There is weak, patchy positivity for ER and negative for PgR and CD34. Thus, a definite diagnosis of aggressive angiomyxoma was established. Tahere is no consensus regarding the pathogenesis of adgressive angiomyxoma. This hormonally responsive tumour is believed to arise from specialized mesenchymal cells of the pelvic–perineal region or multipotent perivascular progenitor cells, which often display variable myofibroblastic and fibroblastic features.
Conclusion: Despite of its rarity, Aggressive Angiomyxoma of the vulva should still be considered as one of the differential diagnoses for any painless swelling in the genitofemoral area. Patient education is vital most especially regarding the term "aggressive" which may be misunderstood for its malignant nature where in fact it actually denotes high risk for local recurrence.

E-PS-24-007
Deceptively pleomorphic, biologically indolent: a case of superficial CD34-positive fibroblastic tumour
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Background & Objectives: Superficial CD34-positive fibroblastic tumour (SCD34FT) is an uncommon mesenchymal neoplasm first described in 2014. It is characterized by pronounced nuclear pleomorphism, low mitotic activity, diffuse CD34 positivity, and focal cytokeratin expression. Despite its sarcoma-like morphology, most cases follow an indolent clinical course with minimal metastatic potential. Over 150 cases have since been reported, improving the understanding of its clinicopathological features. Here, we present a new case to further expand the literature and diagnostic familiarity with this rare entity.
Methods: Clinical, radiological, and pathological evaluations were performed to reach diagnosis.
Results: A 48-year-old male patient presented with a slowly enlarging, painless subcutaneous mass in the left gluteal region, present for approximately ten years. The medical history included partial nephrectomy 13 years earlier, with no other comorbidities or medications.
MRI revealed a well-defined, subcutaneous mass measuring 6.5 cm, showing T2-hyperintense and T1-hypointense signals. The lesion compressed but did not invade the gluteus maximus and extended toward the dermis.
Tru-cut biopsy showed a spindle cell neoplasm of intermediate cellularity with pleomorphism, eosinophilic cytoplasm, pseudo-inclusions, and rare vacuoles. CD34 was diffusely positive;
cytokeratin AE1/AE3 showed focal weak staining. INI1 and H3K27me3 were retained. Findings were suggestive of SCD34FT, but limited sampling precluded definitive diagnosis.
The excised mass measured $6.2 \times 3.7 \times 3.3$ cm and was located 0.4 cm below the skin. Grossly, it appeared soft and heterogeneous. Histology confirmed biopsy findings and showed more extensive pleomorphism, xanthomatous change, and hemosiderin. Mitoses were rare, necrosis absent. CD34 remained positive; cytokeratins (AE1/AE3, OSKAR) were focally positive. Other markers were negative. Ki-67 was 4%.
Integration of clinical, radiological, morphological, and immunohistochemical findings confirmed the diagnosis. The patient remains disease-free without adjuvant therapy.
Conclusion: SCD34FT is a rare, low-grade neoplasm with deceptive morphology. Accurate recognition is essential to avoid overtreatment.

Correlating clinical, histological, and immunohistochemical findings is key to avoiding misdiagnosis.

E-PS-24-008

A rare tumour of soft tissue: Angiomatoid Fibrous Histiocytoma

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Background & Objectives: Angiomatoid fibrous histiocytoma (AFH) is a rare soft tissue tumour of intermediate malignant potential, often seen in children and young adults, and typically arising in superficial extremities. It usually presents as a slow-growing, well-circumscribed mass with prominent haemorrhage and cystic change.
Methods: A 6-year-old male presented with a progressively enlarging subcutaneous mass in the right forearm. Microscopically, the tumour was located in the subcutaneous tissue and displayed extensive haemorrhagic/cystic regions, numerous vascular spaces, and a fibrous capsule with pigment-laden fibrohistocytic cells. Tumour nests were composed of spindle to polygonal cells with moderate, oval nuclei, abundant eosinophilic cytoplasm and inconspicuous nucleoli, showing 13 mitoses/ 10 HPFs. A marked lymphoid infiltrate, sometimes with germinal centres, was noted, along with metastatic focus in one nearby lymph node.
Results: Immunohistochemically, the tumour cells were diffusely positive for Desmin and CD99, with multifocal positivity for EMA and ALK. Ki67 proliferation index was 10–15%. EWSR1 gene rearrangement was obtained by FISH, supporting the diagnosis of AFH.
Conclusion: AFH has intermediate malignant potential with the capacity to recur or metastasize. Diagnosis can be challenging due to non-specific clinical, histological and immunohistochemical features compounded by rarity of this tumour. Wide surgical excision is essential, and thorough clinicoradiologic and pathologic correlation, including molecular testing for EWSR1, is critical. Prognosis can be favourable but long-term follow-up is mandatory, especially in paediatric cases. Consequently clinical observation is advised to detect possible recurrence or further spread.

E-PS-24-009

Lymphomas primarily diagnosed on bone biopsy: a tertiary centre's perspective over the last five years

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Background & Objectives: The diagnosis of lymphoma can be preceded by various symptoms and signs depending, in part, on the primary lesion's location. Lymphomas primarily diagnosed in bone biopsies are sparse in the literature. In the absence of specific symptoms or signs, their identification can be challenging, often leading to delayed diagnosis due to a lack of clinical suspicion of hematolymphoid origin.
Methods: We collected all cases of lymphomas diagnosed in bone biopsies from 2020 to 2024 in ULS-Coimbra. Cases with prior lymphoma diagnosis were excluded.
Results: We identified six cases of lymphomas primarily diagnosed in bone biopsies. Most patients were female (5/6), with a median age of 65 years (range: 33–83). All presented with bone pain, mainly involving the iliac bone. Imaging studies showed lithic lesions, raising the diagnosis of metastasis/primary bone tumour. Flow cytometry analysis in the original biopsy was performed in only one case, as clinical suspicion of lymphoma was lacking in the remaining cases. A diagnosis of diffuse large B-cell lymphomas was retained in all cases, including both germinal centre and non-germinal centre subtypes, as well as one case with *MYC* and *BCL2* rearrangements.
All patients were Ann Arbor stage IVA or IVB at diagnosis. Five underwent R-CHOP treatment: four achieved a complete metabolic response after 6 cycles, being currently alive, with no evidence of disease, and one is still under treatment, presently with a partial response. The oldest patient was treated with 6 cycles of R-mini-CHOP, achieving a partial response.
Conclusion: Our findings highlight that lymphomas primarily diagnosed in bone biopsies are uncommon, with most patients presenting with non-specific findings and no prior clinical suspicion. We emphasize the importance of considering lymphoma in the differential diagnosis of bone lesions, even in clinically and radiologically improbable scenarios, as this leads to an accurate diagnosis and optimal patient management.

E-PS-24-010

Dedifferentiated soft tissue and bone neoplasms: a case series

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Background & Objectives: Dedifferentiation is observed in a subset of mesenchymal neoplasms and generally signifies the emergence of a high-grade tumour that lacks differentiation characteristics of the original neoplasm. This phenomenon can occur de novo or within a recurrent, previously well-differentiated tumour, contributing to a more aggressive clinical course. Histopathologically, a distinct boundary is typically observed between the well-differentiated and dedifferentiated components.
Methods: A retrospective analysis was conducted on patients diagnosed in our clinic between 2016 and 2025. Tumours identified with 'dedifferentiated liposarcoma (DDL)', 'dedifferentiated chondrosarcoma (DCSA)' and 'dedifferentiated solitary fibrous tumour (DSFT)' were retrieved from our clinical archives for further evaluation.
Results: A total of 27 patients met the inclusion criteria, including 22 with DDL, 4 with DCSA, and 1 with DSFT. Among the 22 DDL patients, 14 were male and 8 were female. The average tumour size was 21.3 cm, and the mean mitotic count was 4-5/mm². Necrosis was present in 13 patients. DDL predominantly affected middle-aged adults, with a mean age of 60 years, and the retroperitoneum was the most common site of origin. Among the four DCSA cases, 3 were male and one was female, with a mean age of 54 years. Two of these tumours were located in the femur and two in the pelvis. Our DSFT patient was male, 65 years old, and had a tumour located in the inguinal region.
Conclusion: Dedifferentiated soft tissue and bone neoplasms constitute a morphologically and histologically heterogeneous group. Their aggressive clinical behaviour and diagnostic complexity, due to significant histologic and immunophenotypic overlap, necessitate an integrative diagnostic approach. A multidisciplinary evaluation incorporating clinical, histopathologic, immunophenotypic, and molecular characteristics is crucial for accurate diagnosis and optimal patient management.

E-PS-24-011

Incidental presacral myelolipoma in a patient with prostate carcinoma: a case report

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Background & Objectives: Presacral myelolipoma is a rare, benign extra-adrenal tumour composed of mature adipose tissue and hematopoietic elements. It is usually asymptomatic and discovered incidentally during imaging. Due to its rarity and radiological similarity to other fat-containing lesions, such as liposarcoma or teratoma, histopathological evaluation is essential for accurate diagnosis. This study

aims to present a case of presacral myelolipoma and highlight its diagnostic features and clinical relevance.
Methods: A 72-year-old male with a history of prostate carcinoma underwent pelvic MRI, which revealed a 53×35 mm fat-containing lesion in the presacral space, suggestive of a lipomatous neoplasm. The case was referred as a pathology consultation. Haematoxylin and eosin-stained sections were reviewed. Additional immunohistochemical staining for S100 was performed to confirm adipocytic components. The findings were assessed in line with WHO criteria for soft tissue tumours.
Results: Histological examination showed a well-demarcated lesion composed of mature adipose tissue and trilineage hematopoietic cells, including myeloid, erythroid, and megakaryocytic elements. No cytologic atypia, necrosis, or mitotic activity was observed. The S100 stain confirmed adipocytic differentiation. These findings supported the diagnosis of presacral myelolipoma, a benign tumour requiring no further treatment in the absence of symptoms or growth.
Conclusion: Presacral myelolipoma is a rare but benign lesion that may mimic malignant fat-containing tumours on imaging. Accurate diagnosis relies on histopathological examination, supported by immunohistochemical studies such as S100. Recognition of this entity is important to prevent overtreatment, particularly in patients with an existing oncologic history. In this case, the combination of imaging features and confirmatory pathology allowed for a confident diagnosis and conservative clinical management.

E-PS-24-012
Morphology speaks louder than fusions: a fusion-negative mixed tumour in the scalp diagnosed by classic histopathological approach
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Background & Objectives: Myoepithelial tumours of soft tissue are rare neoplasms that morphologically and immunophenotypically resemble their salivary gland counterparts. The benign end of the spectrum includes myoepithelioma and mixed tumour, the latter defined by the presence of ductal differentiation. Although recurrent gene fusions involving EWSR1 and PLAG1 have been reported in a subset of these tumours, not all cases display identifiable molecular alterations. We present a well-characterized case of a fusion-negative soft tissue mixed tumour with classical histomorphological and immunohistochemical features, underlining the diagnostic power of conventional morphology and the spectrum of presentations within this entity.
Methods: Clinical, histopathological, and immunohistochemical evaluations were performed.
Results: A 48-year-old female presented with a slow-growing, pruritic subcutaneous mass in the left frontal scalp. Examination revealed a firm lesion near the hairline, which was excised under local anesthesia with a preoperative diagnosis of sebaceous cyst.
Grossly, the mass measured $1.2 \times 0.7 \times 0.7$ cm and appeared solid and tan-white. Histologically, it was composed of epithelioid cells with clear, vacuolated cytoplasm arranged in nests within a predominantly chondromyxoid stroma. Micronodular areas within hyalinized stroma and focal ductal differentiation were evident.
Immunohistochemistry showed diffuse positivity for cytokeratin AE1/AE3, S100, and PLAG1. EMA was focally positive. GFAP, brachyury, calponin, and p63 were negative. INI1 expression was retained. Ki-67 proliferation index was approximately 2%. Archer FusionPlex assay revealed no detectable gene fusion.
Diffuse PLAG1 positivity supported the diagnosis of mixed tumour despite the lack of molecular confirmation. The immunoprofile and negative GFAP and brachyury expression excluded morphologically similar entities such as parachordoma. No recurrence was observed during six months of follow-up.
Conclusion: This case emphasizes that even in the absence of detectable genetic alterations, a confident diagnosis of mixed tumour can be established through integrated morphological and immunohistochemical evaluation. Molecular findings may be supportive, but are not essential when classical features are present.

E-PS-24-014
When glomus tumours appear in unexpected places: a report of two rare cases
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Background & Objectives: Glomus tumours are rare, usually benign vascular neoplasms. They typically occur in the subungual area of the fingertips. Their occurrence in atypical locations is as unusual as their malignant transformation. The present report describes two cases of glomus tumours in two unusual locations: the trachea and the sternal manubrium.
Methods: This study presents two rare cases of glomus tumours located at unusual sites: the endotracheal region and the sternal manubrium. The cases were identified through pathological reports from Abderrahmane Mami Hospital in Tunisia, between 2005 and 2024. Diagnosis was confirmed by histopathological examination and immunohistochemical analysis.
Results: The first case involves a 74-year-old male who presented with chronic cough and dyspnea. Bronchoscopy revealed a polypoid mass on the tracheal wall. Computed tomography (CT) showed an intra-luminal obstructive tracheal mass, measuring 30x20mm. Surgical resection was performed. Histological findings revealed a proliferation of oval-shaped glomus cells, arranged in clusters or sheets, surrounding blood vessels. The diagnosis of malignancy was based on high mitotic index (> 5 mitosis/10 HPF), deep location, and tumour size over 2cm. The second case si of a 52-year-old female with a palpable mass at the anterior chest. CT scans revealed a well-circumscribed mass in the manubrium, which was excised. Histopathology concluded to a benign glomus tumour. Immunohistochemical study showed in both cases a positive staining for smooth muscle actin and H-caldesmon, without expression of cytokeratin, CD34, S100 and neuroendocrine markers. Surgical outcomes were successful in both cases, with the first patient requiring ongoing monitoring for potential recurrence due to the malignant nature of the tumour.
Conclusion: Glomus tumours are rare and can arise in unusual locations. While the case of malignant transformation in the trachea emphasizes their potential aggressiveness, the second case highlights their usually benign nature. Therefore, awareness of these rare presentations is essential for accurate diagnosis and proper management.

E-PS-24-015
Clinicopathological analysis of solitary fibrous tumour patients: a single-centre study
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Background & Objectives: Solitary fibrous tumour (SFT) is a rare mesenchymal neoplasm that can exhibit diverse biological behaviour. Identifying prognostic factors is crucial for risk stratification and clinical management. This study aims to evaluate the relationship between tumour necrosis, mitotic activity, tumour size, gender, recurrence and metastasis in patients diagnosed with SFT.

Methods: We retrospectively analysed 83 SFT patients with documented data on tumour size, mitotic count, necrosis, grade, recurrence, metastasis and survival. Statistical correlations were assessed between pathological features and clinical outcomes. All cases re-evaluated by two pathologists.
Results: The mean age was 54.9 years (16-77). Gender and location differences were analysed, but no statistically significant impact on prognosis was observed. Among the patients, 20% developed recurrence, and 8.7% experienced metastasis. The presence of necrosis increased the risk of metastasis by 6.2 times (p-value: 0.008). Mitotic count was found to be one of the strongest predictive indicators of recurrence ($p < 0.001$) and metastasis ($p = 0.003$). Tumours over 15 cm alone carry a 40% risk of metastasis ($p = 0.026$). The four-variable model showed that high-risk patients had the highest recurrence rate (31.3%). The three-variable model also indicated high recurrence risk, but less prominently than the four-variable model. In terms of metastasis, the three-variable model showed that high-grade patients had a higher risk ($p = 0.09$). The four-variable model indicated that both intermediate and high- risk groups were at increased risk of metastasis, though not as distinctly as the three-variable model.
Conclusion: Mitotic activity, tumour necrosis and size appear to be key prognostic indicators in SFT. These findings highlight the importance of comprehensive histopathological evaluation in predicting patient outcomes and follow-up. Further large-scale studies are needed to validate these results and refine risk assessment strategies for SFT patients.

E-PS-24-016
Solitary fibrous tumour of the vena cava-case report: morphological and immunohistochemical insights
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Background & Objectives: Intravascular solitary tumours of the vena cava are rare and often present diagnostic and therapeutic challenges. These tumours may be primary or represent intravascular extensions of adjacent neoplasms, most commonly of renal or adrenal origin. However, solitary growth confined to the vena cava without an identifiable primary source is exceedingly uncommon.
Methods: We present the case of a 57-year-old female patient with an intravascular solitary tumour localized within the inferior vena cava, discovered during physical examination due to abnormal swelling of the lower extremities. The lesion was well-defined, non-obstructive, and showed no continuity with surrounding organs. Imaging studies were followed by surgical resection and histopathological evaluation.
Results: Histological examination revealed tumour tissue composed of hypercellular areas consisting of medium-sized oval to spindle-shaped cells with scant, light eosinophilic cytoplasm and round to oval nuclei, exhibiting mild atypia within a myxoid matrix. Focal angiocentric growth was noted. Less cellular regions were characterized by strands and sheets of tumour cells embedded in a collagenized stroma. Mitotic activity was low, with 1 mitosis per 10 high-power fields (HPF). Blood vessels were moderately numerous, thin-walled, and displayed slit-like, irregular lumina, reminiscent of a "hemangiopericytoma-like" vascular pattern. No necrosis was observed. Immunohistochemically, the tumour was negative for cytokeratin AE1/AE3. Diffuse and strong positivity was noted for vimentin, STAT6, CD34, CD99, and BCL2. MDM2 showed nonspecific cytoplasmic positivity. The tumour cells were negative for CD31, ERG1, alpha-smooth muscle actin, desmin, D2-40, and inhibin. Ki-67 proliferation index was approximately 5%. Based on the morphological and immunohistochemical features, a diagnosis of mesenchymal neoplasm of fibroblastic/myofibroblastic differentiation—**intravascular solitary fibrous tumour**—was established.
Conclusion: Solitary intravascular tumours of the vena cava are rare entities that require thorough evaluation to exclude secondary extension from other primary tumours. Complete surgical excision remains the cornerstone of treatment, and histopathological analysis is essential for diagnosis.

E-PS-24-017
Epithelioid sarcoma of vulva: a rare presentation with molecular characterization
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Background & Objectives: Epithelioid sarcoma (ES) is a rare soft tissue malignancy, accounting for less than 1% of all adult soft tissue sarcomas, and vulvar involvement is extremely uncommon. ES is divided into two subtypes: classic (distal) and proximal-type, with the latter linked to adverse prognosis. Loss of SMARCB1/INI-1 expression is a hallmark of ES. Due to its non-specific clinical presentation, ES is frequently misdiagnosed, leading to delay in treatment and poor prognosis. We present a case of proximal-type vulvar ES, highlighting its histopathological, immunohistochemical and molecular findings.
Methods: A 25-year-old female presented with a painful nodule located on the mons pubis. Initially, imaging suggested a nonspecific inflammatory process. Persistence of symptoms and concomitant weight loss led to further investigation. MRI revealed a subcutaneous mass with 34x32x19mm, harbouring suspicious neoplastic features. Fine-needle aspiration showed atypical epithelioid and plasmacytoid cells, which motivated excisional biopsy and subsequent histopathological analysis.
Results: The excised lesion was whitish-coloured and partially encapsulated with haemorrhagic content. Histology revealed a multinodular and sheet-like growth of pleomorphic epithelioid and rhabdoid cells, with enlarged nuclei and prominent nucleoli, with abundant foci of necrosis and myxoid stroma. Mitotic figures were common and lymphovascular invasion was observed. Immunohistochemistry showed immunoreactivity for epithelial markers (CKAE1/AE3, CKCAM5.2, EMA, BerEp4) and CD34 (heterogeneous staining), and loss of nuclear expression of INI-1, endorsing the diagnosis of ES. Molecular testing (NGS) identified a pathogenic SMARCB1 c.686del mutation (variant allele frequency of 39%), suggesting a potential germline origin.
Conclusion: This case highlights the diagnostic complexity of vulvar ES and the importance of molecular analysis for diagnostic purposes and recognizing potential germline origin. Optimal management of vulvar ES has not been determined due to its rarity, but given the high risk of local recurrence and distant metastasis, early and wide surgical excision is mandatory. The role of adjuvant radiotherapy and/or chemotherapy remains to be established.

E-PS-24-018
Primary diffuse large B-cell lymphoma of the bone, a rare and challenging diagnostic entity
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Background & Objectives: In this study, we describe a case of primary diffuse large B-cell lymphoma of the bone. Primary bone tumours are uncommon diseases, representing only 0,2% of all neoplasms, primary bone lymphomas (PBL) being even more rare, constituting approximately 7% of all malignant bone tumours. They typically arise sporadically and rarely in HIV-positive patients or on the background of longstanding osteomyelitis.
Methods: The patient is a 44 year-old male with no known medical history. Radiologic imaging revealed a large osteolytic mass on the proximal humerus without periosteal reaction. After bone curettage, H&E and immunohistochemical analysis for CD45, CD20, CD3,

CD10, CD5, CD23, CD99, BCL6, MUM1, MYC, BCL2 and Ki-67 were performed.
Results: H&E examination revealed a diffuse proliferation of medium-to-large size cells infiltrating bone lamellae, with prominent necrotic areas, numerous atypical mitoses and crush artefact. The population of tumour cells were CD45, CD20, CD10 and BCL6 positive and CD3, CD5, CD23, CD99, MUM1, MYC and BCL2 negative with a Ki-67 index of 95% which pointed us toward a diagnosis of diffuse large B-cell lymphoma of germinal centre type (according to the Hans algorithm).
Conclusion: Primary bone lymphomas represent 5% of all extranodal lymphomas and <1% off all non-Hodgkin lymphomas. The majority of PBL are diffuse large B-cell lymphomas. Our case report highlights the diagnostic challenges associated with this entity as well as the need for proper patient management.

E-PS-24-019
Too spindly to be a fibrolipoma, too fibrous to be a spindle cell lipoma
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Background & Objectives: The morphologic overlap between fibrolipoma and spindle cell lipoma can pose diagnostic, and mainly academic, challenges, especially in tumours with ambiguous stromal features. Given the known association between spindle cell lipoma and *RB1* deletion, FISH-based evaluation may offer supportive data in diagnostically uncertain cases.
Methods: Seventy-four lipomatous tumours initially diagnosed as fibrolipoma were retrospectively reviewed. Following histologic reassessment, 68 cases were reclassified into three diagnostic categories: fibrolipoma (54), spindle cell lipoma (7), or indeterminate fibrolipoma/spindle cell lipoma (7). *RB1* deletion status was evaluated by FISH in 55 cases on 4-mm-diameter tissue microarray. Eight spindle cell lipomas were included as control and 10/100 signal loss is determined as a cut-off value.
Results: *RB1* FISH analysis revealed higher deletion levels in indeterminate fibrolipoma/spindle cell lipoma [3/6 (50%), losses: 11%, 14%, and 15%] and spindle cell lipoma [1/5 (20%), loss: 21%], while tumours retaining a fibrolipoma diagnosis showed no or minimal deletion [39/44 (89%), mean loss 1,5% range 0-8]. After FISH testing, the morphological diagnosis was changed in 13/68 (19%) of the cases.
Conclusion: In this cohort, *RB1* loss was observed in tumours that, upon clinic and morphologic re-evaluation, were no longer consistent with a fibrolipoma diagnosis. However, some clear-cut fibrolipomas also showed RB1 loss to a lesser extent. *RB1* FISH provides meaningful diagnostic support in lipomatous tumours with overlapping features. Although classification was based primarily on histology, the molecular findings retrospectively aligned with and reinforced the revised diagnoses. These results support the use of RB1 status as a confirmatory adjunct in resolving the diagnostic spectrum between fibrolipoma and spindle cell lipoma.

E-PS-24-020
A case of calcium pyrophosphate crystal deposition disease (CPPD) of the temperomandibular joint
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Background & Objectives: We present a case of calcium pyrophosphate crystal deposition disease (CPPD) of the temperomandibular joint (TMJ) with osteoarthritis. Whilst this diagnosis is not uncommon, CPPD usually affects larger joints such as the knee, wrist, elbow or ankle. Only rarely does CPPD affect small joints such as the TMJ (1).
Methods: An 82 year old female with a one year history of left jaw pain, and with a CT scan demonstrating significant flattening of the articular surface of the left condylar process of the mandible with relatively reduced condylar neck height, underwent total joint replacement. The bone and soft tissue removed during surgery was submitted for histological assessment.
Results: H&E stained sections demonstrated vital bone, benign cartilage, fibrocollagenous tissue, skeletal muscle fibres and benign salivary gland tissue. There was vegetable matter impacted within bone, with associated necrosis and degeneration. The articular cartilage appeared ragged with surface cracks and fissures. Overall the features were in keeping with degenerative joint disease.
Additionally, within the fibrocollagenous tissue focal basophilic aggregates containing rhomboid shaped crystals were noted with scattered macrophages adjacent to these aggregates. The features were suggestive of a crystal arthropathy, in particular CPPD.
Conclusion: CPPD results from an immune response to the pathological presence of calcium pyrophosphate (CPP) crystals inside joints. This process leads to a CPP-crystal inflammatory arthritis, and can present acutely - previously known as pseudogout - or be chronic (1). There is a strong association between CPP crystal deposition and osteoarthritis, called CPPD with osteoarthritis, but the direction of causality is unknown (2). CPPD disease is common, especially in those over 60 years of age, but is underrecognised and undertreated (3).
This case highlights the need to look for CPPD, even at unusual sites. As it is often associated with osteoarthritis, it should be considered as a potential second diagnosis in such cases.

E-PS-24-021
When osteosarcoma takes a twist: a wrist tumour with focal BCOR sarcoma dedifferentiation
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Background & Objectives: We report the first documented case of central low-grade osteosarcoma undergoing dedifferentiation into a sarcoma with BCOR internal tandem duplications (ITDs). Previously, BCOR ITD sarcomas have been almost exclusively identified in the non-appendicular soft tissues of children, with no documented association with osteosarcoma.
Methods: Clinical and pathological information was obtained from institutional EPIC and COPATH information systems, HE and immunohistochemical slides were reviewed by 3 pathologists, and Next-generation sequencing (NGS)DNA and RNA, as well as cytogenomic microarray analysis (CMA) were performed on tumour samples.
Results: We present a 22-year-old male with a progressively enlarging mass in the right thumb at a previous fracture site. The mass exhibited a significant and rapid increase in size two months before presentation. Initial biopsies suggested a low-grade osteogenic tumour. The patient subsequently underwent partial thumb amputation with reconstruction. Gross examination showed a 3.7 cm mass involving the metacarpal bone and invading into adjacent soft tissue. Microscopic evaluation showed low grade central osteosarcoma with transition to round blue cell tumour histology. NGS DNA&RNA and CMA testing showed amplifications of MDM2 and CDK4 genes, numerous other genomic alterations, gains and losses of various chromosome segments, as well as BCOR ITD alteration. The final diagnosis was that of central low-grade osteosarcoma with BCOR sarcoma dedifferentiation.
Conclusion: We present the first documented case of central low-grade osteosarcoma of appendicular bone with BCOR sarcoma dedifferentiation, occurring in the thumb of a young adult, supported by detailed histopathologic analysis and comprehensive genomic profiling,

including NGS (DNA & RNA) and CMA. BCOR ITD sarcomas have been reported exclusively in the non-appendicular soft tissues of infants and young children, with no known association with osteosarcoma. This case underscores the importance of employing NGS and CMA in the evaluation of sarcomas with atypical or heterogeneous histology to improve diagnostic accuracy and guide targeted therapy.

E-PS-24-022

Novel *SMARCA2*::*DDIT3* fusion in myxoid liposarcoma due to an unusual unbalanced chromosomal translocation

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Background & Objectives: Myxoid liposarcoma (MLS) accounts for 20–30% of all liposarcomas, with most cases harbouring the fusion gene *FUS::DDIT3*, while approximately 5% exhibit the *EWSR1::DDIT3* fusion. This report aims to describe a novel fusion, *SMARCA2*::*DDIT3*, identified in a 26-year-old male presenting with a right upper arm mass displaying the classic histologic features of MLS.
Methods: Fluorescence in situ hybridization (FISH) was employed to investigate rearrangements in the *DDIT3* locus. Next-generation sequencing (NGS) was conducted to identify fusion transcripts, and chromosomal microarray analysis was utilized to assess the structural nature of chromosomal alterations.
Results: The tumour displayed the classic histological features of MLS, including small spindle/ovoid cells, variable univacuolated lipoblasts, and a prominent myxoid stroma with delicate arborizing vasculature. Despite these characteristic features, fluorescence in situ hybridization (FISH) revealed no rearrangement of the *DDIT3* locus.
Next-generation sequencing (NGS) identified a novel fusion transcript in which *SMARCA2* exon 4 was fused in-frame with *DDIT3* exon 2. Chromosomal microarray analysis demonstrated the unbalanced nature of the rearrangement, with partial deletions of 0.243 Mb and 0.176 Mb flanking the centromeric end of the *DDIT3* locus on 12q13.3 (which also included *GLI*) and disrupting the *SMARCA2* locus on 9p24, respectively. The resultant chimeric fusion protein is predicted to lack the *SMARCA2* DNA-binding domains while retaining the *DDIT3* DNA-binding and leucine zipper dimerization domains.
Conclusion: These findings indicate an unusual and complex rearrangement, leading to the recruitment of a novel *DDIT3* partner gene through a promoter-swapping-like mechanism. Moreover, they emphasize that the functional aspects of myxoid liposarcoma fusion genes depend on the retention of key *DDIT3* protein domains. Finally, this case highlights the power of traditional morphologic assessment to uncover new molecular genetic discoveries.

E-PS-24-023

***CIC* rearranged sarcoma: a clinical and pathological study**

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Background & Objectives: *CIC*-rearranged sarcoma is a rare and aggressive type of undifferentiated round cell tumour characterized by *CIC* gene fusion, most commonly *CIC::DUX4*. This study presents a series of eleven cases, highlighting their clinical-pathological features.
Methods: Pathology files (2019 to 2024) were searched using "sarcoma with *CIC*" identifying 11 cases, of which seven referred cases were initially misdiagnosed. Pathological and clinical analysis was conducted. Treatment was dictated upon multidisciplinary panel discussion based on tumour stage. Follow-up data (1–25 months) was available for all patients.
Results: The cohort included 6 males and 5 females, aged 14–53 years (median 43), nine in soft tissue and two in bone. Tumour size ranged from 3.5 cm to 20.0 cm (mean 9.8 cm). Most cases showed sheets of undifferentiated cells with focal short fascicles and 1 showed Ewing-like pattern. 1 case showed spindle cells in a fibrotic stroma transitioning to epithelioid cells. Necrosis was present in nine cases, and mitotic count ranged from 2 to 38 (mean=14.2). CD99 was positive in (10/11) cases and WT-1 in (6/9). NKX2.2, S100 and MDM2 were positive in rare cases. *CIC::DUX4* fusion was detected in 4 cases. FISH was positive in 7 cases, two of them confirmed by methylation analysis. Metastasis at diagnosis was common (n=8), primarily in the lungs, with later metastasis to the brain and bone. Eight patients died within 1–19 months (median 10 months), while three are alive, two with controlled disease (6 and 25 months) and one with progression after 10 months. No correlation was seen between overall survival and the presence of metastasis at diagnosis or tumour size (p value= 0.43 and 0.26, respectively).
Conclusion: *CIC*-rearranged sarcomas are rare, high-grade tumours with predilection for soft tissue. Misdiagnosis is frequent, necessitating molecular confirmation. These tumours are treatment-resistant, often present with lung metastasis, and carry a poor prognosis.

E-PS-24-024

Pulmonary epithelioid haemangioendothelioma – case report of a rare entity

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Background & Objectives: Epithelioid haemangioendothelioma is a rare malignant tumour of vascular origin characterized mostly by a WWTR1-CAMPTA 1 fusion with an incidence rate of 0.230 per 1,000,000 person-years. Most lesions are found in the soft tissue and skin, followed by the abdomen, respiratory system, bones and joints. The presentation and prognosis are variable, ranging from asymptomatic incidentally found lesions to aggressive and symptomatic metastatic disease. A study by Zhen Liu and Shuting He found that age > 80, African American and American Indian/Alaska Native/Asian or Pacific Islander ethnicity and respiratory origin were linked to worse survival rate.
Methods: We report the case of a 61-year-old female who was referred to pneumology for incidentally discovered bilateral pulmonary nodules, the largest one being 8 mm of diameter, on imaging done for shoulder pain. Differential diagnosis on imaging included metastases and granulomatous disease. However, past medical history was negative for neoplasia, cardiopulmonary disease, smoking and recreational drugs.
Results: A cone-beam CT-guided lung biopsy was performed and only the cryobiopsy specimen yielded results. Histologic examination revealed epithelioid eosinophilic cells containing intracytoplasmic vacuoles “blister cells”, arranged in nests and cords on a background of myxoid to hyaline stroma. This resulted in the creation of multifocal and bilateral nodules that followed alveolar-filling pattern, characteristic of pulmonary lesions of this entity. IHC was positive for ERG and CAMTA1. Thus, the diagnosis of epithelioid haemangioendothelioma was confirmed and the patient’s management was transfered to hemato-oncology.
Conclusion: The pathological diagnosis for this rare entity can be challenging and a second opinion from an expert could be required.

The management requires a specialized centre and entails surveillance, surgery, chemotherapy or radiotherapy.

E-PS-24-025

An EWSR1::PBX3 fusion-positive intraosseous myoepithelioma in the clavicle

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Background & Objectives: Myoepitheliomas are uncommon benign tumours usually occurring in the soft tissue, but occasionally in an intraosseous location. We present a case of an intraosseous myoepithelioma occurring in the clavicle of a 40 year old male patient, with an EWSR1::PBX3 fusion, the first in this anatomical site. The patient presented to the orthopedics service with complaints of right shoulder pain. Imaging studies showed an radiolucent tumour within the clavicle, measuring up to 2.1cm.
Methods: The lesion was curetted and subsequent histological evaluation showed a tumour with interlacing fascicles of spindled cells with monomorphic cytological features and eosinophilic cytoplasm. There was mild nuclear atypia with very rare mitoses, and no necrosis. No surrounding bone or cartilage formation was noted. The tumour cells were immunopositive for EMA, SMA, S100 and caldesmon, supporting a myoepithelial lineage. The Ki-67 proliferation index was less than 1%. Immunohistochemical staining for keratins and SOX10 were negative.
Archer FUSIONPlex pan solid V2 assay showed an EWSR1::PBX3 fusion.
Results: EWSR1::PBX3 fusions have largely been reported in cutaneous syncytial myoepitheliomas, with less than 10 cases in intraosseous locations, preferentially in the long bones of the lower limb. As this fusion can be seen in both benign myoepitheliomas and malignant myoepithelial carcinomas, the low-grade histology confirms the benign nature in this case, with immunohistochemical studies remaining the cornerstone for diagnosis. No recurrence has been reported by the patient in the 36 months since the curetting.
Conclusion: This case illustrates the need to consider the diagnosis of myoepitheliomas as primary bone tumours that can occur outside the long bones, and lends support to the predilection of this fusion for skeletal involvement. While immunopositivity for myoepithelial markers in conjunction with the morphology may be sufficient for diagnosis in some cases, molecular studies are useful in supporting the diagnosis and appear suggestive of a morphological phenotype and presentation.

E-PS-24-026

A rare case of pleomorphic sarcoma arising in a background of regressive changes associated with giant cell tumour of bone. A diagnostic challenge in a core biopsy

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Background & Objectives: The case illustrates the diagnostic challenge presented in a core biopsy of a pleomorphic sarcoma arising in a fibrohistiocytic background in the upper end of tibia of a 48yr old male. The WHO 5th edition of soft tissue and bone tumours has highlighted that tumours resembling benign fibrous histiocytomas in bone, which occur in sites not typical for non ossifying fibromas, often represent regressive changes in giant cell tumours of bone. Sarcomas in epiphyseal locations of long bones which express histone marker H3.3G34W possibly represent malignant giant cell tumours of bone even without an associated giant cell tumour component. This case illustates both these points.
Methods: A 48 year male presented with pain in his left knee of 2 years duration. His radiology at presentation showed ill defined lytic areas with soft tissue component involving upper end of left tibia. Two earlier biopsies were diagnosed as a histiocytic proliferation. Our lab received the third trucut biopsy.
Results: The biopsy cores showed variable cellularity and a variegated morphology with areas showing a fibrohistiocytic infltrate with a storiform pattern and admixed lymphocytic infiltrate. Also present were few areas showing pleomorphic polygonal to spindle cells with mitosis. The initial IHC work up with histiocytic and mesenchymal markers was non contributary. A review of his earlier radiology in 2024 showed an epiphyseal lytic lesion which prompted IHC for H3.3G34 which was diffusely positive in the spindle cell component of the tumour. There were no areas of classic giant cell tumour seen.
Post 4 cycles of chemotherapy the tumour was excised with a partial response to therapy.
Conclusion: The case highlights the importance of site in interpreting an unusal bone malignancy and illustrates regressive changes in giant cell tumour of bone as a differential diagnosis of fibrohistiocytic epiphyseal bone proliferations.

E-PS-24-027

Diagnostic pitfalls in splenic pathology: a case report

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Background & Objectives: Splenic angiosarcoma is a rare and aggressive malignant vascular tumour with high metastatic potential, with a poor prognosis. Due to the nonspecific presentation, which may be splenomegaly or anaemia, it is frequently misdiagnosed. We present a case in which splenic and hepatic abscesses were initially suspected and later confirmed as splenic angiosarcoma, highlighting the diagnostic challenges and histopathological features.
Methods: A 60-year-old man with multiple comorbidities presented with diffuse abdominal pain and expiratory dyspnea. Initial imaging studies identified liver abscesses, which necessitated further evaluation. CT examination showed multiple hypodense nodular lesions localized to the spleen and liver. The patient decompensated, developing septic shock and multiple organ dysfunction, requiring splenectomy. The excision specimen was analysed in the pathology laboratory for gross, histopathological, and immunohistochemical analyses.
Results: Macroscopic evaluation describes the presence of multiple gray and haemorrhagic areas diffusely distributed in the splenic parenchyma. Histopathological examination of these areas revealed cellular proliferation with various growth patterns including solid areas and vasoforming regions. The solid areas were composed of spindle and epithelioid cells with amphophilic cytoplasm, large nuclei, and prominent nucleoli. The vasoforming areas presented anastomosing vascular channels lined by atypical, large, pleomorphic endothelial cells with high mitotic activity (23 mitoses/10 HPF). The tumour cells were positive for CD31 and CD34. Extensive areas of coagulation necrosis and haemorrhage were also observed. Despite intensive care, the patient developed multiple organ failure and died two days after surgery.
Conclusion: This case highlights the diagnostic challenges of splenic angiosarcoma, which can mimic abscesses radiologically. Histopathological examination, along with immunohistochemical examination, remain crucial for accurate diagnosis. Given the aggressiveness of the tumour, early recognition and treatment are essential for improving the prognosis.

E-PS-24-028

An atypical spindle cell/pleomorphic lipomatous tumour of the thigh with a difficult imaging diagnosis that mimicked a malignant lipomatous tumour

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Background & Objectives: Atypical spindle cell/pleomorphic lipomatous tumours (ASPLT) are categorized as benign lipomatous tumours. However, various MRI findings pose diagnostic challenges. In our case, MRI indicated the possibility of an atypical lipomatous tumour/well-differentiated liposarcoma (ALT/WDL) or a dedifferentiated liposarcoma (DDLPS).
Methods: A 74-year-old woman presented with a mass in her right thigh that had been present for 20 years but had begun to increase in size 1 year prior. MRI revealed a low-intensity signal on T1-weighted images, with scattered high signal and high-signal intensity on T2, with scattered low signal. Heterogeneous enhancement was observed on gadolinium-enhanced T1-weighted images, suggesting that the differential diagnosis was ALT/WDL or DDLPS. Needle biopsy suggested both benign and low-grade malignant lipomatous tumours. Overall, the preoperative findings did not definitively rule out malignant tumours, leading to the decision to perform a wide resection.
Results: A wide range of microscopic appearances and cellularity was observed based on the various proportions of atypical spindle cells, adipocytes, lipoblasts, and pleomorphic (floret-like) cells, as well as variable amounts of collagenous and/or myxoid extracellular matrix. The adipocytic component had predominantly mature morphologies with variations in adipocyte size and shape. Mitotic figures were scarce (0–1/10 HPF), and tumour necrosis was absent. Immunohistochemistry results were as follows: CD34 (+, focal), retinoblastoma (RB1) (−, lost), MDM2 (−), CDK4 (−), S100 (+, focally), and BCL-2 (+, weakly). Fluorescence in situ hybridization revealed no MDM2 amplification.
Conclusion: MRI findings for ASPLT vary due to differences in fat content, making the differential diagnosis broad, including ALT/WDL, DDLPS, and myxoid liposarcoma, suggesting that histopathological findings are crucial for ASPLT diagnosis. Although ASPLT have defined morphological and histopathological features, these findings overlapped with those of other tumours and were not consistently present. Caution should be exercised when distinguishing ASPLT from other lipomatous tumours.

E-PS-24-029

A rare case of malignant calcifying epithelial odontogenic tumour and large neurofibroma

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Background & Objectives: Calcifying epithelial odontogenic tumour (CEOT), also known as Pindborg Tumour, is a rare benign odontogenic tumour with distinct histological features such as sheets and cords of polyhedral cells with nuclear pleomorphism and the presence of amyloid. Extraordinarily uncommon malignant transformation is often difficult to diagnose due to overlapping morphological criteria with benign and recurrent variants.
Methods: We describe the case of a malignant CEOT and a large neurofibroma in an adult female patient using immunohistochemistry and next generation sequencing.
Results: A female patient presented with a slowly expanding ulceration of the lower right alveolar mucosa, clinically giving the impression of oral squamous cell carcinoma. The x- ray and CT scan both showed an osteolysis of the right mandible spanning from regio 47 to the coronoid process with retained tooth 48. Biopsy revealed a CEOT with marked cellular pleomorphism, numerous mitoses and a high Ki-67 labelling index of 30%. Therefore, malignancy was diagnosed, and the patient was planned for partial jaw resection with fibular graft reconstruction. Coincidentally, during MR angiography of the leg vessels another large lesion was found inside the right adductor magnus muscle. Clinical diagnoses included a soft tissue tumour as well as a metastasis. Subsequent biopsy uncovered a neurofibroma with cellular atypia. Finally, jaw resection with additional neck dissection and scapular graft reconstruction was performed. The resection specimen exposed a small area of cortical destruction and mucosal invasion, but no lymph node involvement although a lymphatic vessel invasion was found. NGS of the tumour revealed no special genetic profile. The patient is currently at an eight-year follow-up without recurrence.
Conclusion: While squamous cell carcinoma may be one of the primary causes of progressively enlarging ulcerations in the oral mucosa, odontogenic tumours can also present with aggressive clinical behaviour. This case has been further complicated by the finding of a large neurofibroma.

E-PS-24-030

Case report: a 16-year old adolescent girl with fungal osteomyelitis mimicking malignant neoplasm of calcaneal bone

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Background & Objectives: Blastomycosis is a rare fungal infection caused by *Blastomyces dermatitidis*, typically affecting the lungs but occasionally disseminating to other tissues, including bone. This condition is most commonly reported in Canada and in the midwestern, south-central, and southeastern USA, with an annual incidence of approximately 1 to 2 cases per 100,000 individuals in endemic areas.
Methods: On physical examination, a painful, 6 cm diameter, oedematous, indurated lesion with yellow discharge was noted on the left lateral malleolus. An initial X-ray of the left ankle revealed soft tissue swelling, several areas of subtle lucency in the mid and anterior calcaneus, and a healing, non-displaced lateral malleolus. The X-ray findings raised suspicion of a possible underlying bone pathology, which led to further investigation.
An MRI was performed to evaluate for possible osteomyelitis, which showed destruction of the calcaneus and abnormal signals in the surrounding soft tissue. These findings were concerning for malignancy or a severe infectious process, necessitating further diagnostic workup.
Results: Ultrasound-guided and open biopsies led to the histological finding of acute and chronic inflammation, necrosis, granulomatous inflammation, and fungal organisms. Gomori methenamine silver (GMS) stain confirmed the presence of *Blastomyces dermatitidis*.
Conclusion: This case highlights an atypical presentation of Blastomycosis in an adolescent, mimicking a malignant process in the bone and soft tissue. Despite being a rare condition, Blastomycosis should be considered in the differential diagnosis of osteomyelitis, particularly in endemic regions, even in immunocompetent individuals. Early recognition and appropriate antifungal therapy are crucial to prevent misdiagnosis and delayed treatment complications. This case emphasizes the importance of awareness and consideration of fungal infections in

atypical presentations to ensure timely diagnosis and optimal patient management.

E-PS-24-031

A novel fusion gene EML4-NTRK3 in a case of metastatic infantile fibrosarcoma

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Background & Objectives: Infantile fibrosarcomas (IFS) are locally aggressive non-rhabdomyosarcoma soft tissue tumours. These uncommon tumours usually occur congenitally, affecting 5 in 1 million infants under 1 year of age. The lesions usually involve the extremities, with the lower extremities being the most affected area. They can also be observed in the trunk, head and neck region, and retroperitoneum. Involvement of lymph nodes or metastases is rarely reported.
Methods: A 7-year-old male presented with shortness of breath, fever, and a decline in general condition. Thorax CT revealed an 11x10 cm mass lesion in his left lung. The parenchyma seemed collapsed; extensive pleural effusion filled the left hemithorax. Additionally, a 2 cm metastatic solid lesion at an upper posterior segment and a 7 mm subpleural solitary nodule at the mid-lateral segment of the right lung were observed. The patient had a history of IFS located on his right forearm 5 years prior, followed by receiving chemotherapy and radiotherapy and an amputation operation one year later after the initial diagnosis.
Results: The sign-out diagnosis of the lung mass biopsy was consistent with a malignant mesenchymal tumour of spindle cell morphology. A molecular diagnostic workup with NGS was performed, which resulted in EML4-NTRK3 fusion.
Conclusion: Most IFS cases show ETV6-NTRK3 gene fusions and are sensitive to chemotherapy with favourable clinical behaviour. A few IFS cases were reported to lack ETV6-NTRK3 fusion. Recently, novel fusions such as SEPT7-BRAF, EML4-NTRK3, and TPM3-NTRK1 have been identified in unclassified spindle cell sarcomas, showing morphological overlap to IFS and located at extremities and retroperitoneum. In the setting of unusual clinical presentations with shared tumour morphology, identifying the gene fusions would provide insight into the response to targeted therapy and neoadjuvant regimens in inoperable cases and a chance to avoid maybe morbid surgery and help to predict prognosis.

E-PS-24-033

Citation analysis of the 5th edition WHO classification of tumours soft tissue and bone tumours volume

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Background & Objectives: Evidence-based pathology practice informs the WHO Classification of Tumours (WCT) and should be supported by analysis of the references cited in the previous WCT to guide future editions. Evidence Gap Maps (EGM) and Citation Maps (CM) use a visual approach to identify gaps in cited evidence and detect relations between scholarly articles that could point towards a biased assessment of evidence. We aimed to assess the references cited in the WCT Soft Tissue and Bone Tumours 5th edition (STB-5), summarising gaps and special interests in cited publications, to assist authors and editors during the development of the WCT STB 6th edition.
Methods: We developed an EGM and CM of STB-5 references and provided a descriptive analysis summarising gaps, networks of referenced publications and relations of interests among cited articles. A citation analysis network was developed using VOSviewer®. Two main criteria were applied: maximum number of authors per document (15) and minimum number of documents per author (15).
Results: The CM included 3,373 references from 11,399 authors for 349 tumour types. The EGM we identified gaps in the cytology and macroscopy. The CM showed seven distinct clusters dealing with soft tissue tumour classification, molecular genetics (focussing on sarcoma), bone and cartilage tumours and regional or rare tumour research. All but two showed strong intra and interconnections. Key researchers formed clusters, acting as bridges between them. Main authors in isolated clusters were frequently cited despite weaker interconnections.
Conclusion: Interdisciplinary connections and bridges were observed, indicating that a wide range of tumour characteristics by a variety of key authors in the field are covered. Identifying clusters confirms citations from major research groups, supporting WCT's evidence-based classification. The visual representation of relationships of citations in WCT-5 provides guidance on improvements that can be made in the 6th edition of WCT Soft tissue and Bone volume.

Funding: HORIZON-HLTH-2021-CARE-05 grant number 101057127

E-PS-24-034

A chameleon tumour: unraveling the rare phenomenon of myxoid Liposarcoma with osteocartilaginous differentiation

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Background & Objectives: Myxoid liposarcoma with osteocartilaginous differentiation is a rare variant of myxoid liposarcoma (MLPS) characterized by mature hyaline cartilage within the tumour. Fewer than 10 cases of this phenomenon have been documented in the literature.
Methods: We present the case of a 52-year-old male who presented with pain and functional impairment in his left thigh. A whole-body scintigraphy scan revealed a region with high vascularization in the middle third of the thigh, encompassing a hypercaptant area with intense heterogeneity. SPECT-CT imaging identified a soft tissue tumour in the anterior thigh compartment, measuring 20 x 9.5 x 6 cm, well-demarcated, hypodense, with superior calcifications. A surgical excision was performed, and tissue samples were sent for histopathological analysis and frozen-section examination.
Results: The frozen-section examination revealed a tumour composed of small cells with cytological atypia, arranged in a myxoid stroma. Macroscopic examination identified a well-encapsulated, darkly coloured tumour mass. Paraffin-embedded tissue analysis revealed mesenchymal tumour proliferation with round to oval or spindle-shaped cells with stellate processes. These cells exhibited relatively monomorphic, hypochromatic nuclei with occasional nuclear pseudoinclusions. The stroma surrounding the tumour was myxoid, weakly basophilic, with mucoid extracellular lakes. There were numerous stromal blood vessels with a plexiform appearance. Lipoblast clusters were frequently observed at the tumour periphery, demonstrating atypia and occasional atypical mitotic figures. Multiple areas of haemorrhage and necrosis were noted within the tumour. Notably, there was an area of osteocartilaginous differentiation with hyaline cartilage and a transition to mature bone tissue. Immunohistochemical analysis was positive for S100 (expressed in myxoid areas and lipoblasts), P16, and Ki67 (1-2%) but negative for MDM2 and CD34. These features support a diagnosis of low-grade myxoid liposarcoma.

Conclusion: Myxoid liposarcoma with osteocartilaginous differentiation is a rare tumour seldom reported in the literature. Precise histopathological and immunohistochemical analysis is crucial for ensuring optimal diagnosis, treatment and prognosis.

E-PS-24-035

PD-1&PD-L1 expression in sarcomas

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Background & Objectives: Primary therapy regimen for sarcomas is surgical resection with adequate margins.Aim of study is to assess expression of PD-L1/PD-1 in soft itssue sarcoma(STS) to investigate rationale for immune-checkpint inhibition in patients with PD-L1 positive soft tissue sarcomas.
Methods: CPS was calculated for PD--L1: CPS≥1 positive & CPS<1 as negative. For PD-1 IHC: more than1% membranous staining in tumour & tumour infiltrating lymphocytes and intensity was graded as 1+(weak), 2+(intermediate), 3+(strong).
Results: Of the 167 cases, adequate tissue for IHC was available in 99 cases.Median age of presentation was 44 years (age range: 3 to 94 years), with male predominance.A diverse array of sarcoma types were noted distributed across various primary tumour sites, most common being Ewing sarcoma followed by pleomorphic sarcoma, synovial sarcoma, MPNST, LMS, etc.Evaluation of these markers revealed variable expression patterns in both tumour cells and tumour-infiltrating lymphocytes, which included cytoplasmic and membranous staining pattern, with higher expression noted in higher grade sarcomas with an exceptional lower to nil expression in synovial sarcomas.PDL1 was 170, suggesting a potential for variable immune checkpoint activity among sarcoma subtypes. Of 99 cases, positive CPS was seen in 38 cases with a maximum score of 170.
Conclusion: Evaluation of these markers revealed variable expression patterns in both tumour cells and tumour-infiltrating lymphocytes, with higher expression noted in higher grade sarcomas, with an exceptional lower to nil expression in synovial sarcomas. The diversity in TILS across samples suggests an immunological response gradient, which may correlate with prognosis and immune responsiveness.

E-PS-24-036

CD44-AKT-miR-146a axis targets apoptosis in tendinopathy

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Background & Objectives: Tendinopathy is a debilitating condition characterized by pain and impaired tendon function, with its development linked to chronic inflammation, cellular senescence, and apoptosis. Previous studies suggest that inhibiting CD44 signalling aggravates apoptosis and inflammation in tendinopathic tenocytes. Additionally, microRNA-146a (miR-146a) has been shown to counteract IL-1β-induced senescence in these cells and is upregulated by CD44 in knee osteoarthritis. Given these findings, this study aims to explore the role of the CD44-miR-146a signalling axis in regulating apoptosis in tendinopathy.
Methods: To investigate this mechanism, lentiviral vectors (LVs) were employed to induce overexpression of CD44 cDNA (LVCD44) and the miR-146a precursor (LVmiR-146a) in primary rat tendinopathic tenocytes and tendon tissues. Apoptotic cell death was evaluated using TUNEL staining. To further delineate the involvement of the CD44-AKT-miR-146a pathway, we used the PI3K/AKT inhibitor LY294002 and the CD44-blocking antibody OX-50. Additionally, in situ hybridization (ISH) and immunohistochemistry (IHC) were performed to assess the impact of this pathway on Smad4 expression in tendinopathic cells and tissues.
Results: Overexpression of CD44 and miR-146a significantly reduced apoptosis in tendinopathic tenocytes compared to control cells. The CD44-AKT-miR-146a signalling cascade was found to exert a protective effect against apoptosis in IL-1β-stimulated tenocytes and in a rat model of collagenase-induced Achilles tendinopathy, primarily by downregulating Smad4 expression.
Conclusion: These findings underscore the protective function of the CD44-AKT-miR-146a signalling axis in tendinopathy. By modulating the AKT/miR-146a/Smad4 pathway, CD44 and miR-146a effectively suppress apoptosis in tenocytes and tendon tissues, highlighting their potential as therapeutic targets for tendinopathy management.

Funding: NSTC 113-2314-B-006 -087

E-PS-24-037

Localized form of tenosynovial giant cell tumour: a study of 38 cases

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Background & Objectives: Tenosynovial giant cell tumour (TGCT) is a rare, benign fibrohistiocytic tumour that may be intra or extra-articular. It is divided into two subtypes: localized or diffuse. Our aim is to describe the clinical, histopathological and prognostic features of TGCT in its localized form.
Methods: This is a retrospective descriptive study collected over a period of 17 years from January 2005 to December 2022. The study included 38 patients who were diagnosed with a TGCT in its localized form at Fattouma Bourguiba Hospital in Monastir.
Results: The average age was 42. Thirty patients were women (sex ratio= 0.26). Fifty percent of patients presented with isolated swelling, in 44% of cases the swelling was associated with pain and restricted mobility. On gross examination, 36 cases presented as a well circumscribed nodular formation with yellowish (29%), off-white (26.3%), white (26.3%), or heterogeneous (18.4%) cut surfaces. The mean size was 2.3 cm. Microscopic examination of all cases showed a mesenchymal tumour composed of mononuclear and histiocyte-like cells with multinucleated giant osteoclastic cells. In 42,1% of cases, giant multinucleated cells were matching mononuclear cell density. They were abundant in 7 cases and scarce in 15 cases. There was no cytonuclear atypia. Mitosis were observed in 15,7% of cases. In 20 cases, the tumour was highly cellular, the other cases presented as a hypocellular lesion with an abundant fibrous stroma. Hemosiderin deposit was found in 55.3% of cases while xanthoma cells were observed in 52,3% of cases.
Conclusion: The localized form of tenosynovial giant cell tumour is a benign neoplasm with unclear pathogenesis. It exhibits characteristic clinical and histopathological features. Despite its benign behaviour, a significant recurrence risk exists.

E-PS-24-038

Angiogenic profiles in bone pathologies: an immunohistochemical comparative analysis

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Background & Objectives: Angiogenesis plays a crucial role in fracture healing. However, its precise role in non-unions remains unclear and is addressed by the so-called "vascularization paradox" of non-union (NU) formation: Reduced vascularization can inhibit fracture repair, while its stimulation can facilitate regeneration. In contrast, excessive angiogenesis has been shown to impede fracture healing and contribute to the exacerbation of NU formations.To better understand the vascularization of non-unions, we evaluated the differences in blood vessel density among NU, bone metastases (BM), and femoral head necrosis (FHN), and examined the spatial distribution of blood vessels in these conditions.
Methods: An immunohistochemical analysis was performed using the vascular markers CD31, CD34, and Nestin on a total of 50 samples from three different bone pathologies, namely 15 BM, 15 FHN, and 20 NU. Blood vessel annotation was performed using a self-trained algorithm on whole slide images. The analysis included the examination of the spatial distribution of vessels, comparing vessel count between central and peripheral areas, as well as between fibrotic scar tissue and granulation tissue. Furthermore, comparative analyses across the three different pathologies were conducted.
Results: Significant differences in vascular distribution were observed between NU and FHN, as well as between BM and FHN (both $p<0.0001$). Specifically, NU and BM exhibited significantly higher blood vessel density compared to FHN, indicating distinct angiogenic profiles. Interestingly, no significant differences in vascular distribution were found between BM and NU, or between the central and peripheral areas within the examined tissues.
Conclusion: The similar vascular characteristics observed between NU and BM contrast sharply with those of FHN. These findings suggest common angiogenic profiles that could potentially be targeted with therapeutic intervention. The study underlines the importance of angiogenesis in bone pathologies and suggests directions for future research, including 3D reconstruction and image registration techniques to further assess vascular branching characteristics.

Funding: This study was funded by a grant of the European Union, Ziel ETZ-352 2014–2020, " and by the project BBMRI.cz, reg. no. LM2023033

E-PS-24-039
Malignant gastrointestinal neuroectodermal tumour: case report of an ultra-rare mesenchymal neoplasm
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Background & Objectives: Malignant gastrointestinal neuroectodermal tumour (GNET) is a rare mesenchymal tumour affecting the gastrointestinal tract (GIT). It is known as a clear cell sarcoma (CCS)-like tumour of the GIT. Less than 70 cases have been reported worldwide.
Methods: We present the case of a 67-year-old woman with no relevant medical antecedents. She was admitted to the hospital for gastrointestinal complaints for two years and weight loss of 10 kg in the last few months. Endoscopical evaluation was normal. A mural jejunal thickening, an adjacent lymphadenopathic conglomerate and multiple hepatic nodules were detected in radiological studies. The jejunal segment and the lymphadenopathic conglomerate were surgically removed and a hepatic lesion was biopsied.
Results: The mass was composed of a densely cellular proliferation arranged in nests and cords separated by fibrous septa. The cells were monomorphic, with large clear cytoplasm, round nuclei, and prominent eosinophilic nucleoli. Scattered multinucleated giant osteoclasts-like cells and frequent mitotic figures were seen. Lymphovascular and perineural invasion were found. Lymph node and hepatic metastases were histologically confirmed. The cells were intense and diffusely positive for S100 and SOX10, non-intense and diffusely positive for synaptophysin, and focal positive for CD56. INI1 expression was preserved. Smooth muscle actin, h-caldesmon, melanA, HMB45, MDM4, CDK4, DOG1, STAT6, SS18 and ALK were negative. Molecular studies (Next Generation Sequencing, Archer® FusionPlex® Sarcoma V2) revealed a *EWSR1::CREB1* gene fusion.
Conclusion: GNET is an ultra-rare and aggressive GI mesenchymal tumour characterized by neural markers positivity and melanic markers negativity. The main differential diagnosis is mainly made with a metastatic CSS, but melanic markers are positive; and metastatic melanoma, that do not harbour a EWSR1 gene rearrangement. Other tumours such as gastrointestinal stromal tumour, neuroendocrine tumours, synovial sarcoma or alveolar rhabdomyosarcoma are included in the differential diagnosis. A correct diagnosis of GNET is crucial to early provide an accurate treatment.

E-PS-24-040
From morphologic overlap to molecular precision: VGLL2::NCOA2-fused spindle cell RMS in early infancy
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Background & Objectives: Limited biopsy material, such as tru-cut samples in infants, may lead to diagnostic ambiguity when evaluating spindle cell sarcomas. We present a diagnostically revised case of SC/S RMS, initially labeled as infantile fibrosarcoma (IFS), to highlight the value of clinical, morphological, and immunohistochemical integration in accurate diagnosis and to contribute to the molecular annotation of VGLL2-fused RMS.
Methods: Histopathologic and immunohistochemical analyses were followed by targeted RNA sequencing using a sarcoma-specific fusion panel (ArcherDX Sarcoma Panel v2, Illumina NextSeq 500) for molecular confirmation.
Results: A 6-month-old male infant was referred following a tru-cut biopsy at an external centre, which had rendered a diagnosis of IFS. The clinical differential diagnoses included IFS and Ewing sarcoma. The lesion, initially presenting as a painless swelling in the left elbow, measured 6×3 cm and demonstrated destructive involvement of the distal humerus. MRI revealed a 5.5×3 cm mass extending to the proximal forearm with cortical erosion.
Microscopic reevaluation demonstrated fascicular and focally herringbone-like spindle cell infiltration within a hyalinized stroma. Tumour cells were diffusely MyoD1-positive, focally Myogenin-positive, and negative for desmin, actin, caldesmon, S100, and CD34. Twenty-one mitoses were identified per 10 high-power fields. Based on these findings and clinical context, a diagnosis favoring SC/S RMS was rendered prior to molecular testing.
RNA sequencing subsequently confirmed the diagnosis by detecting a VGLL2::NCOA2 fusion. No MYOD1 mutation or FOXO1 alteration was identified.
The patient received 12 weeks of IRS/IR VAC chemotherapy and two cycles of neoadjuvant radiotherapy. Surgery was deferred at our centre; wide excision is reportedly planned externally. The clinical course remains stable to date.

Conclusion: This case illustrates the diagnostic complexity of SC/S RMS in infancy and demonstrates that clinicopathologic integration can be sufficient in selected cases. Molecular confirmation provided additional diagnostic support and contributes to the genomic understanding of fusion-positive rhabdomyosarcoma.

E-PS-24-041

Small bowel MPNST in a NF1 patient: a case report

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Background & Objectives: Malignant peripheral nerve sheath tumours (MPNSTs) are aggressive sarcomas frequently associated with neurofibromatosis type 1 (NF1). Only 13 cases with gastrointestinal involvement have been reported. We present a high-grade MPNST in the small bowel, initially suspected as GIST.
Methods: A 48-year-old female with NF1 family history presented with numerous skin neurofibromas and symptoms of intestinal obstruction and peritoneal irritation. Contrast-enhanced CT revealed a heterogenous lesion with no clear demarcation from adjacent structures. Right hemicolectomy and right adnexal removal were performed. Histopathological examination and immunohistochemical tests (SOX10, CD117, DOG1, CD34, SMA, MUC4, EMA, S100, and HMB45) were used for diagnosis.
Results: Gross examination showed a relatively well demarcated tan mass with cystic areas, measuring 11 cm in the long axis, originating in the subserosa and progressively invading the full thickness of the small bowel wall, leading to luminal protrusion and mucosal ulceration. Histologically, we described a well-demarcated, unencapsulated, intramural tumour with fascicular architecture, spindle cells, high mitotic activity (50 mitoses/10 HPF), myxoid stroma, and widespread tumour necrosis. IHC revealed focal SOX10 with moderate intensity, while CD117, DOG1, CD34, SMA, MUC4, EMA, S100, and HMB45 were negative. Given the histological features and immunohistochemical profile with focal SOX10 expression, and medical history of NF1, a diagnosis of high-grade MPNST was confirmed.
Conclusion: Gastrointestinal involvement by MPNSTs is extremely rare, with few cases reported so far. Other soft tissue neoplasms such as GISTs are typically included in the differential, although knowing the setting of NF1 allows for a higher index of suspicion in diagnosing MPNST. Taken together with the clinical context, histopathological and IHC evaluation are essential for diagnosis. Given the aggressive nature of MPNSTs, early recognition and preemptive management of plexiform neurofibromas, before transformation, is essential, ideally in a multidisciplinary setting.

E-PS-24-043

Rare variant of fibrous dysplasia: fibrocartilaginous dysplasia

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Background & Objectives: Fibrocartilaginous dysplasia is a rare benign bone lesion seen in children. Our patient is a 10-year-old female who presents to the clinic with left hip pain that has been ongoing for 3 months. The X-ray examination revealed a radiolucent lesion with indistinct borders and areas of ground glass opacity located in the left femoral neck-shaft and left tibia. There is a reduction in the angle of the left femoral neck-shaft, along with outward angulation of the proximal femur (Shepherd's Crook deformity).
Methods: The patient underwent bone curettage biopsy for both lesions. For the lesion located in the left femoral head, histopathological examination of the H&E sections revealed massive cartilage tissue composed of both small fragmented and mostly large nodules in many regions. Focal areas exhibit spindle-shaped benign-appearing fibrous stroma containing disorganized immature bone lamellae fragments within the stroma. Notably, osteoblasts are not prominent around the immature bone tissue in the fibrous stroma. In the cartilage tissue, there is focal cellularity increase and moderate atypia, along with widespread enchondral ossification. Areas of continuity between the cartilage tissue and fibrous stroma are observed.
Results: This lesion is reported as fibrocartilaginous dysplasia. No cartilage tissue is detected in the concurrent curettage biopsy of the tibia, and this lesion is reported as Fibrous Dysplasia.

Conclusion: In the literature, cases where varying amounts of cartilage differentiation accompanying fibrous dysplasia have been reported, though these are very rare. These cases have been described as fibrocartilaginous dysplasia. In these instances, cartilage tissue may sometimes be very prominent. Since atypia may be observed in the cartilage tissue, chondrosarcoma should be considered in the differential diagnosis. In these cases, the identification of the classic fibrous stromal component is crucial.

E-PS-24-044

Correlating nuclear morphometric patterns with immunohistochemical p53 staining and Ki67 labelling index in sporadic primary and long-term recurring chordomas

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Background & Objectives: Pleomorphic nuclear changes as well as tissue architecture can be characteristic for tumour progression or recurrence in solid tumours. Chordomas are malignant bone tumours with a high recurrence rate and uncertain tumorigenesis. Evaluation of nuclear pleomorphism in chordoma recurrences could facilitate the understanding of recurrence development and add a prognostic factor in diagnosis of this rare tumour. This study compares histology, immunohistochemistry and nuclear pleomorphy of non-recurrent chordomas (NRTs) and chordomas with long-term recurrences (RCs) in order to investigate wether tumour progression in chordoma coincides with nuclear pleomorphic changes.
Methods: 26 FFPE tissue samples of 12 patients (eight primary cases and four cases with multiple long-term recurrences) were obtained and stained for: H&E, brachyury, Ki-67, p53, S100, Vimentin, E-Cadherin, EGFR, VEGF, Pancytoceratines, SMARCB1, PD-1 and PD-L1. Nuclear morphometry was assessed by hand-tracing 320 nuclei per sample on digitally captured images.
Results: NRTs display a heterogenous distribution of nuclear morphometric measurements.
A comparison of RCs and NRTs show significant differences in all size and density-parameters as well as three out of four shape parameters and increased variances over time. Primary tumours of RCs had slightly smaller nuclei with higher deviations from a circular shape and were denser than NRTs hinting at a progress in dedifferentiation.

The p53 positivity was generally lower in primary tumours with < 1% compared to recurrent tumours with > 10%. Partial loss of SMARB1 expression could be observed more frequently in recurrences. Remarkably the Ki67 proliferation index showed a significant increase with a labelling index of < 1% in primary tumours and > 5% in the recurrences.
Conclusion: Patients with multiple recurrences showed significant pleomorphic changes over time especially in size and density parameters hinting that changes in clinical presentation and biological aggressiveness can present morphologically. This nuclear heterogeneity can be a feature associated with genetic instability and tumour progression.

E-PS-24-045
Insights into benign bone tumours of the chest wall: a series of 21 cases in a single Tunisian institution
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Background & Objectives: Benign bone tumours of the chest wall are rare entities. The diagnosis of these tumours can be challenging due to their overlapping histological features with other subtypes of bone tumours, especially when biopsy material is limited. In this report, we outline the clinicopathological features of benign thoracic bone tumours, along with their surgical management and prognosis.
Methods: A retrospective review was conducted on 21 patients diagnosed with benign bone tumours of the chest wall between 2002 and 2024. Clinical data, imaging findings, histopathological results, treatment modalities, and follow-up outcomes were retrieved from pathological reports and surgical records at Abderrahman Mami Hospital in Tunisia.
Results: There were 9 men and 12 women. The median age was 36 years, ranging from 20 to 52 years. Chest pain and palpable masses on physical examination were the most common presenting symptoms, reported in 10 and 7 cases, respectively. In 4 patients, the lesions were asymptomatic and discovered incidentally on imaging. Chest radiographs showed well-defined costal opacities in 14 cases. Chest computed tomography revealed a lytic, well-limited medullary costal lesion (17 cases) and a corticalized overgrowth (4 cases). No periosteal reaction or soft tissue infiltration were noted.
Surgical resection was performed in all patients. Pathological examination revealed 13 cases of fibrous dysplasia, 4 cases of enchondroma, 2 cases each of osteochondroma and mesenchymal hamartoma.
No postoperative complications or recurrences were noted during a mean follow-up of 8 years.
Conclusion: Benign bone tumours of the chest wall are rare and usually exhibit a benign course. Surgical resection remains an effective treatment with excellent prognosis and low recurrence rates. Although, radiological imaging plays a crucial role in the initial identification of these tumours, diagnosis confirmation still requires histological examination which accurately differentiate between different tumour types.

E-PS-24-046
Novel and unusual USP6 fusion partners in aneurysmal bone cyst – an update
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Background & Objectives: Aneurysmal bone cyst (ABC) belongs to a heterogenous group of reactive and neoplastic processes collectively known as giant cell-rich lesions of bone. Regarding the histopathological diagnosis, morphological features should be accompanied by clinical data or molecular analysis. A useful diagnostic clue represents the fact that approximately 70% of ABC harbour rearrangements of *USP6* gene. The aim of our research is to identify and report previously unrecognized and rare *USP6* fusion partners in ABCs. These discoveries could aid in both routine diagnostic practices and the exploration of the underlying biology of *USP6*-associated disorders.
Methods: This retrospective, non-randomized study involved a cohort of 14 patients diagnosed with ABCs, who were examined between 2014 and 2025 at Motol University Hospital in Prague. The cases were evaluated through histopathological analysis, immunohistochemistry, and Anchored multiplex RNA methods. In addition, demographic and clinical data were also reviewed.
Results: We discovered four novel *USP6* fusion partners (*ZFX*, *IP6K2*, *DDX6*, and *MORF4L1*), six rare ones (*MEF2A*, *EIF1*, *COL1A2*, *RUNX2*, *PAFAH1B1*, and *FAT1*), and two common partners (*CDH11* and *OMD*) across the 14 ABC cases.
Conclusion: The cases in our study were diagnosed as ABCs based on their distinct clinical and morphological features. However, not all instances present so clearly, and molecular testing remains essential. Recognizing these genetic alterations can help differentiate true ABCs from ABC-like changes seen in a variety of benign and malignant bone tumours. Moreover, the majority of fusion partners identified in our study have been associated with tissue repair according to the literature, which could explain certain clinical peculiarities, such as their connection to trauma in the anamnesis and the self-healing course observed in some cases. We suggest that further exploration of this hypothesis may be desirable.

Funding: The authors report that they received open access funding for their manuscript from research Project of the Ministry of Health of the Czech Republic No. 00064203

E-PS-24-047
Epithelioid haemangioendothelioma: a case report and retrospective review of diagnosed cases in a surgical pathology laboratory
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Background & Objectives: Epithelioid haemangioendothelioma (EHE) is a rare malignant vascular neoplasm with variable clinical behaviour that can arise in diverse anatomical locations. Diagnosing EHE is challenging due to its histological overlap with other vascular and epithelioid neoplasms. This study aims to present an interesting case of EHE and provide a retrospective review of EHE cases diagnosed in our pathology laboratory. We emphasize the diagnostic challenges and highlight the importance of implementing molecular techniques in confirming the diagnosis.
Methods: A retrospective review of EHE cases diagnosed in our pathology laboratory from 2009 to 2025 was conducted. Patient data were collected from pathology reports and medical records, including age, gender, tumour location, histological characteristics, immunohistochemical findings, and molecular analyses when available. Additionally, we present a detailed report of a newly diagnosed EHE case, which served as the catalyst for this study.
Results: A total of 15 cases of EHE were identified, where the diagnosis was either strongly considered or molecularly confirmed. Patient mean age was 60.3 years, with a male-to-female ratio of 2:1. Anatomical sites included the pleura (33.3%), bone (26.7%), soft tissues (20.0%), liver (13.3%), and lungs (6.7%). All cases exhibited morphologic features of epithelioid cells within a myxohyaline stroma. Endothelial differentiation was confirmed through immunohistochemical staining using vascular markers. A definitive diagnosis of EHE was achieved in 4 of 15 cases, with molecular biology techniques utilized in 3 of these cases. We also present a

44-year-old female with a morphologically and mitotically low-grade tumour in the thoracic wall, illustrating the diagnostic complexity and the value of integrating pathology, immunohistochemistry, and molecular studies.
Conclusion: EHE is a rare and diagnostically challenging tumour with diverse clinical presentations. By presenting a unique case alongside a comprehensive institutional review, we aim to enhance awareness and facilitate the accurate diagnosis of this uncommon entity.

E-PS-24-048
***EWSR1-PATZ1* fusion sarcoma. A new case report and review of the literature**
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Background & Objectives: *EWSR1::PATZ1* sarcoma is a exceedingly rare malignant mesenchymal neoplasm with variable morphology and a heterogeneous immunohistochemical profile. So far, only 45 cases have been described in the literature, that is why we report an additional case of this tumour with complete clinico-morhological and molecular data.
Methods: Male, aged 55, was admitted to a hospital due to a subcutaneous tumour of the paravertebral region, growing for 2 months. CT examination showed unencapsulated mass, 23x20x41 mm, localized in the paravertebral soft tissues at the Th11 level. The tumour was radically removed and no adjuvant treatment was administered. The patient maintained free of disease for 13 months.
FFPE and HE stained tumour sections were reviewed by two pathologists. All immunohistochemical staining were made using DAKO Omnis autostainer.
FISH study was performed on FFPE tissue sections using the EWSR1-Dual Color Break Apart Rearrangement Probe set. At least 300 interphase nuclei were analysed. The most common fusion genes were assessed using Archer FusionPlex Sarcoma V2 assay and Illumina MiniSeq sequencer.
Results: **At low power microscopy**, the tumour was partially encapsulated by a variably fibrous tissue and skeletal muscles. **At high power** the tumour texture was consisted of small round cells with moderate polymorphism and moderate proliferative activity. The neoplastic cells formed solid and perivascular arrangements or gathered around pseudocystic spaces. Their immunophenotype was characterized by strong expression of desmin (DER11), S100 protein and MyoD1. The immunohistochemical reactions to cytokeratins, EMA, smooth muscle actine, myogenin, DOG1, and ERG gave negative results. EWSR1-FISH showed the split of two signals in more than 10% tumour cells. NGS study demonstrated EWSR1::PATZ1 gene fusion, with EWSR1 exon 8::PATZ1 exon 1.
Conclusion: Depending on histological texture and the immunofenotype, *EWSR1-PATZ1* sarcoma may histologically resemble rhabdomyosarcoma. The molecular studies (using both FISH or NGS methods) allow to establish the proper final diagnosis.

Funding: Reseach are partially supported by grant of the The National Centre for Research and Development no. GOSPOSTRATEG-VI/0016/2021

E-PS-24-049
Retiform haemangioendothelioma of the index finger: a diagnostic challenge
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Background & Objectives: Retiform haemangioendothelioma (RH) is an uncommon vascular tumour of intermediate biological behaviour, which is prone to local recurrence but rarely shows metastasis to distant sites. It most frequently occurs on the limbs especially the lower extremities. Distinguishing RH from the aggressive angiosarcoma is challenging, as it may mimic well-differentiated angiosarcoma, especially on small biopsies. It is crucial to consider RH in the differential diagnosis of vascular lesions that present with angiosarcoma-like characteristics.
Methods: A 46-year-old woman, with no history, consulted for a painless swelling on the palmar side of her right index finger. The lesion caused mild discomfort without functional limitations. On examination, the nodule was firm, immobile and adherent to deep structures, initially raising suspicion of a tenosynovial giant cell tumour. Imaging findings were in line with this hypothesis. During surgery, unexpected skin adhesion suggested a more aggressive process.
Results: Gross examination revealed a nodule measuring 3.5 × 1.5 cm. Microscopically, the dermis was the site of poorly defined vascular proliferation, forming elongated and branching channels in a distinctive retiform pattern. The endothelial cells exhibited mild nuclear atypia and occasional protrusions into the lumen. Mitotic figures were rare. The surrounding stroma contained moderate lymphocytic infiltration and fibrosis. Immunohistochemical analysis showed ERG positivity and HHV-8 negativity. The diagnosis of RH was retained.
Conclusion: This case illustrates the diagnostic complexity of RH, which can clinically resemble both benign and more aggressive tumours. The unusual location on the finger, combined with its intraoperative and histological characteristics, highlights the need to consider RH in the differential diagnosis of vascular lesions. Given its high recurrence rate, complete surgical resection with negative margins is essential, along with long-term follow-up to monitor for potential regrowth.

E-PS-24-051
Histologic and clinical vagaries of Sclerosing Epithelioid Sarcoma: a series of 23 patients
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Background & Objectives: Sclerosing Epithelioid Fibrosarcoma (SEF) is a rare sarcoma with high local recurrence rates and metastatic potential. Histologically, it contains bland epithelioid cells within a dense fibrous stroma. Immunohistochemistry for MUC4 is highly specific for diagnosis of SEF. We studied 23 patients diagnosed with SEF in our institution from 2019 to 2025 with emphasis on the histologic spectrum, immunohistochemistry and clinical outcomes..
Methods: We obtained clinical data from hospital records and reviewed histopathology findings
Results: The age range of patients was 9 to 70 years; median 40 years. M:F ratio was 60:40. The most common site of occurrence was lower extremity followed by shoulder region, chest wall and paravertebral region. Primary bone involvement was seen in 2 patients. Conventional morphology was seen in most tumours. Areas with spindle cell morphology resembling low grade fibromyxoid sarcoma were seen in 3 cases, necrosis in 3 cases, mitoses in 1 case. Significant nuclear atypia was seen in 2 cases. 86% % of tumours were positive for IHC with MUC4. Molecular testing for EWSR1 gene rearrangement was performed in only 2 patients, both were positive. 11% patients presented with metastasis. 40% experienced local relapse and 16 % had distant metastasis later.

Conclusion: SEF occurred at varied sites and in wide age range, hence required a high index of suspicion. Typical morphology of bland epithelioid cells embedded in dense fibrous stroma was seen in 70% of patients. 30% cases showed unusual findings such as spindle cell areas, foci of necrosis, atypia and increased mitoses. Aggressive clinical behaviour of SEF was evident in spite of its low grade histological features. 40% patients experienced relapse, 27% had metastasis. Lungs, bones, soft tissue and lymph nodes were the commonest sites of metastasis. IHC for MUC4 proved to be specific which helped in ruling out a wide spectrum of differential diagnoses of SEF.

E-PS-24-052

Calcifying Fibrous Tumour of the stomach mimicking Gastrointestinal Stromal Tumour: a report of a rare case

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Background & Objectives: Calcifying fibrous tumour (CFT) is a rare benign soft tissue mesenchymal neoplasm which can occur anywhere and pathogenesis was controversial. Although the gastrointestinal tract is the most common predilection site and often stomach. The histologic examination is the gold standard for the diagnosis. By definition has characteristic morphology thus immunohistochemistry might be of use in the differential diagnosis from other submucosal, more aggressive clinically mimickers and the principle consideration was gastrointestinal stromal tumours (GIST).
Methods: A 52-year asymptomatic woman with gastric lesion found incident in a screening esophagogastroduodenoscopy. Endoscopic ultrasonoscopy showed a mass derived from the muscularis propria and diagnosis of (GIST) was suspected. A laparoscopic wedge resection was preferred. The pathological findings showed grossly well circumscribed submucosal mass 15mm with white to gray cut surface. Microscopically was hypocellular, composed of bland spindle cells with fibroblastic differentiation in a hyalinized collagen stroma and dystrophic type calcifications. Necrosis and mitosis were absent.
Results: Immunostains were negative for the markers CD117, DOG-1, AE1/AE3, SMA, Desmin, S-100 STAT-6, CD34 although SDHB retained. A diagnosis of CFT was rendered. Coexisted a lot lymphoplasmacytic infiltration which are IgG4 positive with IgG4/IgG > 50% in immunohistochemistry. These lesions overlaps morphologically igG4 related disease however the long term follow up showed no evidence especially in patients without other inflammatory or autoimmune diseases and combination of serologic-radiologic findings.
Conclusion: Local resection with clear margins is the most chosen treatment option for CFTs and should be distinguished from other tumours due to their low risk of recurrence and benign biological behaviour with excellent prognosis. When CFT is suspected the patient should be tests for igG4 related disease. The relationship between them remains unclearand only a subset of CFTs may arise in the context of either systematic ig4 disease.

E-PS-24-053

Case series of giant cell rich bone lesions: a 10-year single-centre retrospective analysis of 68 cases

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Background & Objectives: Giant cell-rich bone lesions encompass a spectrum of neoplastic and non-neoplastic disorders characterized by osteoclast-type giant cells, demonstrating diverse clinical and biological behaviours. A multidisciplinary approach incorporating clinical, radiological, pathological, and genetic features is essential to establish a definitive diagnosis and guide appropriate management.
Methods: Between 2014 and 2024, we retrospectively analysed clinical data from 68 patients diagnosed with giant cell-rich bone lesions. The evaluation included demographic characteristics (sex, age), lesion localization, clinical presentation (presence of pain, oedema, pathological fracture), and outcomes (recurrence, metastasis).
Results: In a cohort of 68 patients (35 female, 33 male; mean age 25.5 years, range 2–64) with histologically confirmed bone lesions, the most common diagnosis was aneurysmal bone cyst (ABC) (n=32, 47.1%), followed by giant cell tumour of bone (GCT) (n=17, 25%), chondroblastoma (n=6, 8.8%), non-ossifying fibroma (NOF) (n=4, 5.9%), and giant cell-rich osteosarcoma (n=4, 5.9%). Less frequent entities included reparative granuloma (n=3, 4.4%), chondromyxoid fibroma (n=3, 4.4%), brown tumour (n=1, 1.5%), benign fibrous histiocytoma (n=1, 1.5%), and osteoblastoma (n=1, 1.5%). The femur was the most frequently involved bone (32.4%), followed by the tibia (19.1%) and fibula (16.2%). Pelvic bones (pubis + sacrum) constituted 7.3% of cases (pubis 2.9%, sacrum 4.4%), while small bones of hands/feet (metacarpals + metatarsals) accounted for 8.9% (metatarsals 7.4% + metacarpals 1.5%). Rare sites included the scapula and ribs (1.5% each). Clinically, 92.6% (n=63) presented with pain, 27.9% (n=19) had oedema, and 14.7% (n=10) presented with pathological fractures. Recurrence occurred in 8.8% (n=6), including 3 ABC, 2 GCT, 1 osteosarcoma. Lung metastasis was identified in 1 osteosarcoma case.
Conclusion: The accurate diagnosis of giant cell-rich bone lesions requires comprehensive integration of histopathological characteristics with key clinical-radiological parameters, including patient age, anatomical location, and imaging findings, to distinguish between histologically similar but clinically distinct entities.

E-PS-24-054

EWSR1-PATZ1 fused sarcoma arising in chest wall: a case report

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Background & Objectives: Sarcomas with EWSR1-PATZ1 fusion are rare soft tissue tumour. In the WHO Classification 5th Edition of Soft Tissue and Bone Tumours, it has been classified as Round cell sarcoma with EWSR1-non-ETS fusion. It has been reported to occur across a broad age range (1–81 years) with an approximately equal male-to-female ratio. Notably, it was recently recognized as an entity and demonstrates variable morphology, ranging from low- to high-grade sarcomas, along with a heterogeneous immunohistochemical profile. Due to its low incidence and diverse histologic features, accurate diagnosis is challenging, requiring ancillary immunohistochemistry. Herein, we report an extremely rare case of EWSR1-PATZ1 fused sarcoma.
Methods: Immunohistochemistry and next-generation sequencing (NGS) were used for diagnostic purposes.
Results: A 58-year-old male with no specific symptoms was found to have a 6.5 × 4.3 × 3.6 cm mass in the chest wall on CT. He underwent surgical resection. Grossly, the tumour was well-circumscribed, solid, and fibrotic. Microscopically, it predominantly showed sclerotic areas with low cellularity, interspersed with regions of pleomorphic cells and notable microcystic changes. Most of the tumour cells were spindle-shaped or had a fibrohistiocytic appearance. Immunohistochemically, the tumour showed positivity for GFAP and Desmin, with focal positivity for Sox10, S100, EMA, SMA, and calponin. Based on these findings, EWSR1-PATZ1 fused sarcoma was suspected, prompting NGS analysis, which confirmed an in-frame fusion between EWSR1 exon 7 and PATZ1 exon 1, leading to the final diagnosis.
Conclusion: EWSR1-PATZ1 fused sarcoma is a very rare novel entity of undifferentiated small round cell sarcoma. This case underscores

the importance of considering EWSR1-PATZ1 fused sarcoma in the differential diagnosis of chest wall lesions and highlights the clinical significance of molecular testing in rare sarcomas.

E-PS-24-055

Sclerosing/spindle cell rhabdomyosarcoma. Case series of the last 5 years

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Background & Objectives: Rhabdomyosarcoma (RMS) is a rare malignant neoplasm arising from undifferentiated mesenchyme. Head and neck and extremities are the most frequent locations. It was first classified as a variant of embryonal RMS but it´s been recently recognized as an independent entity.
Methods: A 58-year-old male patient with the complaints of left hand paresthesias. The radiologic studies showed a lesion that involved 3rd and 4th metacarpians and it caused cortical bone rupture.
A 65-year-old female patient assisted with a nodule in the back of the neck that was initially suspicious for sebaceous cyst and it was resected without posterior pathological examination.
Results: Slides of both lesions showed neoplastic proliferation consisting of spindle and epithelioid cells. They had marked cytological atypia, irregular nuclei, vesicular chromatin and prominent eosinophilic nucleoli. In the first case, numerous rhabdomyoblasts could be seen, with a variable cell density that alternates hypercellular and hipocellular zones with stromal sclerosis. The second case standed out with numerous mitosis figures and foci of geographic necrosis and, peripherally, a crown of lymphocytes was observed.
Immunohistochemical staining:
Positive: Smooth muscle actin, desmin, caldesmon, INI1 (nuclear), MyoD1, mioglobin, H3-K27me3, CK AE1/AE3, CK7.
Negative: neural markers, beta-catenin (nuclear), CD34, calponin, CK20, p40, CK5/6, GATA3, EBER.
After histological examination and immunohistochemical staining, both lesions were diagnosed as spindle cell rhabdomyosarcoma.
Conclusion: It`s important of preparing a broad IHQ panel that allows to elaborate a correct differential diagnosis with other spindle cell sarcomas (many of which may have rhadbomyoblastic differentiation).
The fact that a small percentage of spindle cell RMS can express citoqueratine could lead us to mistake with undifferentiated carcinomas, especially in head and neck region.
Spindle cell variant of RMS seems to be an aggressive lesion; despite it has a better prognosis than other adult RMS.

E-PS-24-056

Case report: primary breast soft tissue sarcoma with BCOR genetic alterations

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Background & Objectives: Primary breast sarcomas are rare, accounting for less than 1% of all breast malignancies. Angiosarcoma is the most common type of breast sarcoma but other types have limited clinical, histologic and molecular information, hindering optimal patient management.
Methods: We report a case of a previously healthy 20-year-old female that presented with a 3-week growing, painful breast nodule.
Results: After 2 biopsies inadequate for a histological diagnosis, the patient underwent a tumorectomy. Histological examination revealed a spindle and round cell neoplasm, non-encapsulated, infiltrative, of high malignancy grade with venous invasion and no necrosis. Neoplastic cells were immunoreactive for vimentin, CD10, pS100, CD56, cyclin D1, SATB2, BCL2, and focal SMA and CD99 staining; they were negative for cytokeratins, EMA, p63, GFAP, SOX10, HMB45, melan A, calponin, desmin, myogenin, CD34, ERG, STAT6, MUC4 and TLE1, with a Ki67 of 40%. Together with molecular and NGS ancillary techniques, a non CCNB3-BCOR fusion and a non-homozygotic CDKN2A gene mutation were identified. A diagnosis of primary breast soft tissue sarcoma with BCOR genetic alterations was made after ruling out metastatic endometrial stromal sarcoma. The patient underwent radical mastectomy and chemotherapy. The tumour was poorly responsive to treatment and the patient later developed lymph node and skin metastases and is currently awaiting further treatment.
Conclusion: Primary breast soft tissue sarcomas with BCOR genetic alterations are very rare, with around 200 reported cases, and are associated with a poor prognosis. Given the paucity of data, the management of these patients remains unclear; however, molecular and NGS profiling can identify potentially useful therapeutic targets, thus improving patient overall survival.

E-PS-24-057

Molecular decryption of sarcomas: a 6-year retrospective study revealing new diagnostic perspectives in Marrakech

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Background & Objectives: **Background:** Soft tissue sarcomas are rare tumours whose classifications, based on their appearance and characteristics, often lack consistency. A better understanding of their molecular profiles is essential to improve diagnosis and management.
Objective: To explore the molecular characteristics of soft tissue sarcomas in comparison with their pathological features in patients at the Mohamed VI University Hospital.
Methods: A retrospective study was conducted from January 2019 to January 2025, examining 66 cases of sarcomas (19 PNET/Ewing, 19 synovial, 28 liposarcomas) at the pathology department. Diagnosis was based on standard histology, immunohistochemistry (anti-CD99, anti-cytokeratin, anti-EMA, anti-TLE, anti-MDM2, and anti-CDk4 antibodies) and FISH to detect EWSR1 and SS18 gene rearrangements, as well as MDM2 gene amplification.
Results: The average age of patients was 37 years (13-79 years), with a male predominance. 81% of cases were grade III according to the FNCLCC classification, mainly located in the lower limbs. PNET/Ewing tumours showed proliferation of small round cells, with 85% intense positivity for CD99 and 78.9% EWSR1 rearrangement. Synovial sarcomas presented spindle cells, with >80% positivity for cytokeratin, EMA, and TLE, and 26.3% SS18 rearrangement. Liposarcomas showed positivity for MDM2 and CDk4, with 17.8% MDM2 amplification.
Conclusion: This study underscores the importance of a diagnostic approach combining morphological evaluation and molecular analyses for soft tissue sarcomas. The diversity and complexity of these tumours require a comprehensive approach, allowing for accurate and informed clinical decisions in the management of sarcoma patients.

E-PS-24-058

Tumour necrosis shapes Ewing sarcoma intra-tumoral heterogeneity

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Background & Objectives: Ewing sarcoma (EwS) is the second most common bone malignancy in children and young adults. Most, if not all, EwS oncogenesis is driven by a chromosomal translocation between a member of the Erythroblast transformation specific *(ETS)* family of transcription factors and a member of the *FET* family of RNA binding proteins, most commonly resulting in the *EWS-FLI1* fusion. Despite multimodal therapy, EwS prognosis remains dismal in the presence of metastasis or recurrence, possibly due to its intra-tumoral heterogeneity (ITH). Ewing sarcoma displays one of the lower mutational burdens of all cancers, raising the question of the molecular mechanisms driving its ITH.
Methods: To better understand EwS ITH, we performed single-cell transcriptomics on seven freshly dissociated tumours using full-length single-cell RNA sequencing (SMART-Seq2) and further validated our findings with droplet-based single-nucleus RNA sequencing (10x) on four tumours. In addition, we utilized spatial transcriptomics (GeoMX) to investigate EwS cellular-states spatial distribution and *in-vitro* culture of primary EwS sarcoma cells to decipher molecular drivers of EwS cellular heterogeneity.
Results: We identified six malignant cellular states, including a mesenchymal program predictive of worse prognosis. Spatially, peri-necrotic tumoral cells exhibited a profoundly altered cellular landscape, with enrichment in meta-programs linked to inflammation and mesenchyme-related genes, alongside reductions in cell cycle and metabolic activity. Mechanistically, soluble factors from necrotic tumour cells increased the expression of Activating Protein 1 (AP1) family transcription factors, altering cell state distribution and modulating EWS-FLI1 activity.
Conclusion: Overall, our work provides an atlas of EwS malignant cells, underscores the critical role of tumour necrosis in shaping ITH, and identifies a cell population associated with poorer prognosis, offering potential therapeutic targets and highlighting the role of the mesenchymal cellular state markers in predicting EwS prognosis

Funding: Swiss National Science Foundation (SNSF); Project number P500PM_206713; Name of the project: Dissecting molecular mechanisms driving Glioblastoma heterogeneity

E-PS-24-059

Soft tissue sarcomas: epidemiological criteria and pronostic and predictive clinical and anatomopathological factors for recurrence in the centre of Tunisia

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Background & Objectives: Soft tissue sarcomas (STS) are rare malignant tumours that arise from supportive mesenchymal tissue. Their etiopathogenesis is poorly understood, and several prognostic factors influence patient survival, which varies from 42% to 87% at 5 years. In addition to prognostic factors, it is crucial to identify and manage predictive factors for local recurrence in order to improve treatment outcomes.
The main objective of this study was to analyse the epidemiological, clinical, and pathological characteristics of soft tissue sarcomas, and to identify the predictive factors for tumour recurrence as well as the prognostic factors influencing overall survival.
Methods: This is a retrospective, descriptive, and analytical study based on data from the Cancer Registry of the Centre of Tunisia over a 25-year period (1997-2021). It included patients diagnosed and treated at the orthopedics departments of Monastir and Sahloul hospitals, with diagnoses confirmed by the pathology departments of Farhat Hached and Monastir hospitals.
Results: The study included 142patients,with an average age of 50.7years,ranging from 3 to 93 years.The male-to-female ratio was 1.15.The main symptom was swelling,observed in 85.2%of cases,with an average consultation delay of 20.6 months.The thigh was the most frequent location,involved in 45%of cases.Liposarcomas and fibrosarcomas were the most common histological types,each accounting for 26.8% of cases.The local recurrence rate at 3 years was 45.1%,and the 5-year overall survival rate was 47.9%.Univariate analysis showed that factors such as age,consultation delay,histological type,tumour location,and clinical and radiological characteristics significantly influenced local recurrence and overall survival.
Conclusion: Although rare,soft tissue sarcomas present a great histological and anatomical diversity.Analysis of clinical and therapeutic data allowed the identification of essential prognostic and predictive factors for better disease control and improved outcomes.These results highlight the importance of multidisciplinary management,including multidisciplinary tumour board meetings,in optimizing the treatment and follow-up of patients with soft tissue sarcomas.

E-PS-24-062

Intratesticular leyomioma with degenerative atypia: an unexpected diagnosis of an exceedingly rare benign testicular tumour

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Background & Objectives: Mesenchymal tumours of the testis are extremely rare and they have a tendency to display malignant features. In addition, they are normally difficult to distinguish from other more common testicular tumours. Therefore, radical orchiectomy is the likely choice upon on the presence of a suspicious testicular nodule.
Methods: Here, we report the case of a 46-year-old man who sought medical care after noticing a nodule in his right testicle evolving for nearly 1 month. The ultrasound imaging study described a hypoechoic and highly vascularized nodule with 9 mm. A radical orchiectomy was performed.
Results: A 10 mm whitish well-circumscribed nodule was present in the upper pole of the 5,5x4x3 cm testicle. The histological analysis showed a neoplasm composed of spindle-shaped cells with indistinct cytoplasmic borders, eosinophilic cytoplasm, nuclei with tapered ends and small nucleoli; and epithelioid cells with eosinophilic cytoplasm and rounded nuclei with similar characteristics. There were also frequent cells of increased size, eosinophilic cytoplasm, with irregular nuclear contour, hyperchromasia and a "blurred nuclei" appearance, suggesting degenerative changes. Frequent nuclear pseudoinclusions and occasional multinucleated giant cells were also noted. Mitotic activity was not significant. Necrosis was absent. The immunohistochemistry study showed expression of SMA, Desmin, HHF35 and Caldesmon, while S100 protein and Inibin A were negative. TP53 had wild-type expression. The proliferative index (%Ki-67) was <1%. The diagnosis of a leiomyoma with degenerative nuclear atypia was advanced.
Conclusion: Leiomyomas are benign mesenchymal neoplasms commonly occurring in locations such as the uterus or small bowel. Leiomyomas affecting the male genitourinary tract are extremely uncommon. Of these, intratesticular leiomyomas are exceedingly rare. Given the benign nature of this neoplasm, is of utmost importance to identify

novel markers and imaging features that will prevent unnecessary orchiectomies for a benign testicular tumour.

E-PS-24-063

When rare meets young: paediatric presentation of desmoplastic fibroblastoma

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Background & Objectives: Desmoplastic fibroblastoma (DF) is a benign soft tissue tumour made up of stellate and/or spindle-shaped fibroblasts, embedded in an abundant collagenous or myxocollagenous stroma. DFs are rare neoplasms, predominantly affecting adults. Herein, we present a novel case of paediatric DF, with the aim to expand our knowledge about this entity in childhood.
Methods: The clinical history of the patient was retrieved. Tissue samples were formalin-fixed and paraffin-embedded, then haematoxylin-eosin as well as immunohistochemical staining for CD34, smooth muscle actin (SMA), actin muscle specific (HHF-35), and Ki-67 were performed.
Results: A 12-year-old boy presented with a 4-cm mass on his left thigh. Complete surgical excision was performed. Histology revealed a subcutaneous, well-circumscribed tumour consisting of scattered, stellate and spindle-shaped fibroblasts embedded within an abundant hypovascular, collagenous matrix. Cytologically, no atypia or mitotic activity were noted. CD34, SMA, and HHF-35 were negative; Ki-67% was <1%. After 2 years of follow-up, the patient did not show signs of recurrence.
Conclusion: To date, only 5 additional cases of DF have been reported in paediatric patients (age: 0–18 years), affecting predominantly in males and following a benign clinical course. Our report further confirms the occurrence of this entity in children, underscoring the importance of considering it in the differential diagnosis of benign fibroblastic/fibrocytic lesions even in paediatric population.

E-PS-25 E-Posters Thymic and Mediastinal Pathology

E-PS-25-001

Paraganglioma of the mediastinum: a primary tumour or a metastasis – a case report

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Background & Objectives: Paragangliomas of the mediastinum are rare, slow-growing tumours, associated with high morbidity and mortality.
Methods: 45-year old patient with phaeochromocytoma and mediastinal mass was admitted to tertiary care hospital for additional diagnostics and operative treatment. Pathohistological analysis was performed using haematoxylin&eosin (HE) and immunohistochemistry (CD56, chromogranin, synaptophysin, vimentin, GATA 3, TTF, CD31, calretinin, SMA, S-100, Ki67).
Results: CT and MR were consistent with paraganglioma – benign appearing hypervascular, heterodense soft tissue mass (48mm), located above right atria in close proximity to vascular structures, but without signs of infiltration. MIBG scintigraphy revealed accumulations in right adrenal gland and middle mediastinum. Complete surgical excision wasn't possible due to localization, but removed tissue consisted of tumour composed of eosinophilic, polygonal cells with round nuclei (some of which atypical). Cells were mostly arranged in round formations (Zellballen) and bands, separated by delicate stroma with a large number of small blood vessels. Immunohistochemically, the tumour cells were: CD56, chromogranin, synaptophysin, vimentin and GATA 3 positive, while they were negative for: TTF1, CD31, calretinin and SMA. Sustentacular cells were positive for S-100 while the Ki-67 proliferative index is low (less than 1% of tumour cells).
Conclusion: Typical immunoprofile, low Ki67, rare nuclear atypia and lack of locally invasive growth led to a conclusion of primary paraganglioma rather than metastasis of pheochromocytoma. However, metastatic disease can involve any organ, so immunophenotypes of both tumours must be compared to obtain final conclusion. In addition, possibility of hereditary predisposition and various syndromes and familial conditions must be considered.

E-PS-25-002

Thymectomy specimens: a ten-year review in a Canadian academic pathology department

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Background & Objectives: Thymectomy specimens are infrequently encountered in the surgical pathology laboratory, usually as management of thymic tumours or of myasthenia gravis. Our institution is the main referral centre for the Canadian Maritime provinces (2.1 million population) and we receive most thymectomy specimens in the region. There has been a subjective increase in the number of thymectomy specimens in our department in the past year. Our objective is to review the annual number of thymectomy specimens obtained in our laboratory over the past decade, along with the indication for surgery and the associated histopathologic findings.
Methods: Our laboratory information system was retrospectively searched for thymic resection, obtained for management of thymic tumour or of myasthenia gravis, between 01/01/2016 and 31/03/2025. Surgical date, patient demographics, and histopathologic findings were collected.
Results: From 2016 to 2023, there were 6-14 thymectomy specimens annually (average, 10.4). There were 23 in 2024, and 7 in the first quarter of 2025 (a 145% increase). Thymic tumour is the most frequent indication, and thymoma is the most frequent tumour type. There has been a significant increase in the number of type AB thymomas in 2023 and 2024 (average 6/year) compared to 2016-2022 (average 0.9/year).
Conclusion: There has been a measurable increase in the number of thymectomy specimens and in the incidence of type AB thymoma in our institution in the past two years. This is not explained by a pandemic-related operational slow-down or by an obvious population shift, and has an impact on the laboratory given the specialized resources necessary for their proper evaluation.

E-PS-25-003

Thymic lipofibroadenoma with sebaceous metaplasia and striated myoid cells: a case report

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Background & Objectives: Thymic lipofibroadenoma is a rare benign thymic tumour. While typically composed of adipose tissue, fibrous stroma, and residual thymic elements, unusual metaplastic changes

can occur. We report the rare instance of sebaceous and apocrine metaplasia and numerous myoid cells within a thymic fibrolipoadenoma.
Methods: **Case Report:** A 61-year-old male with aortic dilation underwent preoperative chest imaging, revealing an anterior mediastinal mass which was resected. Grossly, it was a well-circumscribed, encapsulated lesion measuring 11 cm. Microscopically, the tumour displayed the characteristic features of a lipofibtoadenoma, including mature adipose tissue, fibrous stroma, and thymic remnants. Notably, focal areas showed sebaceous gland differentiation, characterized by clusters of cells with foamy cytoplasm and central nuclei. Additionally, apocrine metaplasia was observed, with cells exhibiting abundant eosinophilic cytoplasm. Also the tumour showed a frequent occurrence of polygonal, striated myoid cells with abundant eosinophilic cytoplasm. The myoid cells were positive for SMA and desmin. They also lacked cytological atypia and mitotic figures. The findings were compatible with a lipofiroadenoma of the thymus gland. The patient recovered well.
Results: **Discussion:** Sebaceous and apocrine metaplasia within thymic lipofibroadenomas is an exceedingly rare phenomenon. The mechanisms driving these metaplastic changes are poorly understood. Differential diagnoses include thymolipoma with ectopic sebaceous glands, which is also rare. The presence of apocrine differentiation further distinguishes this case. The incidental discovery of this unusual metaplastic variant highlights the diverse histological spectrum of thymic lipofibroadenomas. It is important to recognize these rare variations to avoid misdiagnosis, particularly with malignant sebaceous or apocrine tumours, though these would rarely present in the thymus.
Conclusion: This case presents a rare thymic lipofibroadenoma with sebaceous and apocrine metaplasia and striated myoid cells, expanding the known histological variations of this benign thymic tumour. Pathologists should be aware of these unusual features to ensure accurate diagnosis and appropriate patient management.

E-PS-25-004

Castleman disease of the thorax: a single-centre case series

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Background & Objectives: Castleman disease (CD) is a rare and heterogeneous complex lymphoproliferative disease. Most commonly, CD is classified clinically as unicentric (UCD) or multicentric (MCD) and pathologically as hyaline vascular variant (HVV) or plasma cell variant (PCV). The HVV is the most common, and is treated with surgical resection. It is most commonly found in the mediastinum, where it classically appears as a unicentric, avidly enhancing mass at computed tomography (CT). This appearance can mimic other avidly enhancing mediastinal masses.
With this report, sharing our experience with five cases of CD, aims to contribute to literature on diagnosing and treating this disease.
Methods: We performed a retrospective study of CD diagnosed at our department of pathology, from 2004 to 2024. Demographics, clinical variables, anatomical site, centricity, histopathology, immunochemistry, and surgical approach were reviewed.
Results: There were 3 females and 2 males. The mean age of the patients was 43 years, average from 24 to 59 years**.** All the patients show enlarging lymph node or mass (n=4) or systemic inflammatory manifestations including fever, anaemia, anasarca, generalized lymphadenopathy and hepatomegaly symptoms (n=1). The histopathological examination based on an excisional biopsy of an affected lymph node (n=2) or on a surgical specimen (n=3). The median mass size was 4.5cm (range 11cm-1.5cm). In our study, histologically, CD is characterized by an onion-skinning of follicular dendritic cells around hyalinized vessels and small, atrophic germinal centres with interfollicular expansion by vascular proliferation and lymphocytes. Helping exclude lymphoma, immunohistochemically (n=3), germinal centres on CD was positive for CD20 and the interfollicular territories was positive for CD3 and CD5.
Conclusion: Castleman disease is a rare, complex and underdiagnosed disorder requiring multidisciplinary management. While UCD is often curable, MCD remains challenging, necessitating ongoing research into targeted therapies.

E-PS-25-005

Thymic adenoid cystic carcinoma with yolc sac tumour pattern

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Background & Objectives: Thymoma is the most common primary tumour of the thymus. Its occurrence is estimated at roughly 0.2%. To present day only singular cases of well documented thymic adenocarcinomas were reported. In this group were noted intestinal adenocarcinoma, pulmonary adenocarcinoma, mucinous adenocarcinoma and singular cases of adenoid cystic carcinoma.
Methods: We present a case of primary mediastinal tumour composed with residual thymoma AB and adenoid cystic carcinoma presenting an unusual yolc-sac like pattern.
Case description. A 65 years old male patient with dyspnoe was admitted to hospital. Computer tomography revealed solid tumour mass in anterior mediastinum measuring 11cm in greater dimension.
Results: Macroscopy presented a well circumscribed tumour mass measuring 11x7x4cm weighing 88g. On the cut surface the tumour was white and shiny with no cystic degeneration and necrosis.
Histologically, we noted infiltration by adenocarcinoma with predominance of adenoid cystic carcinoma. In addition, about 20% of the tumour was composed of a microcystic component lined with flattened atypical epithelium and slit-like spaces with spindle cells closely mimicking microcystic and myxomatous yolc sac tumour. At the periphery a remnant of thymoma AB was noted.
We noted positive steins as follows: PanCK, CK7, SMA, CD117, GFAP, S-100, alcian-pas, mucicarmine. Negative stains were as follows: CK20, TTF-1, GATA-3, OCT3/4, SOX-2, AFP.
Conclusion: The final diagnosis was thymic adenoid cystic carcinoma. The germinal tumour was excluded. Tumour areas presenting yolc-sac patterns were composed with myoepithelial cells.

E-PS-25-008

Primary mediastinal yolk sac tumour: case presentation with molecular study by sequencing

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Background & Objectives: Primary Mediastinal Yolk Sac Tumour is an extremely rare and highly aggressive extragonadal germ cell neoplasm. These tumours typically occur in the anterior mediastinum of young men, usually between the ages of 15 and 59.
Methods: We present the case of a 56-year-old male, a former smoker with a family history of lung cancer, who presented with chest pain. Imaging studies revealed three large tumours compressing the superior mediastinum. The largest tumour, measuring 94 mm in diameter, caused destruction of the left fifth rib and soft tissue involvement. A core needle biopsy was performed and sent to our pathology department for analysis.
Results: Histological examination revealed a high-grade solid neoplasm, positive for pancytokeratin, SALL4, Glypican 3, and CDX2, and negative for GATA3, synaptophysin, OCT4, CD117, CD30, NUT,

HepPar, B-HCG, and WT1. These findings supported the diagnosis of a mediastinal Yolk Sac Tumour, while excluding other differential diagnoses such as thymic carcinoma, large cell neuroendocrine carcinoma, seminoma, hepatocellular carcinoma metastasis, and NUT carcinoma. Next-generation sequencing (NGS) revealed pathogenic point mutations in TP53 and PTEN, as well as several copy number variations (CNVs), including deletions and gains of whole chromosomes or parts of them.
Conclusion: Primary Mediastinal Yolk Sac Tumour presents significant diagnostic complexity due to its rarity and its aggressive clinical behaviour, often leading to confusion with other mediastinal tumours. The molecular profile, including TP53 mutations, is distinct from that of testicular germ cell tumours and plays a key role in the prognosis. TP53 mutations are reported in up to 82% of cases and are considered a prognostic factor associated with resistance to cisplatin based therapies, adding another layer of complexity in the management of these tumours. This case highlights the importance of integrating histopathological, immunohistochemical, and molecular data to achieve an accurate diagnosis and guide treatment decisions for such rare and aggressive tumours.

E-PS-25-009
Uncommon extra-mediastinal bronchogenic cysts: two cases in the cervical and nasopharyngeal regions
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Background & Objectives: Bronchogenic cysts are congenital malformations arising from abnormal budding of the foregut during embryogenesis. They are most commonly found in the mediastinum, while cervical and nasopharyngeal localizations are extremely rare. Due to their unusual locations, these cysts can pose a diagnostic challenge and may be mistaken for other cystic lesions.
Methods: We report two cases of extra-mediastinal bronchogenic cysts: one located in the cervical region and the other in the nasopharynx . Clinical presentation, imaging findings, and histopathological features were reviewed.
Results: Case 1: A 27-year-old male presented with a painless cervical mass. Radiological examination revealed a well-defined cystic lesion. Surgical resection identified a 4×2.5 cm cystic lesion with a 1.8 cm cystic cavity. Histopathological examination showed a cyst wall lined by pseudostratified ciliated columnar epithelium with focal squamous metaplasia, along with underlying skeletal muscle and mucous glands. Case 2: A 54-year-old female was evaluated for a nasopharyngeal mass. A biopsy of a 0.4 cm lesion from the posterior wall of the cavum showed a fibrous-walled cyst lined by regular pseudostratified ciliated respiratory epithelium.
In both cases, histopathological examination confirmed the diagnosis of a bronchogenic cyst. No signs of malignancy were observed.
Conclusion: Bronchogenic cysts in the cervical and nasopharyngeal regions are exceptionally rare and can be misdiagnosed as other congenital or acquired cystic lesions. A thorough histopathological evaluation is essential for accurate diagnosis. Recognizing these atypical locations is crucial for pathologists and clinicians to ensure appropriate management and avoid unnecessary interventions.

E-PS-25-010
A rare malignancy – thymic squamous cell carcinoma
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Background & Objectives: Squamous cell carcinoma of the thymus is an extremely rare neoplasm that originates from epithelial cells. This malignancy is characterized by its aggressive clinical course and potential for local invasion and metastasis.
Methods: A 51 years old female, with no previous medical history, was hospitalized due to a presumed bronchopulmonary tumour. The CT scan revealed in the upper and middle mediastinum, a large mass of tissue, multilobulated that compresses and stenoses the mediastinal anatomical structures. Multiple bronchial biopsis was performed at bronchoscopy. H&E and immunohistochemical analysis for p40, TTF1, CD56, CD5, PAX8, c-KIT were performed.
Results: The videobronchscopy revealed the stenosis of the left upper lobar bronchus due to extrinsic compression, while the left subsegmental bronchus appeared completely stenosed due to extrinsic compression and tumour invasion.
H&E examination revealed multiple fragments of bronchial mucosa extensively infiltrated by a cellular proliferation with a diffuse distribution pattern. The neoplastic cells are of medium size, polygonal, with undefined cellular borders, eosinophilic cytoplasm, and enlarged nuclei, some with hyperchromatic in focal areas, with moderate nuclar atypia. Prominent nucleoli are visible. Immunohistochemical analysis revealed the following: p40 positive, CD5 positive, PAX8 positive and c-KIT positive, TTF1 negative, CD56 negative.
Conclusion: Thymic squamous cell carcinoma is a rare type of cancer, accounting for less than 5% of all thymic tumours. In this case, the immunohistochemical profile was highly suggestive for thymic squamous cell carcinoma. Accurate diagnosis of this entity facilitates further patient management and treatment.

E-PS-26 E-Posters Uropathology

E-PS-26-001
Case report of sperm cell granuloma presenting as a peritoneal nodule: a rare entity
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Background & Objectives: A man in his 30s underwent a reversal of the colostomy procedure. During the surgery a peritoneal nodule was identified and resected for histological assessment.
Methods: The peritoneal nodule measured 12mm in diameter. Histology demonstrated fibroconnective tissue and a population of small-sized cells with hyperchromatic round-to-oval nuclei and scanty cytoplasm which were recognised to be mature spermatozoa. These were associated with a surrounding histiocytic response. The diagnosis of sperm granuloma was made.
Results: Sperm granuloma is a benign condition caused by extravasation of spermatozoa due to vas deferens damage, usually occurring in the epididymis. Sperm granuloma outside of the male reproductive system is very rare and has previously been described in patients with a history of surgery around the urological system.
The underlying aetiology of sperm granuloma development in this patient is unclear. The patient's clinical records revealed a history of previous surgery in the pelvis to correct an inflammatory process which involved the bladder and a suspected fistula formation. Presumably, the inflammation and anatomical distortion have resulted in damage to the vas deferens with subsequent extravasation of spermatozoa into the peritoneum.
Conclusion: Here we present a case of sperm granuloma with an unusual site of presentation as a peritoneal nodule. The diagnosis requires the recognition of mature spermatozoa with surrounding histiocytes, particularly in the setting of previous surgery, inflammation or infection in the proximity of the male reproductive system.

E-PS-26-002

Role of Epithelial-Mesenchymal Transition (EMT) markers SNAIL-SLUG, and TWIST in prognosis of urothelial carcinoma of the bladder: a retrospective study

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Background & Objectives: Bladder cancer, primarily urothelial carcinoma, is a significant global health issue, especially given its high recurrence and poor prognosis. Tumour invasion into the muscularis propria is a crucial prognostic indicator, distinguishing muscle-invasive bladder carcinoma (MIBC) from non-muscle-invasive types (NMIBC). Epithelial-to-mesenchymal transition (EMT) has been implicated in promoting tumour aggressiveness and metastasis, marked by key transcription factors (TFs) like SNAIL, SLUG, and TWIST. This study investigates the association between EMT markers' expression and histopathological features of bladder carcinoma.
Methods: This retrospective study included 36 newly diagnosed cases of urothelial carcinoma at a tertiary care centre. Immunohistochemistry (IHC) was conducted to assess SNAIL-SLUG, and TWIST expression, scored by staining intensity and extent. The statistical analysis evaluated associations between EMT markers, tumour grade, muscle invasion, and clinical stage.
Results: Out of 36 patients, 23 were male, and the age of the patients ranged from 36 to 73 years. Myo-invasive urothelial carcinoma (MIBC) was observed in 21 (58.3%) patients, whereas 15 (41.6%) of them were non-myo-invasive. 80.6% of cases were found to be high-grade invasive urothelial carcinoma. The expression of SNAIL+SLUG showed variable results with 62.1% of the high-grade urothelial carcinoma showing decreased expression. No significant association was observed between them. However, 52.38% of the myo-invasive cases showed an increased expression of SNAIL+SLUG and a strong association was also observed ($p = 0.005$). None of the epithelial-to-mesenchymal transition markers showed an association with lymphovascular invasion.
Conclusion: Increased expression of these transcription markers in advanced stage and grade demonstrates a possible role in identifying the molecular mechanism underlying EMT during urothelial carcinoma pathogenesis. Nuclear expression of SNAIL+SLUG and TWIST in bladder carcinoma was associated with poor outcome indicating the possibility of identifying aggressive lesions.

E-PS-26-003

Collision nodal metastasis of urothelial carcinoma of the bladder and prostatic adenocarcinoma with seminal vesicle involvement

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Background & Objectives: Simultaneous involvement of a lymph node by both urothelial carcinoma and prostatic adenocarcinoma, known as collision metastasis, is an exceptionally rare phenomenon. Additionally, concurrent involvement of the same seminal vesicle by both malignancies is also uncommon, with only a few cases documented in the medical literature. Here, we report the case of a 68-year-old male with a history of T2 high-grade urothelial carcinoma who presented to the hospital with macroscopic haematuria.
Methods: Ultrasonography revealed a thickened bladder wall and a 3 cm tumour mass located in the bladder neck. The prostate measured approximately 40 cm^3. A cystoprostatectomy with bilateral iliac and obturator lymphadenectomy was performed.
Results: Microscopic examination revealed a high-grade urothelial carcinoma extensively infiltrating the bladder wall, predominantly exhibiting a solid growth pattern with areas of squamous and glandular differentiation. It was intricately intermixed with an acinar prostatic adenocarcinoma, which displayed cribriform, trabecular, and solid patterns (Gleason score 9, 4+5). Both the CK7-positive urothelial carcinoma and the PSA-positive prostatic adenocarcinoma invaded the left seminal vesicle. Dual metastases were identified in a left ilio-obturator lymph node, with one component originating from the CK7-positive urothelial carcinoma and the other from the PSA-positive prostatic adenocarcinoma. Additionally, a small component of ductal adenocarcinoma (Gleason score 8, 4+4) with an intraductal growth pattern was present in the prostatic parenchyma.
Conclusion: This case highlights the rare occurrence of collision metastasis, where urothelial carcinoma and prostatic adenocarcinoma metastasized to the same lymph node while simultaneously invading the seminal vesicle. These findings underscore the complexity of diagnosing and managing synchronous genitourinary malignancies. Awareness of such rare presentations is crucial for accurate pathological assessment and appropriate therapeutic strategies.

E-PS-26-004

Secondary hypertension in a young patient: the hidden role of juxtaglomerular cell tumour

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Background & Objectives: Secondary hypertension (SH) is a common condition with multiple underlying causes, the most prevalent being primary aldosteronism. Adrenal gland adenomas and pheochromocytomas are the most frequently suspected tumoral causes, juxtaglomerular cell tumour (JGCT) is a rare but significant differential diagnosis. JGCT is a renin-secreting neoplasm that can lead to hypertension, and surgery is often curative, yet it remains underrecognized due to its rarity.
Methods: We report a challenging case of JGCT in a 29-year-old woman with a five-year history of hypertension, unresponsive to drug therapy, and without prior investigation for secondary causes. Gross examination reveals a well-demarcated brown and yellow tumour measuring 15x15x14mm, confined to the parenchyma. On morphological examination the stroma was prominent with hyalinized areas and rich in vessels displaying variably sized branches, some of them with thick walls. The tumour cells formed groups with an epithelioid pattern, regular nuclei and condensed chromatin, featuring scattered bizarre cells. No mitotic activity or necrosis were observed. Some peripheral entrapped renal tubules were also identified.
Immunohistochymestry (IHC) revealed strong and homogenous positivity for CD34, partial positivity for DOG1, BCL2 and CD99, while ERG, Calponin, Melan-A, HMB45, PAX8, WT1, CK AE1/AE3, Actin, CD31, S100, STAT6 were all negative. There was no loss of INI1 expression.
Results: JGCT is a rare mesenchymal tumour that should be considered in young patients with drug-resistant hypertension. Morphologically angiomyolipoma, solitary fibrous tumour, sarcomas and Nephroblastoma were initially considered, but with help of IHC and clinical features the correct diagnosis was reached.
Conclusion: This case underscores the importance of considering JGCT as a differential diagnosis in patients with unexplained hypertension, particularly in young adults. Raising awareness among clinicians can lead to earlier detection, appropriate surgical management,

and improved patient outcomes. Moreover, nephron-sparing surgery should be prioritized over radical nephrectomy to minimize long-term complications.

E-PS-26-005

An audit of reporting of HPV status in penile squamous cell carcinoma; adherence to current WHO and RCPath dataset recommendations

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Background & Objectives: Penile squamous cell carcinoma (SCC) has an HPV-associated aetiology in up to 50% cases. Both the WHO 2022 and Royal College of Pathologists (RCPath) 2024 guidelines specify that p16 immunohistochemistry should be performed to assess for HPV association, and morphological subtype be stated, with NOS-type reserved only when HPV testing is unavailable. We audited current reporting practices within our department – a supraregional referral centre for penile cancer in the UK – against these recommendations.
Methods: Electronic reports were searched to identify all cases of penile SCC diagnosed at our centre between December 2023- December 2024. The following data was collected: patient age, specimen site, specimen type, morphological subtype of SCC, whether p16 testing and/or HPV genotyping performed, and whether HPV association stated.
Results: 143 cases of penile SCC were diagnosed at our centre within this timeframe. Mean patient age was 69.8 years. 39% (56) cases were resections, (31%) 44 biopsies and 30% (43) excisions. Specimen site was: penis in 46% (66), glans in 37% (53), foreskin in 11% (16), foreskin/glans in 3% (4), glans/corpus cavernosum in 1% (2) and penoscrotal skin in 1% (2) cases. Morphological subtype of SCC was NOS in 52% (74), not stated in 20% (28), mixed subtype in 15% (22), HPV-independent subtype in 7% (10) and HPV-associated subtype in 6% (9) cases. p16 was performed in 90% (129) cases and HPV genotyping in 10% (14) cases. HPV association was reported in 48% (68) cases and HPV independence reported in 34% (49) cases. In 18% (26) cases HPV association was not reported.
Conclusion: Overall there was high compliance with p16 testing at our centre, but efforts should be made to clearly state HPV association in reports and to avoid over-use of the NOS morphological subtype. Recommendations have been made locally, and we plan to re-audit reporting practice at 12 months.

E-PS-26-006

Clinicopathological insights into fumarate hydratase-deficient renal cell carcinoma: a study of 12 Hungarian cases

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Background & Objectives: Fumarate hydratase-deficient renal cell carcinoma (FHd RCC) is a rare and aggressive subtype of renal cell carcinoma. It is characterized by complex histology, biallelic inactivation of the FH gene, frequent loss of FH expression, and accumulation of S-(2-succino)-cysteine (2SC).
Methods: We retrospectively analysed 12 cases of FHd RCC, reviewed by two pathologists (AJa and LK). Clinical data were obtained from electronic records, while pathological features were extracted from histopathology reports.
Results: Ten tumours were identified in nephrectomy specimens (mean size: 91.5 mm; median: 90 mm; range: 23-220 mm), one in a renal mass biopsy, and another in a biopsy of a metastatic infraclavicular lymph node. The cohort included seven males and five females (mean age: 52.8 years; median: 48.5 years; range: 22-78 years). Three female patients had undergone prior hysterectomy for leiomyomas. Histologically, the tumours exhibited eosinophilic cells with high-grade nuclear atypia, predominantly forming a tubulo-papillary pattern. CMV inclusion-like nucleoli were observed in nine cases. FH expression was lost in all but one tumour, and 2SC staining (performed in seven cases) showed strong nuclear and cytoplasmic positivity, including the FH-retained tumour. Genetic analysis (six cases) identified pathogenic FH mutations in all, with one confirmed as germline. Three patients had distant metastases at diagnosis, and five developed metastases during follow-up. Four patients died of cancer-related causes.
Conclusion: FHd RCC is a diagnostic challenge due to its rarity and lack of specific morphology. However, accurate diagnosis is crucial due to its aggressive nature and possible association with hereditary leiomyomatosis and renal cell carcinoma syndrome. We strongly advocate FH and 2SC immunohistochemical testing for all high-grade or large RCCs, particularly in younger patients or those with a history of uterine or cutaneous tumours, suggesting a syndromic link.

Funding: This study was funded by HUN-REN-ONKOL-TTK-HCEMM Oncogenomics Research Group

E-PS-26-007

Inflammatory myofibroblastic tumours of the urinary bladder: 25-year single-centre experience

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Background & Objectives: Inflammatory myofibroblastic tumour (IMT) is a rare mesenchymal tumour, rarely seen in the urinary bladder. We aimed to document our 25-year single-centre experience on the histopathological and immunohistochemical characteristics of IMTs of the urinary bladder.
Methods: A database search was performed on urinary system materials diagnosed as IMT between 2000 and 2025 in our institution. Clinical data, histopathological features, immunohistochemical characteristics and fluorescent in-situ hybridization results were retrieved from archival records.
Results: Among 14 cases, 11 (78%) were male. Mean age was 48.35±14.38 years (median:43, [range: 28-72]). All cases were localized in the urinary bladder and underwent transurethral resection. Seven were consultation cases, among which the primary diagnosis differed in only one. Six (42%) demonstrated atypia and pleomorphism, while none showed necrosis. Three (21%) cases showed infiltration into the muscularis propria. Myxoid stroma was seen in 3 (21%) cases. On immunohistochemical examination, 50% (6/12) showed at least focal expression for anaplastic lymphoma kinase (ALK D5F3), 58% (7/12) for pancytokeratin, 71% (10/14) for smooth muscle actin. Fluorescent in-situ hybridization for ALK gene rearrangement revealed positive in 2 among 3 cases that were analysed. Follow-up data of 9 (64%) patients were available. During a mean follow-up period of 64 ± 70 months (range 1-200), one patient, with muscularis propria invasion, had recurrence after five months.

Conclusion: Inflammatory myofibroblastic tumour is a mesenchymal tumour that should be considered in the differential diagnosis of spindle cell lesions of the urinary bladder. Ancillary tests such as immunohistochemistry and fluorescence in situ hybridization for ALK are helpful in diagnosis.

E-PS-26-008

Biphasic squamoid alveolar renal cell carcinoma: a report of three cases with immunohistochemical and FISH analysis

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Background & Objectives: Biphasic squamoid alveolar renal cell carcinoma (BSARCC) is a recently described rare morphological variant of papillary renal cell carcinoma (PRCC). Due to its rarity, limited data exist regarding its histopathological, immunohistochemical, and molecular features. Herein, we present three cases of BSARCC, aiming to further characterize its clinicopathological profile.
Methods: Immunohistochemistry(IHC) was performed using CK7, PAX8, AMACR, P63, Cyclin D1, and Ki-67. Additionally, MET/CCP7 FISH analysis was conducted to assess chromosomal alterations.
Results: The cohort included two male and one female patient, with a mean age of 63.3 years (range: 59–69). Two cases were partial nephrectomy, one was core biopsy. The mean tumour diameter was 33 mm (range: 25–38). Tumours were well-circumscribed with a whitish or pale yellow appearance.
All cases exhibited a biphasic architecture characterized by nests of larger squamoid cells surrounded by a single layer of smaller cuboidal cells in an alveolar pattern. Emperipolesis was noted in two partial nephrectomy specimens but was absent in the biopsy.
IHC analysis showed diffuse positivity for CK7, AMACR, and PAX8 in both cell populations, while P63 was negative. Cyclin D1 was expressed exclusively in large cells. The Ki-67 index was higher in large cells compared to small cells(5-30% vs. 1%).
FISH analysis revealed chromosome 7 polysomy in all three cases, while MET gene amplification was observed in one case, with no difference between large and small cells.
At a mean follow-up of 26 months (range: 4–68 months), all patients remained alive without evidence of recurrence or metastasis. One patient underwent cryoablation following biopsy and follow-up continues without surgical resection.
Conclusion: Chromosome 7 polysomy links BSARCC to PRCC, reinforcing its classification within the PRCC spectrum. Our findings support BSARCC as a distinct variant of PRCC, with consistent histopathological and immunohistochemical characteristics. Further studies are needed to clarify its molecular pathogenesis and clinical implications.

E-PS-26-009

***CTNNB1* mutations characterize a subset of testicular Adult Granulosa Cell Tumours**

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Background & Objectives: Testicular adult granulosa cell tumour (AGCT) is a rare sex-cord stromal tumour (SCST) that, unlike its ovarian counterpart, rarely harbours *FOXL2 p.Cys134Trp* mutation. Previous analyses of cases originally diagnosed as AGCT have shown that their genomic features are heterogeneous. The aim of this study was to perform genomic analyses on an expanded series of testicular SCSTs diagnosed as AGCTs.
Methods: In total, 15 AGCTs were collected and selected slides were centrally reviewed (Indiana University) to confirm the diagnosis. Cases were analysed using two DNA-NGS panels comprising 34 genes, including those with alterations identified in previous studies of testicular AGCT (i.e. *FOXL2*, *NRAS*, and *TP53*).
Results: NGS was successfully performed in 9/15 (60%) tumours; the remaining 6/15 (40%) did not yield DNA suitable for sequencing. No alterations were found in 6/9 (66.6%) tumours. Three tumours (3/9; 33.3%) harboured *CTNNB1* alterations: *CTNNB1 p.Ser37Phe* (VAF:42%), *CTNNB1 p.Gln322_Trp338delinsArg* (VAF: 54%), and *CTNNB1 p.Gly34Arg* (VAF: 42%). Of note, 2/3 tumours with *CTNNB1* alterations showed a focal tubular architecture, a feature not seen in tumours without *CTNNB1* alterations. No tumours showed *FOXL2* alterations.
Conclusion: The results of this study suggest that a subset of AGCTs exhibit *CTNNB1* alterations, a genomic finding seen in other SCSTs (in particular Sertoli cell tumour, not otherwise specified) and associated with a focal tubular histology. Additionally, this study confirms that testicular AGCTs do not typically harbour *FOXL2* alterations. Further studies with β-catenin immunohistochemistry in selected cases is underway.

E-PS-26-010

GATA3 immunostaining and clear cell renal tumours with fibromyomatous stroma

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Background & Objectives: There are limited number of studies investigating GATA3 expression in renal tumours with fibromyomatous stroma. We aimed to identify the GATA3 expression in carbonic anhydrase 9/cytokeratin 7 positive renal tumours with fibromyomatous stroma and tubulopapillary morphology.
Methods: We retrospectively re-evaluated expressions of GATA3, carbonic anhydrase 9, cytokeratin 7, CD10 and histopathological features of 13 renal tumours with fibromyomatous stroma/tubulopapillary morphology were diagnosed in our centre between 2012-2024 years.

Results: In this series of 13 patients, five patients (39%) were female and eight patients (61%) were male. The mean age of the patients was 55,3 years (range; 30-76 years). According to World Health Organization (WHO) 2022 renal tumours classification systems, eight (61%) tumours were clear cell papillary renal cell tumour (CCPRCT). Three tumours (3/8) showed nuclear reactivity for GATA3 diffusely and four (4/8) tumours stained with CD10 focally. The other five (39%) tumours were morphologically similar to *ELOC* mutant renal cell carcinoma. However, since molecular methods could not be applied, they were classified as "renal cell carcinomas with fibromyomatous stroma (FMS-RCC)". These tumours except one (4/5) tumour were GATA3 diffusely and CD10 focally positive.
Conclusion: According to the 2022 WHO classification, renal tumours with fibromyomatous stroma were classified as "*ELOC* mutated RCC" and "CCPRCT". However, there is no clear consensus on "*TSC/MTOR* mutated FMS-RCC", which has not yet been classified. Our study suggests that GATA3 expression can potentially be used in the differential diagnosis of FMS-RCC. Investigation of GATA-3 expressing fibromyomatous stroma renal tumours using molecular diagnostic methods will allow the classification of new tumour subtypes.

E-PS-26-011
Clinicopathologic and immunohistochemical features of oncocytic and chromophobe renal tumours: a single-centre retrospective study
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Background & Objectives: Oncocytic renal tumours and chromophobe renal cell carcinoma (ChRCC) are low-grade renal neoplasms that often display overlapping histomorphological features. However, they differ significantly in biological behaviour. Oncocytic tumours are typically benign and do not require further treatment after surgical excision, while ChRCC is a malignant tumour with metastatic potential, necessitating distinct clinical management. Immunohistochemistry (IHC) serves as an important adjunct tool in distinguishing between these entities. This study aimed to evaluate the clinicopathologic and immunohistochemical characteristics of renal oncocytic and chromophobe tumours and to analyse their associations with capsule invasion, tumour multiplicity, and survival outcomes.
Methods: We retrospectively reviewed 45 renal tumour cases diagnosed between 2016 and 2021 at Akdeniz University, Türkiye, comprising oncocytic (n=10), hybrid (n=3), and ChRCC (n=32) tumours. Clinical and pathological data were collected. IHC markers (CD117, CK7, CK18, CD10, E-cadherin, AMACR, and Vimentin) were evaluated semi-quantitatively. Statistical analyses were performed using the Chi-square test in SPSS version 28.0.
Results: The mean patient age was 59.3 years (range: 28–80), and 55.6% were male. Most tumours were left-sided (60%), solitary (95.6%), and classified as stage I (91.1%). Capsule invasion was observed in 24.4%, and positive surgical margins in 8.9% of cases. Recurrence occurred in 2 cases, and 3 patients died due to unrelated causes. Common comorbidities included hypertension (40%) and diabetes mellitus (13.3%). CD117 and CK18 were the most frequently expressed markers. While most IHC markers showed no significant association with capsule invasion or multiplicity ($p > 0.05$), AMACR was significantly associated with tumour multiplicity ($p = 0.010$). No correlation was found between IHC profiles and overall survival.
Conclusion: This study highlights the importance of immunohistochemical evaluation in distinguishing oncocytic from chromophobe renal tumours. While AMACR expression may be more frequent in multifocal tumours, further studies with larger cohorts are needed to determine its potential clinical significance.

E-PS-26-012
PD-L1 expression in neuroendocrine urothelial and prostate tumours
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Background & Objectives: Small Cell Neuroendocrine Carcinomas (SCNECs) of the genitourinary tract are rare, with urothelial and prostate being the most common sites. These tumours are often diagnosed at advanced stages, leading to poor prognosis. Recent studies, including a phase 1b trial combining pembrolizumab with platinum-based chemotherapy, have shown promising results for stage III-IV SCNECs. This study aims to summarize the clinicopathological features of SCNECs and assess PD-L1 expression.
Methods: A retrospective study of genitourinary SCNECs at our hospital was conducted over a 10-year period (2015-2025), identifying 7 cases: 5 from the bladder (3 pure, 2 mixed with high-grade urothelial carcinoma) and 2 from the prostate (1 pure, 1 mixed with Gleason 9 acinar adenocarcinoma). PD-L1 expression was independently assessed by two pathologists using the combined positive score (CPS).
Results: The cohort consisted predominantly of men (5/7), with a mean age of 66 years (range 45-78). Four cases were diagnosed at stage IV, 2 at stage III, and 2 at stage II. Five patients received palliative chemotherapy, 1 underwent surgery followed by a clinical trial, and 1 case was monitored closely. Tumour cell PD-L1 positivity was observed with a mean of 0.8% (range 0-3%), while immune cell PD-L1 expression was positive with a mean of 8% (range 0%-25%). CPS scoring revealed PD-L1 positivity in four cases (all bladder-origin), with CPS scores ranging from 1-10, and three cases (1 bladder, 2 prostate) were negative with a CPS score of 0. The highest CPS score (5.2) was observed in the disease-free patient.
Conclusion: This study is the first to evaluate PD-L1 expression in genitourinary SCNECs. While expression varied, bladder-origin tumours showed higher PD-L1 positivity compared to prostate-origin tumours. These findings suggest that bladder-origin SCNECs may benefit from immunotherapy, though larger studies are needed to confirm these results.

E-PS-26-013
When clear cells turn dark: unraveling the aggressive nature of renal cell carcinoma with sarcomatoid differentiation
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Background & Objectives: Renal cell carcinoma (RCC) with sarcomatoid differentiation represents a highly aggressive type of RCC. This study aims to characterize the clinicopathological features and the immunophenotypic profile of clear cell RCC with sarcomatoid differentiation diagnosed in our institution between 2016 and 2024.
Methods: A total of five cases of renal cell carcinoma with sarcomatoid differentiation between January 2016 and December 2024 were retrieved from the pathology archives of Colentina Clinical Hospital. The studied cohort comprised 3 male and 2 female patients. Immunohistochemical analysis was performed using the Leica BOND immunostaining system.
Results: In four of the five cases, the neoplastic process originated within the left kidney. All documented cases exhibited extensive areas of necrotic tissue, indicative of aggressive tumour progression. Immunohistochemically, carbonic anhydrase IX (CA IX) as well as CD10 demonstrated positive staining across all cases, with a patchy

distribution within the sarcomatoid component and a diffuse pattern within the clear cell component. PAX8 expression was absent in the sarcomatoid component across all cases while the clear cell component showed patchy positivity only in two cases. In contrast, cytokeratin 7 (CK7) was negative in four cases across both tumour components, while one case exhibited patchy CK7 positivity within the sarcomatoid component, particularly noteworthy for its marked pleomorphic features.
Conclusion: This findings enhance our understanding of the clinicopathological characteristics and immunophenotypic profile of this phenomenon. The different expression patterns of CA IX, CD10, PAX8 and CK7 highlight the distinct phenotypic divergence between the clear cell and sarcomatoid component. Such insights hold importance especially in metastasis wherein the renal origin remains ambiguous or in instances where the clear cell constituent presents atypical features.

E-PS-26-014
Renal hydatid cyst: diagnostic and treatment considerations
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Background & Objectives: A renal hydatid cyst is a rare parasitic infection of the kidney caused by *Echinococcus granulosus* or *Echinococcus multilocularis*. It develops when hydatid larvae reach the kidney, forming fluid-filled cysts. Symptoms vary and may include flank pain, haematuria, or a palpable mass. Rupture can lead to severe complications such as anaphylactic shock or secondary infection. Diagnosis relies on imaging techniques (ultrasound, CT, MRI) and serological tests. Treatment options include surgery (partial or total nephrectomy), percutaneous drainage, and antiparasitic therapy with albendazole.
Methods: We report a case of a 40-year-old woman who presented to the Urology Department with a large multilocular tumour mass in the right kidney. The tumour was located at the lower pole of the kidney, extending into the renal sinus and protruding beyond the renal contour. It appeared heterogeneous on imaging, with fluid densities, septa, and microcalcifications. The CT findings suggested either a multilocular cystic nephroma or a multilocular cystic renal carcinoma.
Results: Gross examination of the nephrectomy specimen (14 × 9 × 6 cm) revealed a multilocular cystic cavity at the lower renal pole, containing multiple smaller cysts filled with citrine fluid. Histological analysis showed a multilocular cystic structure surrounded by a hyalinized and partially calcified fibrous pseudocapsule. A peripheral inflammatory response consisting of lymphoplasmacytes, histiocytes, and eosinophils was observed. Inside the cyst, multiple eosinophilic, acellular lamellar membranes with a distinct proliferative layer were present, along with ovoid structures resembling protoscolices, findings characteristic of a hydatid cyst.
Conclusion: This case underscores the rare presentation of renal hydatid cysts and emphasizes the importance of early diagnosis to prevent severe complications such as rupture or infection. Accurate identification through imaging and serological tests is crucial, and timely treatment significantly improves patient outcomes.

E-PS-26-015
Applications of 12p *Fluorescence in situ hybridization* (FISH) in testicular germ cell tumours (TGCTs)
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Background & Objectives: Gains of the short arm of chromosome 12 (12p), often in the form of isochromosome 12p (i12p), are considered hallmarks of postpubertal-type GCNIS-derived TGCTs, being diagnostically useful. FISH is commonly used for detecting 12p gains. We aimed to review TCGT cases where this FISH assay was ordered and its diagnostic purpose.
Methods: All TGCT cases where 12p FISH was ordered in our institution between 2021 and 2024 were retrieved. Clinicopathological data and cytogenetic test results were collected.
Results: Our study included nine patients. The most frequent reason was for supporting the diagnosis of prepubertal-type teratoma (n=4) by showing absence of gains in 12p, which were diagnosed after puberty, in patients aged 20 to 28 years.
Two cases were ordered to support a diagnosis of somatic-type malignancy in the metastatic setting. One was a 47-year-old patient presenting with a retroperitoneal mass adherent to the duodenum, initially suspected to be a gastrointestinal-tract tumour. Confirmation of i12p, together with a personal history of a TGCT >20 years previously, confirmed the diagnosis of somatic-type adenocarcinoma arising from a TGCT.
The second was a 30-year-old patient presenting with a large retroperitoneal mass, mostly composed of carcinoma with solid and glandular pattern and unspecific immunophenotype, adjacent to teratoma foci. The detection of i12p led to investigation of the testis, which showed features of regressed TGCT with postpubertal-type teratoma.
The remaining three cases corresponded to spermatocytic tumours, with absence of 12p, in patients aged 36, 41 and 62.
Conclusion: The 12p FISH can be useful in three main settings: for the differential diagnosis between prepubertal-type and postpubertal-type teratoma, considering that both could occur at post-pubertal age; for supporting the diagnosis of spermatocytic tumour, which can occur at a wide age range; and for supporting the diagnosis of somatic-type malignancy arising in TGCT, especially at metastatic sites with limited clinical history.

E-PS-26-016
SMARCB1-deficient medullary-like renal cell carcinoma: report of two cases with emphasis on morphological spectrum and differential diagnosis
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Background & Objectives: SMARCB1-deficient medullary renal cell carcinoma (RCC) is a very rare and aggressive tumour, considered within the group of molecularly defined RCC. It represents <0.5% of RCCs and often presents in patients with sickle cell trait. Even rarer, some tumours occur in patients without haemoglobinopathies, being considered SMARCB1-deficient medullary-like RCC. We reviewed two patients diagnosed at out institution.
Methods: Patient A (PtA) presented with a 9.3cm right renal mass, with extensive necrosis. The patient underwent a radical nephrectomy 5 months later. Patient B (PtB) presented with lumbar pain and haematuria and a 15cm right renal mass.
Results: Both showed a high-grade carcinoma with infiltrative features, invading peri-renal tissues and renal hilum, with extensive lymphovascular invasion, high mitotic index and necrosis. PtA showed a tumour with tubulo-papillary to solid architecture, raising the hypothesis of papillary RCC or MiTF-family RCC. PtB showed a mostly solid and poorly-differentiated tumour, with both epithelioid and spindle cell areas, which in some foci raised differential diagnosis of a small round cell tumour. The tumours were PAX8+, cytokeratin+, FH/SDHB/SMARCA4 retained, OCT3/4-, ALK-. FISH for TFE3/TFEB/gains in 7/17 were negative. FISH for EWSR1/CIC/SS18 in PtB were negative. Both tumours had complete loss of INI1

immunoexpression. DNA/RNA were extracted from both tumours, and NGS studies revealed no fusions and presence of SMARCB1 pathogenic variants as the single alteration.
Despite systemic therapy, both patients died at 1.5years and 8months post-resection with metastatic disease.
Conclusion: SMARCB1-deficient RCC with medullary-like features is a rare entity which lacks association with haemoglobinopathy. It can have variable morphological resemblance to "classical" SMARCB1-deficient medullary RCC, being often poorly differentiated and raising several differential diagnoses, but shows a similar INI1 loss and poor clinical behaviour.

E-PS-26-017
Langerhans cell histiocytosis in renal cell carcinomas: a multicentre case series
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Background & Objectives: Langerhans cell histiocytosis (LCH) is a rare neoplasm characterized by neoplastic Langerhans cells intermixed with reactive mononuclear cells and granulocytes, particularly eosinophils. LCH can be associated with non-hematologic neoplasms. This study compiles cases from three hospitals to describe the clinicopathological and molecular features of renal cell carcinomas (RCC) with LCH.
Methods: A retrospective, multicentre study including five cases of renal tumours with a Langerhans cell component.
Results: All patients were male, with a mean age of 61 years (range: 50–70). All cases presented as well-defined solid lesions, with a mean tumour size of 4.26 cm (range: 2–6.5 cm). Most (4/5) were clear cell RCC (ISUP grade 2 [3/4], grade 3 [1/4]), including one collision tumour with papillary RCC (ISUP grade 3). One case (1/5) was high-grade RCC with rhabdoid transformation (ISUP grade 4). The histiocytic component demonstrated epithelioid histiocytes (4/5), eosinophilic cytoplasm (5/5), histiocytes with prominent nucleoli (4/5), multinucleated giant cells (1/5), and eosinophilic infiltration (5/5). Immunohistochemistry showed positivity for CD68 (4/4), S100 (3/3), CD1a (3/4), Langerin (2/2), and Cyclin D1 (1/1). BRAF V600E mutation was detected in all tested cases (2/2). None of the three assessed patients had systemic histiocytosis, though one had monoclonal gammopathy of undetermined significance (MGUS). Another patient is pending systemic evaluation.
Conclusion: Recognizing LCH in renal neoplasms poses a diagnostic challenge, as these cells may be misinterpreted as part of the renal tumour, potentially leading to overestimation of grade and impacting prognosis. Eosinophils may serve as a diagnostic clue. Immunohistochemical or molecular testing for BRAF V600E helps confirm diagnosis. While our cases were renal-limited, systemic disease has been reported, highlighting the need for further evaluation.

E-PS-26-018
***FGFR3* and *PIK3CA* mutations in non-muscle invasive bladder cancer: novel variants and prognostic value**
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Background & Objectives: Urothelial bladder cancer is a prevalent urological malignancy, particularly among Tunisian men. Non-muscle invasive bladder cancer (NMIBC) is characterized by heterogeneity and variable recurrence/progression risks. *FGFR3* and *PIK3CA* mutations are frequent in NMIBC. This study aimed to identify *FGFR3* and *PIK3CA* mutations in NMIBC and evaluate them with clinicopathological features.
Methods: Clinicopathological data from 42 NMIBC cases from the pathology department at Charles Nicolle Hospital (Tunis, Tunisia) were analysed. *FGFR3* (exons 7, 15) and *PIK3CA* (exon 9) hotspot regions were sequenced using Sanger sequencing.
Results: Cases were equally distributed between pTa and pT1 stages (50% each; pT1 substaged as pT1a [n = 4 (19%)] and pT1b [n = 17 (31%)]). Carcinoma in situ (CIS) was present in 3 cases (7%) of pT1 tumours. Thirteen distinct FGFR3 variants were identified in exon 7, including eight known (S249C, P250R, P250S, H251Q, S249S, S249Y, S249A, T264T) and five novel mutations (P250A, H251L, A257S, P253P, I254V). S249C was the most frequent alteration, observed in 22 cases (85% of FGFR3-mutated cases). FGFR3 mutations were found in 26 cases (68%) and correlated with tumour stage ($p = 0.03$).
Conclusion: *FGFR3* and *PIK3CA* molecular testing may complement cystoscopy and urinary cytology for NMIBC prognosis. Novel *FGFR3* mutations and their association with tumour stage suggest their potential as prognosis biomarkers. Further studies are needed to validate these findings.

E-PS-26-019
HPV-induced penile squamous cell carcinoma with subsequent CDKN2A (P16) deletion
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Background & Objectives: The WHO classification of tumours currently recommends stratifying penile squamous cell carcinoma (pSCC) by HPV status. Studies investigating clinicopathologic and prognostic differences variably define HPV status by P16 immunohistochemistry (IHC) and/or HPV viral detection (e.g. polymerase chain reaction-restriction fragment length polymorphism [PCR-RFLP], in situ hybridization [ISH]). We present a case of P16-positive HPV-induced pSCC with subsequent loss of P16 protein expression secondary to biallelic inactivation of *CDKN2A*.
Methods: A patient with pSCC was seen at our institution, and all specimens (initial biopsy, penectomy and recurrence biopsy) were evaluated by HPV ISH, PCR-RFLP, P16 IHC, and next-generation sequencing (NGS).
Results: A 70-year-old man initially presented with gross haematuria and a groin mass. Cystoscopy revealed a papillary neoplasm arising from the distal penile urethra, and biopsy confirmed an invasive keratinizing squamous cell carcinoma. This initial biopsy was block-positive for P16 by IHC, positive for high-risk HPV by ISH, and positive for HPV subtype 16 by PCR-RFLP. He subsequently underwent partial penectomy and immune checkpoint inhibitor therapy. Unfortunately, his disease progressed, and repeat biopsy 5 months after surgery demonstrated pSCC with positive HPV ISH but negative P16 IHC. Genomic testing of the penectomy and post-penectomy biopsy revealed a homozygous *CDKN2A* deletion, explaining the acquired loss of P16 expression.
Conclusion: To our knowledge, this is the first case of HPV-induced pSCC with subsequent P16-loss reported in the literature. This case underscores the complexity of pSCC pathogenesis and the limitations of P16 as a surrogate for HPV status.

E-PS-26-021
Relevance of Von Hippel Lindau protein (pVHL) expression in biological behaviour of renal cell carcinomas in Indian subcontinent
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Background & Objectives: Von Hippel Lindau (VHL) is tumour suppressor gene; alterations in gene product (pVHL) of which leads to development of Renal Cell Carcinoma (RCC). pVHL functions through transcription dependent nuclear-cytoplasmic trafficking for it's action. Present study is an aim to evaluate and correlate the frequency of pVHL expression with Renal Carcinoma subtypes, grades and stages.
Methods: Total 78 cases of RCC which included three subtypes viz. clear cell, papillary and Chromophobe were analysed for pVHL expression using polyclonal antibody to pVHL (pVHL30/ pVHL19). Age of the patients varied from 50 to70 years with mean age of 54.5±12 years. Of these 70 cases expressed positivity. Among these 55,11 and 04 were clear cell, papillary and Chromophobe respectively. Stage wise distribution of these cases was as 44% (I),28% (II),18% (III)and10% (IV).
Results: pVHL expression across tumour cells was predominantly nucleo-cytoplasmic (83%) followed by exclusive cytoplasmic (11%) and nuclear(06%) expressions. TNM staging wise, exclusive nuclear expression was confined to early stages (I and II) only, whereas cytoplasmic exclusivity showed a predominant predilection for advanced stages viz. 23% and29% for stages III and IV as against 6% in early stages (I and II). Nucleo-cytoplasmic expression also was skewed towards early stages (84%) as compared to locally metastatic(77%) and advanced metastatic(71%) stages. Fuhrman's nuclear grading in clear cell RCC cases too accounted for all the exclusive nuclear positive pVHL expression in grade I while the cytoplasmic alone expressive pVHL cases shared60% of grade IV labelled carcinomas. Statistical significance was achieved for most of the results.
Conclusion: To conclude, the results emphasize that VHL gene mutations leading to structural alterations in pVHL have significant relevance in biological profile of Renal Cell Carcinomas.

E-PS-26-022
Renal metastasis of sinonasal adenoid cystic carcinoma: a case report
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Background & Objectives: Adenoid cystic carcinoma (ACC) is a malignant epithelial tumour which arises from salivary glands. They can present with metastases many years after the initial resection. We describe the clinical, radiological and morphologic features of a case of a patient with sinonasal ACC with metastasis to the kidney. Renal metastasis of ACC is uncommon and presents diagnostic challenges. Histological examination is key in confirming the diagnosis and excluding a primary renal tumour.
Methods: A 54-year-old female had previous sinonasal ACC, treated with resection and adjuvant radiotherapy. She presented with epistaxis 8 years later and was diagnosed with local recurrence of the tumour. Imaging revealed a tumour within the left kidney, with no other evidence of distant metastases. The tumour was hypo-enhancing on the arterial phase, with progressive enhancement on the portovenous phase. The radiological impression was that of papillary renal cell carcinoma. The patient opted for resection of the local tumour recurrence and surveillance for the kidney tumour. Surveillance imaging subsequently showed interval growth of the left kidney tumour and a radical nephrectomy was performed.
Results: The kidney contained a 6.0 cm tan-white tumour at the interpolar region. Microscopically, the tumour had a biphasic appearance, comprising basaloid luminal cells and clear abluminal cells with surrounding basement membrane material. On immunohistochemical staining, the luminal cells were positive for CD117, while the abluminal cells were positive for p40. The histologic features were those of ACC.
Conclusion: The clinical-radiological features of renal metastasis may resemble a primary renal tumour. Increased venous enhancement during a contrasted CT study has been suggested as a finding that favours metastasis over a primary renal tumour. The radiological features in our case support this observation.

E-PS-26-024
Next-generation sequencing (NGS) and PD-L1 immunohistochemistry in plasmacytoid urothelial carcinoma of the urinary bladder: a single institution experience
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Background & Objectives: Plasmacytoid urothelial carcinoma (PUC) of the urinary bladder is an aggressive urothelial carcinoma subtype characterized by single infiltrating cells with plasmacytoid appearance, and somatic CDH1 mutations leading to loss of E-cadherin expression. This variant has been previously described in limited case series and thus warrants further investigation.
Methods: 32 cases with this diagnosis and slides available for review were found in our pathology archives from 2018-2024. Next-generation sequencing (NGS) data were available in 18 cases, and PD-L1 immunohistochemistry in all 32 cases. Both tumour proportion score (TPS) and combined positive score (CPS) were calculated for PD-L1. Survival analysis was performed using Kaplan-Meier method and log-rank test.
Results: Median patient age was 72.5 years (IQR: 64.3-78.8). The cohort consisted predominantly of males (29/32, 91%). 25 patients (78%) underwent radical cystectomy (RC), while 7 (22%) had transurethral resection. Median tumour size was 5.2 cm (IQR: 3.6-8.0). Most RCs (22/25, 88%) were high-stage (pT3-4). Lymph node dissection was performed in 23/25 RCs, and of those 12 (52%) were pN1-2. Lymphovascular invasion was identified in 22/25 RCs (88%). 17/32 cases (53%) showed a PD-L1 TPS≥1% (6/17 received immune-checkpoint inhibitors – ICIs), while 21/32 (66%) exhibited a CPS≥1% (8/21 received ICIs). Recurrently mutated genes included TP53, TERT, RB1, CREBBP, and ERBB2, among others; our NGS panel does not cover CDH1. Most frequent copy number alterations were losses of RB1, CDKN2A, and CDKN1B. Median tumour mutational burden (TMB) was 10.3 mut/Mb (IQR 5.4-15.73). Median overall survival (OS) was 13.0 months (95% CI: 4.2-21.8). There was a trend for superior OS among patients with PD-L1 expression.
Conclusion: Our study shows that PUCs frequently feature a high TMB and/or PD-L1 expression, suggesting a potential for intervention with ICIs. Additionally, there is a strong rationale for NGS testing as actionable mutations are frequently present, including ERBB2 mutations.

E-PS-26-025
Collision metastasis of urothelial carcinoma and neuroendocrine tumour to para-aortic lymph node: a case report
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Background & Objectives: Collision tumours involve the simultaneous presence of two distinct malignant neoplasms. In nodal metastasis, this refers to the occurrence of metastatic deposits from two separate primary tumours within the same lymph node, a rare phenomenon. We present a case of collision metastasis in para-aortic lymph node, involving urothelial carcinoma of the renal pelvis and a neuroendocrine tumour from the small intestine.
Methods: A 63-year-old female with a history of high-grade urothelial carcinoma of the renal pelvis and well-differentiated neuroendocrine tumour of the small bowel (status post right nephroureterectomy and small bowel resection). Approximately one year after the operation, the patient presented with bilateral leg oedema and

abdominal/groin pain. A CT scan revealed a 3.6 x 6.1 cm conglomerate paraaortic lymph node, which was biopsied.
Microscopic examination of the biopsy revealed two distinct populations of epithelioid cells:
• Urothelial Carcinoma Component: Atypical cells with hyperchromatic, irregular nuclei and large cytoplasm, resembling the previously resected urothelial carcinoma.
◦ Immunohistochemistry: GATA-3 (+), p40 (+), CK7 (+), CK20(+), CK-pan (+)
• Neuroendocrine Tumour Component: Small, round cells with pink cytoplasm and speckled "salt-and-pepper" nuclei arranged in nests, similar to the previous neuroendocrine tumour from the small bowel resection.
◦ Immunohistochemistry: CK-pan (+), Synaptophysin(+), Chromogranin(+)
Results: The needle biopsy showed a collision of high-grade urothelial carcinoma and well-differentiated neuroendocrine tumour infiltrating fibrous tissue, with findings that were morphologically and immunohistochemically consistent with previous resected primary tumours.
Conclusion: In conclusion, collision metastases involve the co-occurrence of metastatic deposits from different primary tumours within the same lymph node. Accurate diagnosis requires close clinical-pathology correlation and detailed histologic examination to differentiate the individual tumour components. The recognition of collision tumours is crucial, as the individual components may necessitate different treatment strategies. Awareness of collision tumours is essential to ensure comprehensive evaluation of patients with multiple cancer diagnoses, appropriate management, and optimized patient outcomes.

E-PS-26-026
Machine learning-based integration of transcriptome and digital pathology for predicting chemoresistance in muscle-invasive bladder cancer
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Background & Objectives: Muscle invasive bladder cancer (MIBC) presents with variable clinical and pathological features, leading to inconsistent responses to standard treatments such as neoadjuvant chemotherapy (NAC). Although transcriptome profiling has shown differences in NAC response, reliable predictors of treatment outcome remain elusive.
Methods: Machine learning workflows analysed transcriptome data from four independent cohorts (n=376) to extract molecular classifiers associated with the response to NAC. Spatial protein expression was assessed by computational pathology using two in-house cohorts (n=91). The digital pathology datasets, encompassing 74 protein markers, were further interrogated using deep learning models to identify an optimal antibody panel for immunohistochemistry (IHC)-based diagnostics. Survival outcomes were assessed through computational pathology-driven prediction modelling. Functional assays evaluating gene expression, cell proliferation, and apoptosis were conducted to elucidate the role of the KEAP1/NRF2 pathway on modulating chemoresistance in MIBC.
Results: The machine learning analysis of multi-cohort transcriptome datasets, incorporating diverse gene classifiers, uncovered key molecular features associated with NAC response, which highlighted key genes involved in stress, immune responses, and cell adhesion. The clinical relevance of these markers was validated by digital pathology for analysing spatial protein expression. The machine learning frameworks reduced complex digital pathology datasets to a clinically manageable number of biomarkers for IHC-based diagnostic or therapeutic applications. Computational pathology-driven predictions of NAC response demonstrated a strong correlation with survival outcomes in MIBC patients, highlighting their potential clinical utility. Furthermore, targeting KEAP1 resensitized MIBC cells to cisplatin, highlighting a potential therapeutic approach for overcoming chemoresistance and enhancing treatment efficacy.
Conclusion: This study improves the predictive power of the NAC response by integrating machine learning-based transcriptome profiling to refine gene classifiers and applying digital pathology analysis to increase clinical relevance. This approach advances precision medicine in MIBC by offering a more personalized, predictive, and feasible framework for treatment decision-making.

Funding: This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (Ministry of Science and ICT) (RS-2024-00422023) and by grants (2023IP0034) from the Asan Institute for Life Sciences, AMC, Seoul, Korea

E-PS-26-027
Osseous metaplasia in kidneys
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Background & Objectives: Osseous metaplasia (OM) in kidneys is a relatively rare finding, which has only a few research studies, with less than 50 reported cases in English literature.
The objective of this study was to investigate the prevalence of OM in kidneys or parts of kidneys removed for any reason between 2020 and 2024 in one laboratory.
Methods: Routine pathological reports from partial or total nephrectomy, conducted for various reasons, were retrospectively evaluated for mentions of OM. These reports included side, patient's age, sex and for tumours: size, tumour type (WHO classification), pTNM classification and histological grade (WHO/ISUP).
Results: 44 cases of OM were detected:
- 40 in tumours (main mass or capsule),
- 4 outside of tumours (renal pelvis, wall of simple renal cyst, perirenal adipose tissue and renal blood vessel), but each of them occurred within a kidney, which contains neoplasm (2 papillary renal cell carcinoma, 2 urothelial neoplasm).

The sex distribution included 16 females and 28 males in scope of report.
The arithmetic mean patient's age was 65 (range of age 41-82).
Histological types of tumours were: 37 renal cell carcinomas /RCC/ (34 clear cell /CCRCC/, 2 chromophobe, 1 papillary /PRCC/) and 3 oncocytomas.
The mean tumour size was 5,2cm (1,7cm – 13cm).
In RCC distribution according to TNM classification was: pT1 - 22 (pT1a - 11 , pT1b - 11), pT2b – 1, pT3a - 14.
Histological grade (CCRCC and PRCC) was: G1– 8, G2– 19, G3– 6, G4- 2 (1 with rhabdoid features, 1 with sarcomatoid features).
5 tumours contained necrosis (1-30%).
There was no confirmed case of OM in the kidney removed due to non-tumour conditions.
Conclusion: OM in the kidney occurred within benign and malignant renal neoplasms as well as it was detected outside of renal tumours.

E-PS-26-028

A pleomorphic rhabdomyosarcoma, arising from spermatic cord

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Background & Objectives: Rhabdomyosarcoma is a malignant tumour of mesenchymal origin. Pleomorphic rhabdomyosarcoma is an uncommon subtype that affects older adults and is characterized by aggressive behaviour and poor prognosis. Spermatic cord tumours are rare and rhabdomyosarcomas arising from spermatic cord are extremely uncommon. Here we present a case of a 76 year old male diagnosed with pleomorphic rhabdomyosarcoma of the spermatic cord.
Methods: A 76 year old male presented to the emergency department with left inguinal pain, swelling for one year along with elevated Beta-HCG. Physical examination revealed a firm, non-testicular 9 x 5 cm mass extending into the scrotum without overlying skin changes. Imaging studies including MRI pelvis, ultrasound of the testis and CT abdomen-pelvis identified a suspicious mass in the left inguinal soft tissue raising suspicion for a spermatic cord tumour. The patient underwent left radical orchiectomy.
Results: Gross examination of the specimen revealed a 9 x 5.3 cm tan white tumour with areas of necrosis and haemorrhage. Microscopic evaluation showed sheets of high grade malignant cells with abundant atypical mitosis, necrosis, spindle cell morphology and plasmacytoid features. The adjacent testis was uninvolved. Immunohistochemistry demonstrated diffuse desmin positivity, weak focal positivity for SMA and MYOD1 and negativity for epithelial, melanocytic and vascular markers. A diagnosis of pleomorphic rhabdomyosarcoma was made. After multi disciplinary meeting discussion no chemotherapy was required, the patient is being followed and is doing well.
Conclusion: Paratesticular rhabdomyosarcoma can occur at any age. Histopathology and immunohistochemistry play a crucial role in distinguishing it from other paratesticular tumours. In our patient aggressive surgical management was the mainstay of treatment.

E-PS-26-029

Mesothelioma of the tunica vaginalis: report of a rare entity and lights on differential diagnosis from 5th WHO classification of urinary and male genital tumours

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Background & Objectives: Mesothelioma of the tunica vaginalis (MVT) is rare, with less than 300 cases reported since the first description in 1957. It accounts for less than 1% of pleural and peritoneal mesotheliomas and of testicular neoplasms.
In Italy, the mean standardized incidence rate of MTVT is 0.095 per million person-years, with a peak incidence in the sixth decade.
Herein we report a rare case of mesothelioma of the tunica vaginalis with immunohistochemical and molecular assessment.
Methods: An 83-year-old patient, with no history of trauma came to our urological unit in January 2024, for left testicular swelling.
He worked as a railway station systems technician.
Clinically the mass resembled a cyst and a routinary ultrasound was performed. Results were consistent with a cyst with associated thin papillary projections on tunica vaginalis.
The patient underwent orchiectomy.
Results: Macroscopically, the tunica vaginalis was covered by multiple white thin papillae, measuring from 2 to 0,1 cm. Testicular parenchyma did not present macroscopical alterations.
Microscopically, a proliferation of epithelioid elements with marked atypia and pleomorphism covered tunica vaginalis, forming papillae and pseudoglandular structures, with invasive foci.
Psammomatous bodies were present. Necrosis was absent.
Atypical cells expressed calretinin, WT1, CK5/6, BAP1 (pathcy) and were negative for BEREP4, CEA, CK20 and ER.
Molecular test showed deletion of CDKN2A in 30% of cells (cut off 15%) with FISH.
For all these features, a diagnosis of epithelioid MVT was made.
Conclusion: MVT is rare and aggressive, with no AJCC/IUCC classification nor standard treatment available.
The diagnosis is challenging, as it must be distinguished from other mesothelial lesions (well-differentiated papillary mesothelial tumour), ovarian type epithelial tumours, tumour originated from the collecting duct and rete testis and metastases.
A combination of immunohistochemistry and FISH analysis showing deletion of CDKN2A is mandatory.

E-PS-26-030

Coexistence of low-grade oncocytic tumour (LOT) and multifocal angiomyolipomas: a unique case report

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Background & Objectives: LOT is an emerging renal neoplasm recently delineated in the 2022 WHO classification as part of a heterogeneous group of oncocytic tumours not fitting into conventional categories. LOT characteristically shows diffuse CK7 positivity, absent CD117 expression, and frequently harbours mutations in mTOR pathway genes. In addition, angiomyolipomas (AMLs) – tumours that may be associated with tuberous sclerosis complex (TSC) – often display similar mTOR dysregulation. We report a unique case of a 61-year-old male that combines LOT with multifocal AML foci in radical nephrectomy specimen, raising strong suspicion for an underlying TSC/mTOR-driven pathology.
Methods: The patient presented with urinary symptoms and imaging studies identified a left renal mass and incidental hepatic AML. The radical nephrectomy specimen underwent thorough gross and microscopic examination. Immunohistochemical studies were performed to distinguish LOT from other oncocytic renal tumours and to characterize the AML components.
Results: Gross examination revealed a well-circumscribed, cream-colored tumour measuring 5.2 cm in the upper pole of the kidney, with cystic and haemorrhagic areas. Histologically, the lesion exhibited uniform low-grade nuclei eosinophilic voluminous cytoplasm, a solid nested architecture, and a prominent perinuclear halo – features consistent with LOT. Immunohistochemistry confirmed diffuse CK7 and PAX8 positivity and lack of CD117 expression. In addition, random sampling of the apparently normal renal parenchyma uncovered multiple, scattered AML foci (largest 1.5 cm) that displayed a classic triphasic pattern and robust expression of melanocytic markers (HMB45, MelanA, Cathepsin K) alongside SMA positivity.
Conclusion: This case illustrates the rare coexistence of LOT and multifocal AML, suggesting a shared TSC/mTOR-driven molecular basis. Despite the patient's demise due to non-neoplastic causes precluding genetic consultation, the morphological and immunohistochemical findings align with literature implicating mTOR pathway dysregulation and underscore the importance of considering TSC. Recognizing this association may have significant implications for genetic counselling and potential targeted therapeutic strategies.

E-PS-26-031

Metanephric stromal tumour of the kidney: a case presentation

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Background & Objectives: Metanephric stromal tumour (MST) is a rare, benign renal tumour found primarily in children, typically diagnosed at the average age of around 2 years. It's very uncommon in adults, which can complicate diagnosis.

Methods: A 23-year-old male noticed right abdominal enlargement and underwent an ultrasound, which revealed a space-occupying lesion in the right kidney. A contrast-enhanced CT scan showed a large lesion in the right kidney with right-sided hydronephrosis. The patient underwent right radical nephrectomy.

Results: On gross examination was presented the kidney weighed 3024g and measured 22x20x15 cm, with most of it replaced by tumour mass (18x21x14 cm). Macroscopically the tumour was grayish-pink, flabby, and solid-cystic, with predominant solid components and smooth-walled cysts (0.5 to 4.5 cm) containing yellowish fluid. The renal pelvis was compressed but not infiltrated. On microscopic examination the tumour was mainly spindle-shaped, with monomorphic cells forming multidirectional bundles around stromal vessels. There were minimal fat components, pronounced degenerative changes (sclerosis, necrosis), and unlined cysts. The mitotic count was 1 per 10 hpf. No infiltrative growth into the renal capsule or pelvis was noted, and the tumour's morphology resembled angiomyolipoma. Immunohistochemical results revealed negative status of tumour cells for PanCK, Desmin, SMM, S100, MelanA, HMB45, and CD99. CD34 showed focal expression in spindle cells around vessels and renal tubules. The patient was diagnosed with metanephric stromal tumour, and molecular testing for BRAF p.V600E was recommended.

Conclusion: Surgery is the main treatment for MST, with preoperative diagnosis often requiring differentiation from other renal conditions. While CT, ultrasonography, and CEUS are commonly used, recent studies suggest BRAF mutation detection may provide a valuable diagnostic tool. MST is primarily diagnosed through exclusion, with imaging techniques playing a crucial role in distinguishing it from other renal tumours.

E-PS-26-033

A primary well-differentiated neuroendocrine tumour of the bladder in a young male: a case report of a rare entity

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Background & Objectives: Neuroendocrine neoplasms are a diverse group of tumours that can arise in any organ system. They are much rarer in the genitourinary (GU) system, constituting around 1% of bladder neoplasms, with the least common subtypes is well differentiated neuroendocrine tumour (NET). We present a case of a young man, presenting with hypertension and renal impairment who was diagnosed with a primary well- differentiated NET of the bladder.

Methods: A 29- year-old man underwent an USS KUB to investigate symptoms of hypertension and renal impairment. Further CT and MRI imaging showed an organ- confined bladder tumour with no nodal disease or distant metastasis. A transurethral resection of the bladder tumour (TURBT) was performed.

Results: Microscopically, the initial TURBT showed a tumour consisting of bland, monotonous cells with mild nuclear pleomorphism and speckled chromatin with scarce mitoses. Immunohistochemistry was positive for AE1/AE3, synaptophysin, CD56 and chromogranin A but negative for NKX3.1 and GATA3. Ki67 labelling index was low (5-10%). This was consistent with a well- differentiated NET. Correlation with clinical and radiological findings were recommended to exclude metastases from elsewhere before considering the rare primary bladder origin. Following his initial diagnosis, the patient underwent a partial cysto-prostatectomy with ureteric reimplantation. Analysis of the resected specimen concurred with that of the initial TURBT with a diagnosis of a grade 2 well- differentiated NET of the bladder.

Conclusion: A range of neuroendocrine neoplasms have been described in the GU tract including large and small cell carcinomas, paragangliomas and well- differentiated NET. The latter is exceedingly rare in the bladder, with fewer than 30 having been described in the literature. These tumours share architectural and cytological features with similar tumours from other sites. Metastases to other organs has been known. Given its rarity, there is no current standard of care for patients presenting with these tumours.

E-PS-26-034

Association of intertubular growth pattern with prognosis and prognostic parameters in pure seminomas

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Background & Objectives: Testicular cancers are the most common solid neoplasms among young adults aged 20–40, with germ cell tumours accounting for approximately 95% of cases. About 55–60% of germ cell tumours are pure seminomas. Intertubular seminoma(ITS) is an entity that has been described in recent years, and its prognostic significance remains not fully established.

Methods: 81 patients diagnosed with stage 1 seminoma between 2007 and 2023 were identified at Dokuz Eylül University Hospital. Haematoxylin and eosin (H&E) stained slides of these patients were examined for the presence of ITS and other prognostic parameters.

Results: The median patient age was 33, and the median tumour size was 45 mm. The presence of an intertubular pattern was significantly associated with younger age($p=0.025$), smaller tumour size($p=0.009$), necrosis($p=0.001$), intratubular pattern ($p=0.014$), and rete testis invasion ($p<0.001$). In multivariate logistic regression, only rete testis invasion remained an independent predictor of intertubular pattern. Tumour size was not significantly associated with rete testis invasion ($p=0.163$), and no significant associations were found with vascular invasion or tumour localization. The distance between the main tumour mass and an ITS focus, measured in high power fields (HPFs), was inversely correlated with tumour size (Spearman $\rho=-0.35$, $p=0.033$). ITS were observed in association with germ cell neoplasia in situ (GCNIS) and/or tubular atrophy in 27/37 cases, with seminiferous tubules showing normal spermatogenesis in 3/37 cases, and with both ITGCN-positive and histologically normal tubules in 7/37 cases.

Conclusion: It is not yet clear whether ITS is associated with a more aggressive course; however, the presence of rete testis invasion should be considered in terms of the disease's potential for spread. The association of ITS with GCNIS and tubular atrophy may provide insights into the tumour's development process. Further research is needed to determine whether ITS can be used as a biological marker in early-stage seminomas.

E-PS-26-036

Recurrent clear cell adenocarcinoma in the urethral diverticulum: a case report

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Background & Objectives: We report a case of recurrent clear cell adenocarcinoma (CCA) in the urethra following an initial occurrence involving the urethral diverticulum. CCA of urethra is a rare and aggressive malignancy, with only about 250 cases reported in the English literature.
Methods: A 43-year-old female presented to the hospital with abdominal pain. Imaging studies demonstrated a periurethral mass in urethral diverticulum. A urethral diverticulectomy was performed and clear cell adenocarcinoma was identified. Three and half years later, a residual mass was observed in the urethra inferior to the bladder. Finally, a total urethrectomy was performed.
Results: Gross finding of urethral diverticulectomy specimen shows a gray-white soft polypoid mass. Histologic examinations demonstrate a combination of solid, papillary and tubulocystic growth pattern. The atypical cells show clear to eosinophilic abundant cytoplasm and luminal hobnailing of nuclei with moderate nuclear atypia. In immunohistochemical staining, PAX8, CK7, p53 and Napsin A were positive and GATA3 was focal and weak positive. Three and half years later, the patient visited the hospital with complaints of haematuria and dysuria. In imaging studies, there was about a 3cm mass confined into urethra inferior to the bladder. Total urethrectomy was done. The pathologic findings were similar to those of the previous urethrectomy specimen. Following the diagnosis of recurrent CCA of the urethra, the patient is undergoing palliative chemotherapy.
Conclusion: CCA of urinary tract, especially urethra is a rare malignancy with a relatively poor prognosis compared to non-CCA cancers. This case presents a rare disease of recurrent CCA originating in the urethral diverticulum, highlighting the importance of pathological and immunohistochemical findings in diagnosing CCA.

E-PS-26-037

High-grade urothelial carcinoma of the renal pelvis with trophoblastic differentiation and micropapillary subtype: a rare case report

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Background & Objectives: Urothelial carcinomas (UC) typically exhibit classic transitional cell morphology, but some cases may present with distinct histological features. Trophoblastic differentiation is rare and warrants detailed evaluation due to its prognostic significance. The aim of presenting this case is to emphasize the clinical and histopathological characteristics of rare variants and contribute to existing literature.
Methods: A 73-year-old male with a history of prostate adenocarcinoma presented with left flank pain. Imaging revealed grade 4 hydronephrosis in the left kidney and a soft tissue density filling the lumen of the left ureter. Left ureteronephrectomy was performed.
Results: Macroscopic examination identified a tumour in the proximal ureter and papillary lesions filling the renal pelvis. Histopathological evaluation showed high-grade UC areas alongside syncytiotrophoblastic cells with abundant eosinophilic cytoplasm, pleomorphic nuclei, and micropapillary structures. Extensive necrosis and haemorrhage was present, with faint cytoplasmic staining for β-hCG and SALL4 in syncytiotrophoblasts.
Conclusion: UC originates from the uroepithelial cells lining the urinary system. While most cases involve transitional cells, approximately 25% exhibit squamous, glandular, sarcomatoid, or micropapillary features, which are often aggressive. Trophoblastic differentiation in UC is rare and can range from syncytiotrophoblasts to choriocarcinoma. Only 7 cases of UC with trophoblastic differentiation of the renal pelvis have been reported in the literature. Syncytiotrophoblasts are giant cells with eosinophilic cytoplasm and large nuclei, observed in 28–35% of UCs and associated with β-hCG production. This differentiation is linked to high-grade, advanced stages, poor therapy response, and early hematogenous spread, indicating a poor prognosis. Immunohistochemically, β-hCG is expressed in trophoblastic/syncytiotrophoblastic cells and frequently in malignant urothelial cells. Elevated serum β-hCG levels independently correlate with poor prognosis. SALL4 is focally positive in <50% of cases but negative in syncytiotrophoblasts. To date, there have been no other reported renal pelvis UC case with micropapillary and trophoblastic differentiation other than our case in the literature.

E-PS-26-038

Immune landscape alterations in renal cell carcinoma under transplant-related immunosuppression: clinical implications for personalized therapy

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Background & Objectives: The tumour microenvironment (TME) plays a critical role in renal cell carcinoma (RCC) progression and response to immunotherapy. However, the impact of long-term immunosuppression in transplant recipients on immune cell composition in RCC subtypes remains poorly defined. This study aimed to characterize immune differences between immunocompetent and immunosuppressed post-transplant (post-Tx) patients in both clear cell RCC (ccRCC) and papillary RCC (pRCC), and to explore their clinical relevance.
Methods: Tumour samples from 81 RCC patients (49 ccRCC, 32 pRCC) were analysed, including 43 post-Tx patients under systemic immunosuppression (glucocorticoids, calcineurin and mTOR inhibitors, MMF). Immune cell infiltration and checkpoint expression were assessed using histology, immunohistochemistry, mRNA expression profiling (PanCancer IO360™ panel), mRNA-FISH, and AI-assisted digital pathology. Clinical and pathological data and prognostic scores (MSKCC, IMDC, UISS) were correlated with molecular findings.
Results: PD-L1 expression positively correlated with tumour grade, stage, size, and UISS classification in the whole cohort.
In ccRCC, immunosuppressed patients exhibited markedly reduced densities of $CD4^+$, $CD8^+$, $FOXP3^+$ T cells and $CD20^+$ B cells, with corresponding downregulation of *PDL1*, *CTLA4*, and *LAG3* at the mRNA level. PD-L1 protein expression was consistently lower across tumour cells, immune cells, and combined scoring systems. These immune alterations correlated with impaired renal function and higher clinical risk profiles.

In pRCC, post-Tx patients showed decreased macrophage density and lower PD-L1 protein expression, but only minimal differences in T or B cell infiltration compared to controls. Overall, immune activity was lower in pRCC than ccRCC, regardless of immune status.
Conclusion: Transplant-related immunosuppression significantly reshapes the immune microenvironment in ccRCC, while pRCC appears inherently less immunogenic. These findings underscore the clinical value of immune profiling and support PD-L1 as a potential biomarker to guide risk stratification and personalized therapy in RCC.

Funding: This study was supported by Grants of Wilhelm Sander Foundation (2019.035.1) and Else Kröner-Fresenius-Stiftung (Promotionsprogramm DigiStrucMed 2020_EKPK.20)

E-PS-26-039
Prognostic, clinical and pathological significance of HER-2 expression in urothelial carcinoma: a retrospective study
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Background & Objectives: HER-2 (Human Epidermal Growth Factor Receptor 2) is an emerging biomarker of interest in various solid tumours, including urothelial carcinoma (UC). The current study aims to evaluate HER-2 expression and its association with clinicopathologic characteristics and patient outcomes in UC.
Methods: This retrospective cohort study included 100 patients diagnosed with urothelial carcinoma. HER-2 expression was assessed immunohistochemically and scored as negative/(+1), (+2), or (+3). Clinicopathological variables including tumour subtype, grade, stage, metastatic profile, invasion patterns, and survival outcomes were analysed with respect to HER-2 status.
Results: HER-2 overexpression (+3) was observed in 32% of patients and was significantly more frequent in patients with micropapillary (18.8%) and nested (12.5%) histological subtypes (p=0.018). Patients with HER-2 (+3) had higher rates of advanced-stage disease and distant metastasis, particularly bone (28.1%) and liver (12.5%) involvement. Although not statistically significant, HER-2 (+3) cases showed trends toward poorer overall survival and higher rates of perineural and lymph node invasion. Patients with HER-2 (+2) expression had lower survival and progression-free survival, though numbers were limited. Mean event-free survival was shorter in HER-2 (+2) patients (16.0±16.4 months) compared to HER-2 negative/(+1) (24.5±23.3 months), and HER-2 (+3) (23.4±25.3 months), albeit without statistical significance. Progression-free survival similarly varied across HER-2 categories but did not reach statistical significance.
Conclusion: HER-2 overexpression, especially at the (+3) level, is associated with adverse histologic subtypes, higher rates of invasion and metastasis, and a trend toward worse clinical outcomes. Although HER-2 was not an independent prognostic marker in multivariate models, its strong association with aggressive disease features supports further investigation into its role as both a prognostic biomarker and a potential target for anti-HER-2 therapies in urothelial carcinoma.

E-PS-26-040
The value of the tumour-stroma ratio as a prognostic marker is low in clear cell renal cell carcinomas
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Background & Objectives: The tumour-stroma ratio (TSR) is of interest as a new prognostic factor in many tumours. In clear cell renal cell carcinoma (CRCC), the aim was to investigate the relationship between TSR measured using image analysis and tumour prognosis.
Methods: Seventy patients diagnosed with CRCC who underwent nephrectomy between 2017 and 2021 were included in the study. TSR was calculated by marking the slides scanned on the digital scanning device. Patients were divided into 2 groups as stroma-poor and stroma-rich from the TSR median value of 86%. Differences between variables evaluated with the Chi-square test, T test and One Way Anova. Kaplan-Meier method were used for comparison of survival curves.
Results: Fifty-two males (74.3%) and 18 females (25.7%) were included in the study. The mean age was 58.5 ± 12.2, and tumour size was 6.5 ± 3.3. The effect of TSR on OS and MFT was examined using Kaplan-Meier log-rank analysis. It was determined that there was no significant difference between the TSR groups. When OS and MFT, grade groups were compared with the log-rank test, a significant difference was found (p:0.046, p:0.038, respectively). No statistically significant difference was found between TSR groups and overall survival (OS) and metastasis-free survival (MFS) (respectively, p=0.29, p=0.47). When the grade groups were compared with OS (p=0.32), MFT (p=0.01), and stage (p=0.01), a statistically significant difference was found; however, no significant difference was found with diameter groups (p=0.053), TSR groups (p=0.48), and lymphovascular invasion (p=0.06). When the stage groups were compared with diameter groups (p=0.02) and lymphovascular invasion (p=0.01), a statistically significant difference was found; when compared with OS (p=0.72), MFT (p=0.12), and stage (p=0.59), no significant difference was found.
Conclusion: In CRCCs, diameter criteria are associated with prognosis, while TSR, which has been reported as a new prognostic marker in other studies, is not associated with prognosis.

E-PS-26-041
Clear cell renal cell carcinoma with extremely cystic changes presents diagnostic challenges for pathologists and clinicians
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Background & Objectives: Clear cell renal cell carcinoma (ccRCC) is the most common type of RCC in adults. The classic ccRCC shows golden-yellow, variegated cut surface with focal haemorrhage, fibrosis, or necrosis. Cystic change is frequent especially in low-grade ccRCC, and most of them are focal. In rare cases, however, the cystic changes can be extensive or to extreme extent make the tumour resemble a renal cyst or multilocular cystic renal neoplasm of low malignant potential (MCNLMP) based on radiology, histology, or intraoperative appearance. This can pose diagnostic challenges for pathologists and clinicians. It may be misdiagnosed or mistreated as benign renal cyst or indolent MCNLMP, significantly affecting patient care.
Methods: Here we presented a 50 year-old female patient with bilateral multifocal ccRCCs, two of which show extremely cystic changes.
Results: The biggest tumour is a 10.6 cm, unilocular, smooth-walled cystic mass containing haemorrhagic and necrotic material. The cystic wall is thickened and grossly adherent to adjacent organs including pancreas, spleen, and adrenal gland. Histologically, cystic wall shows extensive fibrosis, focal chronic inflammation, and scattered small foci of tumour cells with clear cell features. Immunohistochemical stains show that tumour cells are positive for Pax 8, AE1/AE3, and CA IX, confirming the diagnosis of ccRCC. The second tumour was excised as a simple renal cyst after confirming with intraoperative ultrasound, but the histology showed small clusters of ccRCC cells in the cystic wall.
Conclusion: This case demonstrates ccRCC with extensive cystic changes as an important differential diagnosis for renal cystic lesions.

Funding: Institutional Research Grant program at the University of Texas MD Anderson Cancer Centre, USA

E-PS-26-042

Non-urothelial tumours of the urinary bladder: a decade-long single-centre retrospective study

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Background & Objectives: Non-urothelial tumours of the urinary bladder are rare but clinically significant, including primary tumours, secondary extensions from adjacent organ malignancies, and distant metastases. These tumours present diagnostic and therapeutic challenges due to their diverse origins and pathological features. This study aims to analyse their clinicopathological characteristics, prevalence, and distribution to improve understanding and management strategies.
Methods: This retrospective observational study reviewed histopathologically diagnosed non-urothelial bladder tumours at Timișoara County Hospital from January 2015 to December 2024. Data were collected from electronic medical records, including patient age at diagnosis, gender, histological subtype, microscopic features, and tumour staging. Tumours were categorized into three groups: (1) primary bladder tumours, (2) secondary extensions from adjacent malignancies (e.g., prostate, cervix, rectum), and (3) distant metastases from extravesical primary tumours (e.g., breast cancer, melanoma).
Results: A total of 176 cases were identified, distributed as follows: primary bladder tumours - 59 cases (33.14%); secondary extensions from neighbouring tumours - 115 cases (64.60%); distant metastases to the bladder - 4 cases (2.24%). The mean age at diagnosis was 67 years (range: 36–90), with a slight male predominance (54.81%). Among primary bladder tumours, squamous cell carcinoma (11.23%) and sarcomatoid carcinoma (8.42%) were the most common histological subtypes. Among secondary extensions, colorectal adenocarcinomas were the most frequent (26.70%). Among the four cases of distant metastases, one stemmed from invasive lobular breast carcinoma, another from gastric adenocarcinoma, a third from non-Hodgkin lymphoma, and the final one from metastatic melanoma.
Conclusion: Although rare, non-urothelial bladder tumours present significant diagnostic and therapeutic complexities. Most cases involve secondary extensions from adjacent organs, while distant metastases are less common. These findings underscore the importance of early detection and personalized treatment approaches to improve patient outcomes. Further research is needed to better understand the clinical behaviour and optimal management of these tumours.

E-PS-26-043

Low grade mucinous tubular and spindle cell renal cell carcinoma (MTSCC): a case report of a quite rare, newly described entity

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Background & Objectives: Mucinous, tubular and spindle cell renal cell carcinoma (MTSCC) is a quite rare subtype of renal cell carcinoma that was first included in the WHO classification of renal tumours in 2004. To our knowledge, up to now, there are fewer than 100 reported cases of MTSCC in scientific literature.
Methods: We report the case of a 44-year-old female, with no relevant medical history, who was referred to the surgical department of our hospital due to a renal mass found incidentally during an ultrasound examination. Additional imaging tests were performed that verified the presence of a 5,5 cm tumour in the parenchyma of the left kidney. Subsequently, the patient was subjected to laparoscopic partial nephrectomy and oncectomy and the specimen was sent for further histopathological examination.
Results: In our histopathological laboratory we received a specimen of partial nephrectomy of 6,5 cm in maximum diameter. At dissection a well-circumscribed, solid, white-tan mass of 5,5 cm was observed. Microscopic examination showed a low-grade epithelial neoplasm that consisted of elongated, tightly packed, anastomosing epithelial tubules of cuboid cells and a spindle cell component embedded in a mucinous stroma. The neoplastic cells were positive for AE1/AE3, vimentin, PAX-8 and CK7, while CD10, CK20 and 34βE12 were negative. Consequently, the diagnosis of MTSCC was established.
Conclusion: MTSCC accounts only for 1% of renal cell carcinomas and shows a predilection for women of middle age. The prognosis is very good, with very low rates of recurrence and metastasis after surgical treatment with no additional chemotherapy/radiotherapy. The microscopical diagnosis is based almost exclusively on its characteristic 3-element morphology. Our case report presents a case of a quite rare and newly described entity and poses questions with regards to its immunohistochemical and molecular profile.

E-PS-26-044

Establishing non-HPV induced penile squamous cell carcinoma cell lines to advance research in rare urogenital tumours

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Background & Objectives: Rare urogenital tumours, including penile squamous cell carcinoma (PSCC) are significantly understudied which partly explains the lack of major treatment options beyond surgery. There is a critical need for models to facilitate further research and develop novel therapies. Here, we present preliminary data on cell culture establishment of three patients with HPV-independently induced PSCC, each exhibiting distinct biological characteristics.
Methods: All cell lines were enzymatically isolated from surgical specimens of primary PSCC operated at Medical University of Graz, Austria.
Results: Cell line PeniCA1 is derived from a 49-year-old patient with a pT2, G3 PSCC featuring pathogenic *CDKN2A* missense and *TP53* missense mutations. PeniCA2 was isolated from a pT3, N1, G2 PSCC of a 78-year-old man featuring a disruptive *CDKN2A* mutation, and missense mutations in *TP53*, *HRAS*, and *FBXW7*. PeniCA3 was obtained from a 75-year-old man with pT2, G2, N1 PSCC with a missense *TP53* mutation. Additionally, HPV6 DNA was detected despite a morphological lack of a productive HPV infection. PeniCA1 exhibited a medium maturation rate while PeniCA2 displayed the lowest maturation rate, but highest doubling time. PeniCA3 cell culture showed a low proliferative activity but high maturation rate with large mature squamous cells and individual koilocytes. Despite the lack of morphological criteria of HPV infection in the primary SCC, cultured keratinocytes were able to differentiate into a stratified epithelium with koilocytes.
Conclusion: All three cell lines match their primary tumour histologies. We postulate that the mutation profiles influence the doubling time and growth rate of the cells in culture. They can serve as a functional model of HPV-independent PSCC in vitro and in vivo. We postulate that basal keratinocytes serve as a reservoir for HPV in latent infections, and that in a supportive culture environment allows virus production and assembly.

E-PS-26-045

HRR testing in Croatia; metastatic castrate-resistant prostate cancer; target for potential PARPi therapy

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Background & Objectives: Homologous recombination repair (HRR) mutations, including those in key genes such as BRCA1/2, play a significant role in DNA repair mechanisms. Defective HRR pathways, especially in advanced cancers like metastatic castrate-resistant prostatic adenocarcinoma (mCRPC), make tumours susceptible to targeted therapies such as poly ADP-ribose polymerase inhibitors (PARPi). This study aims to start evaluating the prevalence of HRR gene mutations in mCRPC patients in Croatia and assess their potential for guiding PARPi-based therapeutic strategies.
Methods: A total of 30 mCRPC patients were selected for HRR mutation testing using formalin-fixed paraffin-embedded (FFPE) tissue samples. The HRR gene panel included full-length sequencing of the following genes: ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCD2, MRE11, NBN, PALB2, PPP2R2A, RAD51B, RAD54L, and TP53. Patohistological findings (GG, pTN, tumour volume) and clinical data (age, stage, therapy,OS) were compared to molecular testing results.
Results: Of the 30 patients, 25% (n=7) displayed pathogenic mutations in HRR-related genes. The most frequently mutated genes were BRCA2 (10%), followed by ATM (6%), and CDK12 (3%). Mutations in CHEK2 and PALB2 were observed in a smaller subset of patients. No cases of co-occurring mutations in multiple HRR genes were found. These genetic alterations were strongly associated with poor prognosis, indicating aggressive disease and an accelerated progression to metastatic castration resistance. Mutations were find in patients with higher GG and stage, often within cribriform pattern.
Conclusion: HRR gene testing is pivotal for identifying mCRPC patients who could benefit from PARPi therapy. A significant proportion of patients in our study carried mutations in BRCA2 and ATM genes, highlighting the potential of personalized treatment approaches. Targeted PARPi therapies offer promising therapeutic opportunities, especially in HRR-deficient tumours. Further clinical validation is essential to refine therapeutic strategies and expand the use of PARPi in clinical settings.

E-PS-26-046

The association of tertiary lymphoid structures and benign lympho-epithelial lesions in human prostate: their role in high grade chronic asymptomatic prostatitis NIH category IV

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Background & Objectives: NIH-category IV prostatitis (histologic prostatitis, HP) is an asymptomatic chronic inflammation of the prostate. Chronic inflammation has been associated with the most frequent socially important prostate diseases like benign prostatic hyperplasia (BPH) and prostate cancer (PCa). Tertiary lymphoid structures (TLS) develop within the inflamed tissue, but changes in adjacent prostatic ducts are poorly studied. It remains unclear if these modifications are part of organized immune structures, leading to the hypothesis that they may represent benign lympho-epithelial lesions (LEL).
Methods: We investigated TLS and ductal epithelial cell changes (LEL presumably) in 110 different cases of prostatic inflammatory and normal specimens, in the context of basic prostate pathology – benign prostatic hyperplasia (BPH) and prostatic adenocarcinoma (PCa). HP is scored in low and high grade (LG and HG) using the severity of inflammation.
Results: We observed an association between TLS and LEL in the investigated 110 patients from the basic group with HP. A combination between both TLS and LEL was found in 45/110 cases (40.9%). Statistical analysis shows a significant correlation of the presence of both LEL and TLS examined separately or together, with HG-HP ($p<0.001$). There is lack of significant correlation between the presence of LEL and TLS with BPH and PCa.
Conclusion: The study is the first attempt to examine qualitatively and quantitative LEL and TLS in normal an inflammatory human prostate. Their presence, triggered by antigenic stimuli and external factors, reflects a chronic inflammatory microenvironment. The strong association between LEL/TLS and their link with HG-HP reflects HP aggressiveness. The data from this study suggest that LEL and TLS may be key players in the pathophysiology and morphogenesis of NIH-category IV prostatitis. LEL/TLS formation can be considered as a hallmark of tissue autoimmunity and probably reflects the immune/autoimmune phase of NIH category IV prostatitis.

E-PS-26-047

L1CAM expression defines low-grade oncocytic tumours among eosinophilic renal neoplasms

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Background & Objectives: The classification of renal eosinophilic tumours has expanded with the recognition of new entities, including Low-Grade Oncocytic Tumour (LOT). Differentiating LOT from eosinophilic chromophobe renal cell carcinoma (E-chRCC), renal oncocytoma, and eosinophilic vacuolated tumour (EVT) may sometimes be complex due to shared morphological and immunohistochemical characteristics, particularly in small bioptic samples. This study aimed to assess the diagnostic utility of L1 cell adhesion molecule (L1CAM), a transmembrane glycoprotein involved in neural development and oncogenesis, as a marker for LOT.
Methods: A retrospective, multicentre study was conducted on a cohort of 50 eosinophilic renal neoplasms, including morphologically and immunophenotypically confirmed cases of low-grade oncocytic tumour (LOT), renal oncocytoma, eosinophilic chromophobe renal cell carcinoma (E-chRCC), and eosinophilic vacuolated tumour (EVT). All cases underwent centralized histopathological re-evaluation by expert uropathologists to assess architectural and cytological features. Immunohistochemical analysis was performed using antibodies against

L1CAM, keratin 7 (KER7), GATA3, CD117, and cathepsin K. The specificity and sensitivity of L1CAM for the identification of LOT were analysed in comparison to other eosinophilic renal tumours.
Results: LOT cases commonly displayed a "small nested" growth pattern, along with perinuclear halos and irregular nuclear contours—features occasionally shared with other eosinophilic renal tumours. Their immunophenotype (KER7 and GATA3 positive; CD117 and cathepsin K negative) was not consistently definitive for diagnosis. Notably, L1CAM expression was observed as strong and diffuse membranous staining in 100% of LOTs, but was entirely absent in oncocytoma, E-chRCC, and EVT. These findings highlight the superior sensitivity and specificity of L1CAM in identifying LOT.
Conclusion: L1CAM is a highly specific and sensitive marker for distinguishing LOT from other eosinophilic renal neoplasms, offering valuable support in challenging differential diagnoses. These results support the integration of L1CAM immunostaining into diagnostic workflows. Further investigations are warranted to assess its expression across the broader spectrum of oncocytic renal tumours.

E-PS-26-049
Paratesticular smooth muscle hyperplasia imitating malignancy: a possible link to epididymitis – a case report
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Background & Objectives: Paratesticular smooth muscle hyperplasia (PT-SMH) is a rare benign mass-forming lesion, primarily affecting the epididymis but also the spermatic cord and tunica albuginea. Its resemblance to malignant neoplasms poses a significant diagnostic challenge, often resulting in unnecessary orchiectomies. Differential diagnoses include leiomyoma, leiomyosarcoma, and other mesenchymal tumours, requiring thorough histopathological evaluation. While its exact aetiology remains unclear, some evidence suggests an association with obstructive processes like epididymal or vas deferens duct ectasia. Epididymitis, a common inflammatory condition, may contribute to ductal obstruction and reactive smooth muscle proliferation; however, a direct causal relationship has not been established. This study presents a case of SMH-TA with concurrent epididymitis, highlighting their potential association.
Methods: A 66-year-old male presented with an incidental intrascrotal mass, clinically suspected to be a neoplasm, leading to a radical orchiectomy. Histopathologic examination showed a proliferation of smooth muscle bundles arranged in interstitial and perivascular patterns, lacking atypia, mitotic activity, or necrosis. The lesion surrounded dilated epididymal ducts, some containing spermatozoa. Adjacent testicular parenchyma exhibited severe tubular atrophy and extensive chronic and acute epididymitis with microabscess formation. Immunohistochemistry confirmed smooth muscle origin (SMA+, desmin+), ruling out neural and vascular neoplasms (S100-, CD34-).
Results: Findings support a hyperplastic rather than a neoplastic process, confirming the diagnosis of PT-SMH, likely secondary to chronic inflammation and obstruction.
Conclusion: PT-SMH remains an extremely rare entity and should be considered in the differential diagnosis of epididymal masses. The coexistence of PT-SMH with severe epididymitis may provide insight into a possible causal relationship, though further studies are needed to establish a definitive link. While few cases of PT-SMH have been reported, even fewer have highlighted this association. Increased clinical and pathological awareness, along with thorough histopathological evaluation, is crucial to avoid misdiagnosis and unnecessary surgical intervention.

E-PS-26-050
Eosinophilic vacuolated tumour: a case report of an emerging entity in uropathology
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Background & Objectives: Eosinophilic vacuolated tumour (EVT) is a rare, emerging entity recently acknowledged in the 2022 WHO classification. It poses significant diagnostic challenges due to overlapping features with oncocytic, clear cell, and other eosinophilic renal neoplasms. Despite high-grade nuclear features, EVT generally demonstrates an indolent behaviour and favourable prognosis. However, limited data regarding its long-term clinical course necessitate further studies and extended follow-up to better elucidate its biology and prognostic implications. We present a case of EVT to detail its pathology, highlight diagnostic hurdles, and emphasize its rarity.
Methods: A 68-year-old female presented with a 2 cm exophytic lesion in the lower pole of the right kidney, initially suspected as clear cell renal carcinoma, papillary variant, based on MRI findings. A partial nephrectomy was performed. Histopathologic examination revealed a neoplasm composed of cells with abundant oncocytic cytoplasm and focal intracytoplasmic vacuoles, along with prominent nucleoli. The tumour exhibited a solid and nodular architecture, with trapped renal tubules and areas of sclerosis. Immunohistochemistry showed PAX-8 positivity, focal CK7 and CD117 reactivity, and negativity for CD10 and Carbonic Anhydrase IX.
Results: The morphological findings and immunoprofile supported the diagnosis of an oncocytic renal tumour, yet its features did not align definitively with either oncocytoma or chromophobe carcinoma. Instead, the tumour's characteristics were most consistent with EVT.
Conclusion: This case highlights a diagnostically challenging oncocytic renal tumour that defies conventional classification and stands as a testament to the evolving landscape of renal neoplasm classification. Classifying EVT within the 2022 WHO "Other Oncocytic Tumours" category marks a significant advancement in our understanding, yet it also reveals the gaps in our knowledge. This case exemplifies the importance of meticulous pathological evaluation for accurate diagnosis and classification of emerging renal neoplasms, paving the way for future research and clinical advancements in uropathology.

E-PS-26-051
Expression of Programmed Death-ligand 1 (PD-L1) in urothelial carcinoma of bladder
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Background & Objectives: Bladder cancer is the second most common cancer in the genitourinary tract with urothelial carcinoma (UC) being the commonest histologic subtype. PD-L1 is used for selecting patients with urothelial bladder cancer for immunotherapy. The objective of our study was to evaluate the immunohistochemical expression of PD-L1 in UC of bladder and to study its association with the clinicopathological characteristics of UC.
Methods: A retrospective study was conducted of 65 patients who underwent transurethral bladder resection for UC from January 2020 to December 2024. The tumour was graded as per WHO classification. Immunohistochemistry staining for PD-L1 was done on the archived blocks. The expression of PD-L1 (SP 263) (membranous positivity) was analysed using the standard combined positive score (CPS) scoring system. A CPS equal to or greater than 10 was considered positive.

PD-LI positivity was compared with morphological features such as grade, tumour infiltrating lymphocytes and muscle invasion.
Results: PD-L1 expression was categorised as positive (41/65) and negative (24/65). The cases included 39 muscle invasive and 26 non-muscle invasive tumours. Of these, 53 (82%) were high grade and 12 (18%) were low grade. Tumour infiltrating lymphocytes (TILs) in the stromal compartment were calculated based on the stromal tissue occupied by mononuclear inflammatory cells relative to the total area of the stroma within the tumour and grouped as low (0–10%), intermediate (15–50%) and high (55–100%) grade of stromal lymphocytic infiltration. 75% of the cases showed the grade of TILs to be in the low category. There was a significant relationship between PD-L1 positivity, TILs grade and muscle invasive status of bladder UC. There was no significant association between tumour grade and PD-L1 positivity.
Conclusion: PD-L1 expression correlates with increased TILs and muscle invasive status, suggesting that PD-L1 as a potential biomarker for tumour aggressiveness and guide immunotherapy for advanced UC.

E-PS-26-052
Staining patterns of cancer-associated fibroblast markers and CD8+ T-cell distribution in the stroma of bladder cancers
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Background & Objectives: The components of the mesenchymal environment of the tumour stroma are significant. Investigating tumour-infiltrating lymphocytes and cancer-associated fibroblasts (CAF) is important for bladder cancers. Finding markers of these cells that can be used in future drug therapy is vital.
Methods: Immunohistochemistry was performed on material from 27 BCG-treated patients (1) and 40 non-treated patients (2). A study used CD8 T-lymphocyte markers. The evaluation was done quantitatively, determining the mean by counting cells in 10 high-power fields. FAP (fibroblast activate protein) and FSP1 (fibroblast specific protein 1/S100A4) were used to identify CAF. The evaluation employed a mark method for staining intensity, ranging from 0 for negative staining to 3 for maximum intensity.
Results: Group (1) had 1.2-fold more CD8+ T-cells in cases without relapses after BCG therapy than in cases that relapsed, confirming the protective function of the peritumoral inflammatory infiltrate. There is a higher rate of CD8-T cells in high grade MIBC (1.2-fold greater infiltration in comparison to low grade MNIBC). FAP reaction was exclusively observed in invasive bladder cancers and high-grade BC in both groups. In FAP+ urothelial carcinomas, CAFs were associated with poor CD8+ T-cell infiltration ($p<0.001$), indicating a lack of tumour cytotoxic potential. FSP1 showed reduced intensity and area of staining in tumour cells and the invasive margin of recurrence specimens compared to primary tumours ($p < 0.001$). In group (2) there was a positive correlation of FSP1 marker and FAP in the stroma of the invasive margin ($p < 0.001$).
Conclusion: Research into using more different CAF markers combined with other components of the mesenchymal environment in the context of bladder cancer is required. Analysing the markers' association with clinical data in large groups will help update tests and genetic markers for urothelial carcinomas, which is important for refining the criteria for BCG therapy in a Russian cohort.

E-PS-26-053
A rare collision: seminoma and teratoma coexisting in a young male's testis
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Background & Objectives: Testicular germ cell tumours (TGCTs) are the most common malignancies in young men, with seminomas and non-seminomatous germ cell tumours (NSGCTs) as the primary subtypes. Collision tumours, defined as two histologically distinct neoplasms coexisting within the same testis without intermixing, are exceptionally rare. We report a rare case of a 21-year-old male diagnosed with a right testicular collision tumour composed of seminoma and teratoma.
Methods: A 21-year-old male presented with a palpable right testicular mass. Scrotal ultrasound revealed a hypoechoic, non-homogenous tumour with a multilobulated contour. The patient underwent right orchiectomy via an inguinal approach. The excised specimen underwent histopathological and immunohistochemical evaluation.
Results: Gross examination revealed a whitish, nodular tumour occupying 85% of the testicular parenchyma. Histologically, the tumour was composed of two distinct, colliding tumours: one with an epicentre in the testicular parenchyma and the other originating from the epididymal region, separated by a fibrous pseudocapsule. The seminomatous component was characterized by a monomorphic malignant germ cell proliferation, with large, atypical, mostly uninucleated germ cells arranged in nests and sheets. The cells had prominent nucleoli and eosinopholic cytoplasm.The teratoma consisted of well-differentiated elements from all three germ layers (including glandular, neural, and mesenchymal structures), alongside primitive neuroectodermal, rhabdoid and lipoblastic elements. Immunohistochemical staining confirmed the dual nature of the tumour, with seminoma cells expressing CD117, OCT4, Glypican3, SALL4, S100, while teratomatous elements demonstrated variable differentiation markers SALL4, P63, GFAP, Desmin, Synapthophisin and S100, reflecting its complex differentiation.
Conclusion: Testicular collision tumours, though rare, should be considered in the differential diagnosis of complex, heterogenous testicular masses in young males. Comprehensive histopathological and immunohistochemical evaluation is essential for accurate diagnosis and individualized treatment strategies.

E-PS-26-054
Immunomorphology of Post-Atrophic Hyperplasia of the Prostate
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Background & Objectives: The post-atrophic hyperplasia (PAH) of the prostate is a precancerous lesion, whose morphogenesis is insufficiently clarified. The histological components of an immune inflammation are diverse, but the most important elements that are also relatively easy to evaluate are as follows- the presence of lymphoid follicles (tertiary lymphoid structures: TLS) and benign lymphoepithelial lesions (BLEL). We examined TLS and BLEL in PAH.
Methods: We studied the combination of TLS and BLEL with PAH quantitatively and qualitatively in 165 prostatic biopsy, surgical and autopsy specimens.
Results: 37.3% of the cases show a combination of PAH and TLS. The statistical analysis of the results does not show any significant relationship between the presence of PAH and TLS ($\chi^2 = 2,38$; $p = 0,126$).
A combination of PAH and BLEL can be found in 44.9% of the patients. The statistical analysis of the results shows there is a significant link between the presence of PAH and BLEL ($\chi^2 = 20,95$; $p < 0.001$). In 75% of the cases the two lesions show a close topographic assiciation, with a distance between them <2mm. 85% of these cases involve residual BLEL. PAH is often shown as a proliferative lesion developing in the wall of prostate canalicules with BLEL. It is clearly visible on longitudinal histological sections.

Conclusion: This study represents the first effort to quantitatively and qualitatively analyse the immunopathologic patterns of PAH. PAH is a lesion, which represents an extension and an end stage of the prostate duct damage (BLEL) and reflects the chronic inflammatory prostate microenvironment.

E-PS-26-055

Heterogeneity of expression of potential CAF markers in prostate cancer

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Background & Objectives: Cancer associated fibroblasts (CAF) are an important component of the tumour microenvironment. No universal marker has been identified for CAF due to their subpopulation division. Multiple substances are being considered for the role of potential CAF markers in tumours. However, there is evidence for heterogeneity in the expression of these markers.
Methods: We performed immunohistochemical staining of 75 samples with antibodies to periostin (POSTN) and 34 samples with PDGFRa+β from patients with prostate cancer. PDGFRα+β and POSTN staining in the prostate were assessed in the stroma around tumour glands. The aim of our study was to investigate the staining patterns of these CAF markers and their correlation with clinical and morphologic parameters and survival of patients.
Results: Immunohistochemical staining of both markers was distributed from no staining (0) to significant staining (3+). A significantly higher number of recurrences was shown in the group with a high PDGFRa+β (3+) reaction (p=0.0018). No relationship was found between grade (p=0.21112), invasion level (p=0.2757) and PDGFRα+β intensity. There was also no correlation between intensity of POSTN expression and clinical and morphologic parameters and recurrence.
Conclusion: Th1e obtained data confirm the heterogeneity of CAF markers in prostate tumours, as well as their potential to be used as prognostic markers. PDGFRa+β may be a significant diagnostic marker for predicting prostate cancer recurrence. The role of POSTN staining remains the subject of further study.

E-PS-26-056

L1 Cell Adhesion Molecule (L1-CAM) expression in oncocitomas scars

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Background & Objectives: Renal oncocytomas (RO) often present with a central scar. Cell groups adjacent to or encompassed by the scar often exhibit a morphology distinct from the rest of the tumour: tubular or cord-like pattern, cells with ovoid-spindle-shaped nuclei, clear cytoplasm, and absence of typical oncocytic features. Several previous studies have shown that these morphological changes are accompanied by immunophenotypic changes. Some of the observed markers, such as racemase or Napsin A, suggested an adaptive change reminiscent of renal tubules. Recently, it has been shown that the marker L1CAM (CD171), a type 1 multidomain transmembrane glycoprotein of the immunoglobulin superfamily, is differentially expressed in P-cells of the normal renal collecting duct, as well as in nephrogenic adenomas. Our main objective is to study L1CAM expression in RO scar areas with morphological changes such as those described previously.
Methods: We selected 25 RO cases diagnosed between 2016 and 2025 that contained a central scar area along with morphological changes in clusters of cells within it. Immunohistochemical staining for L1CAM was performed.
Results: Twenty-five cases that contained areas of tubular morphology within the fibrous scar were studied. These areas, unlike the rest of the tumour, showed intense positivity for L1CAM in 22/25 cases and weak positivity in 3/25. Positivity was observed in normal distal tubules of the non-tumour parenchyma. The remainder of the tumour was negative.

Conclusion: Scarred areas in RO often encompass groups of cells with a morphology and immunohistochemical profile distinct from the rest of the tumour. These include intense immunoreactivity for CK7 and Vimentin, negativity for CD117, and weak-irregular staining for AMACR and Napsin. The expression of L1CAM in the scar area in all cases, along with the expression of other renal tubule markers, reinforces the hypothesis that this morphology could be an adaptive change similar to nephrogenic metaplasia.

E-PS-26-057

Molecularly defined tumour microenvironment ecosystems enhance prognostic stratification in low- and intermediate-risk prostate cancer

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Background & Objectives: Tumour progression in prostate cancer (PCa) is shaped by complex interactions between epithelial cancer cells and the surrounding tumour microenvironment (TME). While some relations are evident on haematoxylin and eosin (H&E) slides, transcriptomic profiling offers deeper functional insights. This study aimed to integrate RNA-seq and histopathological data to identify TME-defined tumour ecosystems (Ecotypes) and functional cell states, assessing their association with pathological features and clinical outcome.
Methods: On a clinicopathological well-annotated multi-institutional cohort of 400 prostate tissue samples (179 benign and 221 malignant) with matched bulk RNA-seq, we applied EcoTyper, a computational framework that deconvolutes transcriptomic data into distinct cell types with unique transcriptional states ("cell states") and assigns to each PCa an overall TME molecular profile called "Ecotype" (E). Associations between Ecotypes, cell states, Grade Groups (GG), and morphology were assessed. A graph neural network was trained to predict Ecotypes from H&E images.
Results: A predominant Ecotype was identified in 181/221 (82%) PCa cases. Interestingly, GG1 PCa (n=62) were enriched in E6 (*normal-like TME*), however GG1 patients lacking E6 showed a markedly higher recurrence rate with nearly fivefold increased odds (OR= 4.76, 95% CI: 0.83–40.0). Whereas in GG2-3 PCa (n=70), E10 (*longer overall survival*) showed a negative correlation with the percentage of Gleason pattern 4 (p=0.02). Moreover, specific cell states (e.g., myofibroblasts, chymase-positive mast cells) were enriched in low-grade tumours. Finally, distinct H&E patterns predictive of Ecotypes were identified.
Conclusion: Characterizing the TME using transcriptome-based, ecosystem-level tools provides relevant biological and clinical information beyond conventional clinicopathological features. Ecotype E6 may help identify truly GG1 indolent PCa suitable for active surveillance, while Ecotype E10 could refine prognostic stratification in intermediate-risk cases. Integrating these molecular ecosystem signatures with standard

histopathological evaluation has the potential to enhance diagnostic accuracy and shape tailored treatment strategies.

E-PS-26-058

Predictive influence of phenotypic characteristics in upper urothelial carcinoma to expression of CD44

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Background & Objectives: CD44 acts as a cell adhesion molecule and is involved in regulation of the malignant biological behaviour of tumour cells. Objective of this study was to determine the predictive influence of phenotypic characteristics - histological grade, pathologic stage, growth pattern, lymphovascular invasion, presence of necrosis and divergent differentiation in upper tract urothelial carcinoma (UTUC) to expression of CD44.
Methods: This study included 92 patients with UTUC who had undergone open type nephroureterectomy. H&E-stained slides were used to assess phenotypic characteristics. Immunohistochemistry was performed to detect membranous expression of CD44 which was categorized as normal or altered. Monoclonal antibody against CD44 (Dako, Glostrup, Denmark) at dilution 1:50 with a standard En Vision system was used. Slides were reviewed independently by three researchers (LJV, ARP, SS) and areas with greater positivity were selected.
Results: Pathological stage, growth pattern and lymphovascular invasion have significant influence to expression of CD44 in UTUC ($p<0.0001$; 0.05; 0.005, respectively), however, differentiation, necrosis and divergent differentiation have no significant influence. In regression analysis, parameters with predictive influence to expression of CD44 in UTUC included stage ($p=0.001$) and lymphovascular invasion ($p=0.024$).
Conclusion: This investigation detected that the loss of CD44 was determined with high stage and presence of lymphovascular invasion.

E-PS-26-059

Somatic-type malignancies in testicular germ cell tumours: a diagnostic challenge

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Background & Objectives: The most common group of testicular tumours is germ cell tumours (GCTs). Somatic-type malignancies (STMs), which are more common after chemotherapy, arise from teratomas and yolk sac tumours. Diagnosing and managing STMs can be highly complex and challenging.
Methods: We retrospectively re-evaluated the morphological and immunohistochemical features of eight cases diagnosed with STM in metastases after GCT treatment and the molecular characterization of one patient.
Results: The median age of the cases at the time of STM diagnosis was 33 years. The median time from the initial diagnosis of GCT to the development of metastatic STM was 45.6 months. Adenocarcinoma was the most common STM in metastases (n=5), followed by sarcoma (n=1) and embryonic-type neuroectodermal tumour (ENT) (n=1). One tumour previously classified as STM was re-diagnosed as an epithelioid trophoblastic tumour (ETT). Among five adenocarcinoma cases, three (3/5) were SALL4 positive. Sarcoma case was SALL4 and Glypican-3 positive. ENT cells expressed synaptophysin, while ETT cells were positive for GATA3 and p63. NGS was performed only in one STM case (adenocarcinoma) and revealed a pathogenic variant in the PTEN gene that caused loss of function.
Conclusion: Most STMs associated with GCT are found in association with teratomas, leading to the assumption that teratomas are the tissue of origin. As in our metastatic sarcoma and testicular tumour YST case, SALL4 and glypican-3 positivity support that SMT may also originate from YST. The developmental origin of STM formation and the underlying molecular mechanisms remain unclear. Although there is no standard treatment for STM, treatment is generally tailored according to the stage of disease and histology (e.g. sarcoma, carcinoma). The existence of patients who are refractory to treatment suggests that despite the morphological similarity between STM and true somatic malignancy there are molecular differences. We believe that elucidation of the etiopathogenesis of STM will contribute to patient management.

E-PS-26-060

Defining the molecular profile: histomorphological evaluation and a sporadic somatic TSC2 mutation in fibromyomatous RCC

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Background & Objectives: Renal cell carcinoma (RCC) with fibromyomatous stroma is a rare subtype characterized by distinctive histopathological features. Here, we present a case where the diagnosis was established based on histomorphological criteria, subsequently supported by the identification of a novel somatic TSC2 variant through genetic analysis. This case expands the molecular spectrum of RCC and underscores the role of integrative diagnostics.
Methods: A 60-year-old male underwent partial nephrectomy for a 3×3×2 cm right renal mass. Given the unusual morphology, additional genetic analysis was performed using peripheral blood. Somatic variant analysis identified the TSC2 NM_000548.5:c.984A>G variant.
Results: Histopathological examination revealed a well-circumscribed tumour composed of elongated, branching tubular structures lined by clear to lightly eosinophilic cells, set within a dense fibromyomatous stroma. There was no evidence of perirenal fat, lymphatic, or vascular invasion, and the surgical margins were clear with a 2 mm parenchymal clearance. Immunohistochemically, tumour cells were positive for PAX8, HMWCK, and CK7, with focal CAIX positivity and a low Ki67 index (1-2%). AMACR and c-kit were negative. The surrounding stroma exhibited SMA positivity with focal desmin staining.
Conclusion: The combination of histomorphological features, immunophenotypic findings, and somatic TSC2 variant analysis supported the diagnosis of RCC with fibromyomatous stroma. The tumour displayed bland nuclear features (ISUP 2013/Fuhrman grade I) and a low proliferation index, indicating a likely indolent clinical course despite the presence of a novel genetic alteration. This case emphasizes the critical role of histopathology in diagnosing RCC with fibromyomatous stroma while highlighting the utility of targeted somatic genetic analysis for refining classification. Further studies are needed to elucidate the clinical implications of TSC2 variants in this rare RCC subtype.

E-PS-26-061

Correlation of serum prostate-specific antigen with Gleason's score/ grade group in prostate carcinomas

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Background & Objectives: Prostate-specific antigen (PSA) is a key screening tool for prostate cancer, despite its high sensitivity and low specificity. Gleason's grading remains a strong predictor of tumour

aggressiveness. We studied the correlation between PSA levels and Gleason's score/grade group.
Methods: A retrospective study was conducted on prostatic adenocarcinoma cases diagnosed at Habib Thameur Hospital (January2021–February2025).
Pathologic reports were reviewed to extract data including: PSA levels, specimen type (needle biopsy, transurethral resection of the prostate [TURP], or radical prostatectomy), Gleason score/Grade group and histological type.
The relationship between PSA levels and Gleason score/Grade group was evaluated using linear regression modelling to assess correlations and trends.
Results: Of 83 prostate specimens received in the selected period, 51 (61.4%) were needle biopsies, 17 (20.5%) TURPs, and 15 (18.1%) radical prostatectomies. Mean age was 70.5 years (range: 52–85). Median PSA was 28ng/ml. With extremes of 5.2 ng/ml (Gleason 7(3+4)) and 6021ng/ml (Gleason 10(5+5)). Gleason Group 5 was the most frequent (28.9%), followed by Group 2 (21.7%). The most common Gleason scores were 7(3+4) (21.7%) and 6(3+3) (16.9%). A significant positive correlation (p=0.047) of moderate strength (r=0.218) was observed between PSA levels and Gleason scores. Acinar adenocarcinoma predominated (97.6%), with 1 case each of ductal and mucinous adenocarcinoma.
Conclusion: A significant positive correlation (p=0.047, r=0.218) was found between PSA levels and Gleason grades. Patients with high serum PSA concentrations are likely to have high tumour grade group. Our findings demonstrate that Gleason's score is one of the factors determining serum PSA concentration in patients with prostate carcinoma and its part is 21.8%.

E-PS-26-062
Interobserver reproducibility of PD-L1 interpretation in urothelial carcinoma
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Background & Objectives: Programmed death-ligand 1 (PD-L1) expression by tumour cells suppresses anti-tumour T-cell responses, making it a key immunotherapy target. Accurate PD-L1 assessment is critical in urothelial carcinoma. It is essential for optimizing immunotherapy decisions and improving clinical outcomes but interobserver variability may impact its clinical utility. This study evaluates the reproducibility of PD-L1 interpretation in urothelial carcinoma.
Methods: A retrospective study was conducted on urothelial carcinoma cases diagnosed at Habib Thameur Hospital (2017–2021). PD-L1 immunohistochemical staining using the Tissue MicroArray (TMA) technique for the 22C3 clone was independently assessed by a senior pathologist (P1) and a pathology resident (P2). Based on the Combined Positive Score (CPS), cases were classified as positive (CPS >10) or negative (CPS ≤10). Interobserver agreement was analysed using Cohen's kappa coefficient.
Results: 105 specimens of urothelial carcinoma were received during the 5-year selected period, out of which 4 cases (3.8%) were classified as PD-L1 positive (CPS >10). Pathologist P1 identified 4 positive and 101 negative cases, while P2 identified 3 positive cases. Only one case showed discordance (P1: CPS=19; P2: CPS=9.2). The interobserver agreement, assessed using Cohen's kappa coefficient, was $\kappa = 0.852$, indicating strong reproducibility between the two pathologists.
Conclusion: PD-L1 evaluation play a pivotal role indetermining eligibility for immunotherapy in urothelial carcinoma. The high agreement among pathologists, regardless of experience, demonstrates strong interobserver reproducibility using the 22C3 clone. In cases of discordance, retesting may be required to confirm treatment suitability, thereby optimizing outcomes. Standardized training and protocols are crucial to minimize variability and ensure accurate patient selection for anti-PD-L1 therapy.

E-PS-26-063
MTSCC: insights into morphological variability and differential diagnosis with papillary RCC
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Background & Objectives: This study aims to characterize the morphological features of mucinous tubular and spindle cell carcinoma (MTSCC) and highlight diagnostic pitfalls with papillary renal carcinoma (PRCC).
Methods: A retrospective clinicopathological analysis was conducted on MTSCC cases diagnosed at the Portuguese Oncology Institute-Porto (IPO-Porto). Clinical and pathological parameters were assessed and relevant literature was reviewed.
Results: Six cases of MTSCC were identified, corresponding to three female and three male patients, aged 41 to 73 years. Mean tumour size was 8.3 cm (range: 3.1-14.5cm). Macroscopically, only one case showed extension to the pelvicalyceal system. Three cases were pT1b, one pT2a, one pT2b and pT3a. Microscopically, three cases had a predominant tubular pattern, two had a predominant spindle cell pattern, and one had equal proportions of both. Mucinous areas were abundant in three cases, moderate in two and focal in one tumour. All tumours exhibited haemorrhage, areas of cytoplasmic clarification, and no mitotic figures were found nor sarcomatoid or rhabdoid features. Other findings included psammomatous calcifications (three cases), hyalinized stroma (two), cholesterol clefts (five), xanthogranulomatous macrophages (five), and hemosiderophages (two). CD10 was negative/focal in 4/2, respectivelly. One case was studied with FISH and showed no gains in 7/17.
Conclusion: MTSCC is a rare renal tumour which can mimic PRCC, as mucinous areas may be present in both entities. Presence of more than focal papillary features favours PRCC. Immunohistochemistry may be overlapping, although CD10 is reported to be negative or focal in MTSCC, as verified in all MTSCC cases of our study. In difficult cases, the demonstration of gains in 7/17 in PRCC may be of help, since these are not observed in MTSCC. Upon review, we identified such a case, which had focal mucinous stroma, but showed gains in 7/17 being diagnosed as PRCC. These molecular differences, combined with thorough histopathological evaluation, are crucial for accurate diagnosis.

E-PS-26-064
Neuroendocrine differentiation in prostate cancer: clinical and pathological insights from a case series
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Background & Objectives: Neuroendocrine proliferations in prostate cancer range from focal neuroendocrine differentiation within conventional adenocarcinomas to aggressive neuroendocrine carcinomas. Although rare, these entities display distinct biological behaviours and have significant therapeutic implications. This case series explores the pathological and clinical characteristics of patients diagnosed with neuroendocrine differentiation in prostatic malignancies.

Methods: A retrospective analysis was conducted using the electronic database of Timişoara County Hospital to identify male patients diagnosed with prostatic malignancies exhibiting non-focal neuroendocrine differentiation between January 2020 and February 2025. Clinical data, including age at diagnosis, sample type, treatment details (where available), histologic classification, Gleason score/grade group, and stage (if applicable), were collected. Histopathological assessment and immunohistochemical analysis using markers such as chromogranin A and synaptophysin were performed to evaluate neuroendocrine differentiation.
Results: Seven cases of prostate cancer with neuroendocrine differentiation were identified, with a median patient age of 71 years (range: 60–81). The sample types included biopsies (n=2), transurethral resection specimens (n=4), and radical prostatectomy specimens (n=1). These cases were classified as follows: prostatic adenocarcinoma with extensive neuroendocrine differentiation (n=5), prostatic adenocarcinoma with Paneth cell-like change (n=1), and small cell neuroendocrine carcinoma (n=1). Among cases of conventional prostatic adenocarcinoma with extensive neuroendocrine differentiation, the most common Gleason score was 9 (Grade Group 5). The patient with Paneth cell-like change had undergone hormonal therapy before prostatectomy and was staged as pT3a.
Conclusion: Neuroendocrine differentiation in prostatic malignancies is rare and encompasses a diverse morphological spectrum. A thorough histopathological evaluation using standard staining techniques, combined with immunohistochemical analysis, is essential for accurate classification. Further research is necessary to determine the clinical significance of these findings and to develop optimized treatment strategies.

E-PS-26-065

Dermal nerve sheath myxoma of the penis: the first histopathologically confirmed case

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Background & Objectives: Dermal nerve sheath myxoma (DNSM) is a rare benign peripheral nerve sheath tumour, classically involving the distal extremities. Penile localization has never been reported. We present the first histopathologically confirmed DNSM in the penis, with clinical correlation to a prior incompletely excised lesion.
Methods: A 58-year-old male presented with a 2 cm ventral penile nodule at the site of a lesion excised 10 years earlier without pathological examination. Excisional biopsy was performed. Histomorphologic evaluation and comprehensive immunohistochemistry (S100, Ki67, CD34, PanCK, desmin, calponin) were conducted.
Results: Histopathological examination revealed a hypercellular, multilobular tumour composed of bland spindle cells arranged in interconnecting cords and syncytial clusters within a prominent myxoid stroma, devoid of nuclear atypia or mitotic activity. Immunohistochemical analysis demonstrated diffuse strong S100 positivity, confirming Schwann cell lineage, and a low proliferative index (Ki67 <1%). The tumour was negative for CD34 (excluding cutaneous myxoma), PanCK, and desmin. Additional markers were uniformly negative, further excluding vascular, smooth muscle and other mesenchymal differentials. These findings aligned definitively with the WHO diagnostic criteria for dermal nerve sheath myxoma.
Conclusion: This report presents the first documented case of DNSM in the penis, expanding the anatomic spectrum of this rare tumour. The diagnosis relied on histomorphology (cord-like/syncytial architecture) and S100 positivity, with CD34 negativity excluding cutaneous myxoma. The clinical history suggests this likely represented recurrence after incomplete excision a decade prior, emphasizing the necessity of pathological evaluation for all penile masses, even those clinically deemed benign.

E-PS-26-066

Investigation of concordance between prostate core biopsy and prostatectomy tumour grade over one year at MMUH, Dublin

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Background & Objectives: Prostate cancer grading is persistently the most important predictor of overall outcome in localized disease. In 2014, the ISUP modified the Gleason score system to reduce the degree of upgrading from biopsy to radical prostatectomy specimens and improve reproducibility. The objective was to investigate the correlation of prostatectomy specimen and prostate core biopsy Gleason score and grade group.
Methods: Between September 2023 and September 2024 89 prostatectomy specimens were processed at MMUH. Reports were reviewed and compared to reports of correlating prostate core biopsy. Report deemed concordant if there was no difference in tumour grade between prostate core biopsy and prostatectomy specimen using the Gleason score system or grade group.
Results: The most common Gleason grade on prostatectomy and prostate core biopsy was 3+4 (n=60). Concordance was identified in 85% of the cases (n=77). Of the disconcordant Gleason grades, 8 (66%) were upgraded on prostatectomy specimen, 4 (33%) were downgraded. The highest rate of upgrading was seen in biopsies with Gleason score 3+3 (66%) and downgrading was seen in 50% of biopsies with Gleason score 3+5. Grade Group 2 was the lowest grade a prostatectomy specimen was downgraded to
Conclusion: The concordance of 85% is relatively high compared to previous studies which have demonstrated concordance of 54.8%-68%. Under grading is frequently seen when evaluating Gleason scores at biopsy. However, there are many factors which impact Gleason score correlation, for example, smaller prostate glands and higher percent tumour volume. Recommendations to expand this study include; a follow-up study to compare concordance, to identify and review clinical details which may demonstrate predictive factors, such as Prostate Specific Antigen and timing of the prostatectomy and identify number of core biopsies and percentage of tumour seen on core and to assess whether they are contributing factors in the upgrading or downgrading of the tumour grade.

E-PS-26-067

Expression and prognostic value of PD-L1 in urothelial bladder carcinomas: a retrospective study

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Background & Objectives: PD-L1 expression serves as both a predictive biomarker for immunotherapy response and a potential prognostic indicator in advanced bladder cancer. While its predictive role is well established, its prognostic significance remains controversial.
We evaluated PD-L1 expression in urothelial bladder carcinomas (UBC) and its associations with survival outcomes and clinicopathological features in Tunisian patients.
Methods: We retrospectively studied UBC patients treated surgically at Habib Thameur Hospital between 2016 and 2021. PD-L1 status was assessed by immunohistochemistry (clone 22C3) using the Tissue MicroArray (TMA) technique, with positivity defined as Combined Positive Score (CPS) ≥10. Comprehensive clinicopathological data were collected, and survival analyses were performed using Kaplan-Meier and Cox proportional hazards regression models.

Results: This study included UBC 142 patients. The mean patient age was 67.4 years (range: 29–90), with a male-to-female ratio of 8.46. The Tumours were classified as low-grade in 47.88% and high-grade in 52.12%.The most frequent pathological stage was pTa (35.21%). PD-L1 positivity (CPS ≥10) was identified in 10 cases (7%), showing predominant immune cell staining patterns. With a median follow-up of 54 months, PD-L1+ patients exhibited significantly reduced overall survival compared to PD-L1- cases (60.86 vs. 86.79 months; p=0.04). Multivariate analysis confirmed PD-L1+ as an independent predictor of poor prognosis (HR=4.42, 95% CI: 1.41-13.86; p=0.011), along with nodal metastasis (p=0.05) and increasing age (p=0.009). PD-L1+ tumours demonstrated significant associations with advanced stage (p=0.032) and concomitant carcinoma in situ (p=0.006).
Conclusion: Our findings demonstrate that PD-L1+ (CPS ≥10) represents an independent prognostic marker in UBC, associated with worse survival and aggressive characteristics (CIS, advanced stage). These results underscore the need for expanded research on PD-L1's prognostic role in bladder cancer and warrants further investigation of its biological mechanisms and clinical implications.

E-PS-26-068

Has CK20 alone the power to improve pT1 urothelial carcinoma stratification? Molecular phenotypes meet sub-staging

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Background & Objectives: The classification in molecular phenotypes (MP) is still poorly understood in non-muscle-invasive bladder urothelial carcinoma. We characterized with immunohistochemistry the MP of a cohort of pT1 high-grade urothelial carcinomas (HGUC) to investigate MP correlation with extension of lamina propria (LP) invasion and predictive value for progression and recurrence.
Methods: Immunohistochemical markers (CD44, CK5/6, CK20, P-PARg) and a simple score system were employed as a surrogate of molecular analysis to stratify into Luminal and Basal phenotypes a series of pT1 HGUC diagnosed between 2013 and 2021 on TUR specimens. ROL system was adopted to quantify LP invasion, and classified cases were classified in ROL1 (<1mm) and ROL2 (>1mm).
Results: A total of 192 confirmed pT1 HGUC were analysed. Mean age was 73yrs, with male predominance (74%); 83 cases were ROL1 (43%) and 109 ROL2 (57%). Luminal and basal phenotype was present in 141 (73%) and 10 cases (5%); 32 showed a Mixed phenotype (17%) and 9 were Null (4,7%). Of the 156 pts with FUP, most cases were Luminal (117, 75%), only 9 Basal (6%), 27 Mixed (17%) and 3 Null (2%); at a median FUP of 24 months (IQR: 12.3-40), 24 patients had progression (15%) and 52 recurrence (33%). At multivariate Cox regression analysis, CK20 expression showed a protective effect for progression on all cases (HR=0.40, 95% CI 0.17-0.94; p=0.036); on the contrary, no correlation was found between ROL and MP, and no significant predictive role was detected when stratifying for ROL categories.
Conclusion: Clinical management of pT1HGUC patients is often challenging and relatable tools for risk stratification are still needed. Our results suggest that MP with immunohistochemistry is not able to stratify patients risk of progression, nor to improve sub-staging predictive value; interestingly CK20 expression alone might be protective, independently from MP, but further validation is needed.

E-PS-26-069

Immunohistochemical evaluation of potential prognostic and predictive markers in bladder transitional cell carcinoma

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Background & Objectives: Urinary bladder carcinoma belongs to the most common cancers and represents the ninth leading cause of death in men. Diagnosis is based on histological evaluation of tumour surgical specimens, which is classified into several subtypes, the most frequent being the urothelial carcinoma, subdivided into low-grade and high-grade papillary lesions, non-invasive or invasive. The diagnosis of the different subtypes is then supported by detection of certain protein-expression profiles. In the presented work, prognostic value of several such proteins expression is evaluated in a retrospective study.
Methods: Over 250 cases of urothelial bladder carcinoma were diagnosed according to the WHO 2022 criteria. Expression of CK 5/6, CK7, CK20, p63, E-cadherin, AIF (apoptosis inducing factor), survivin and Ki67 were evaluated by immunohistochemistry. Products of staining intensity (0-3) and percentage of positive cells (1-10) were calculated for cytoplasmic/membrane expressions, nuclear expressions were evaluated as percentage only. Correlation of expression profiles with tumour stage and grade were statistically evaluated.
Results: Except for AIF, staining intensity did not show any significant differences between the different stages and the grades of the tumours. Evaluation of cytokeratin positive cells percentages showed significant differences between stage pTa and pT1 or pT2. Cytokeratin expression was not significantly different between low grade and high-grade carcinomas. The percentage of AIF, survivin and Ki67 -positive cells was significantly increased in high-grade versus low-grade tumours, the expression of p63 showing the opposite difference. The percentage of survivin and Ki67 -positive cells was significantly increasing from stage pTa through pT1 to pT2.
Conclusion: Evaluation of cytokeratins 5/6, 7 and 20 is of limited diagnostic or prognostic significance. The number of AIF-positive cells correlate with the grade of the tumour. Expression of survivin and Ki67 was increasing with both, the stage and the grade of bladder carcinomas, providing useful prognostic and predictive factors of the tumour.

Funding: EU NextGenerationEU through the Recovery and Resilience Plan for Slovakia under the project No. 09I03-03-V03-00046

E-PS-26-070

miRNA-371 in testicular germ cell tumours

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Background & Objectives: Patients with testicular tumours require adequate diagnostics and follow-up, currently done through classic protein serum biomarkers evaluation: lactate dehydrogenase, alpha fetoprotein and beta chorionic gonadotropin. However, research of miRNA's, especially miRNA-371 as more specific and sensitive biomarker has emerged.
Methods: Serum levels of lactate dehydrogenase, alpha fetoprotein, beta chorionic gonadotropin and miRNA-371 were measured in 16 patients with testicular tumours (seminoma or non- seminoma) during initial disease presentation and post-orchidectomy in order to evaluate

and compare miRNA-371 to classical markers. miRNA- 371 values were analysed and compared to different histological components. miRNA value was expressed in relation to referent sample (<5 as negative with small probability of tumour, 5-10 as indetermined, >10 as positive with great tumour probability).
Results: All sixteen cases were initially grouped according to the type of testicular tumour and stage of the disease, there were 9 pure seminomas and 7 mixed germ cell tumours. All patients had positive miRNA values (far higher than 10) before orchiectomy, while number of cases with other 3 positive markers was significantly lower. The lowest percentage of miRNA levels had cases with smaller tumour size. Depending on the stage there were positive cases after surgery as well.
Conclusion: Testicular tumours affect great number of patients, especially those of younger age, therefore research of new, more reliable markers is necessary in order to enable better diagnostics and follow-up. miRNA's as potential biomarkers have a role in carcinogenesis, as oncogenes or tumour suppressors. According to current findings regarding miRNA-371 in testicular tumours, it appears to be more sensitive and specific biomarker compared to the ones routinely used.

E-PS-26-071
Same stage, different fate: pelvic fat invasion independently identifies high metastases risk in pT3a RCC. A call for subclassification
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Background & Objectives: Pathologic T3a renal cell carcinoma (RCC) includes tumours with extension into perirenal fat, renal sinus fat, or renal vein; however recent evidences have shown that these distinct invasion patterns may have different prognostic implications, supporting the need to reconsider the current classification to better reflect the different biological behaviour of p T3a tumours. The aim of our study is to evaluate the prognostic impact of specific infiltration patterns and pathological features (grade, necrosis and lymphovascular invasion) of pT3a RCC patients.
Methods: We retrospectively analysed 102 patients with clear-cell pT3a RCC. Tumours were classified by site of extra-renal extension: pelvic vs. perirenal fat invasion. Metastatic events were taken into account, and both univariate and multivariate analyses were performed to identify independent predictors of metastases.
Results: Metastatic progression occurred in 69 of 102 patients (67.7%). Pelvic invasion was present in 53 cases (52%), and perirenal invasion in 49 (48%). Metastases occurred more frequently in patients with pelvic fat invasion (43/53, 81.1%) than in those with perirenal invasion (26/49, 53.1%) ($p = 0.002$, chi square test). At multivariate analysis, pelvic fat infiltration was an independent predictor of metastases (OR: 2.19, 95% CI: 1.08–5.91, $p = 0.04$), along with lymphovascular invasion (OR: 4.56, 95% CI: 1.16–17.9, $p = 0.03$). Necrosis and tumour grade were not significantly associated (all $p > 0.3$).
Conclusion: Pelvic fat invasion is associated with a significantly higher risk of metastasis compared to perirenal fat invasion in pT3a RCC, regardless of tumour grade and necrosis. These findings reinforce the need for redefining subclassification of pT3a disease to enhance prognostic accuracy and inform postoperative surveillance strategies.

E-PS-26-073
Adult Wilms tumour: a rare case of epithelial-predominant nephroblastoma mimicking renal cell carcinoma
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Background & Objectives: Wilms tumour (nephroblastoma) is a malignant renal neoplasm that typically affects children, while its occurrence in adults is exceptionally rare, representing less than 1% of all adult renal tumours. Due to its rarity, adult Wilms tumour is often misdiagnosed as renal cell carcinoma, posing a significant diagnostic and therapeutic challenge.
Methods: We present the case of a 40-year-old male with a renal mass identified during imaging. A total nephrectomy was performed under clinical suspicion of renal cell carcinoma. Gross examination revealed that the entire kidney was replaced by tumour tissue measuring up to 180 mm, with nodular architecture and focal myxoid degeneration.
Results: Microscopic analysis showed that the tumour was composed predominantly (over 90%) of epithelial cells, round to cuboidal in shape, with scant basophilic cytoplasm, hyperchromatic nuclei, and prominent nucleoli. These cells formed glandular, cribriform, and occasional rosette structures. The blastemal component accounted for less than 10%, while the stromal component was sparse to nearly absent. Focal necrosis was present in less than 10% of the tumour. The tumour infiltrated the renal capsule and extended into the renal sinus. Immunohistochemically, tumour cells showed diffuse positivity for TLE-1, CD99, Bcl-2, CD56, CK AE1/AE3, and CAM5.2, and focal positivity for Chromogranin A, CK8/18, MyoD1, Vimentin, Cyclin D1, NSE, WT-1, and p63. INI1 was retained. The tumour was negative for a broad panel of other markers including RCC, CAIX, EMA, and CD34, excluding other types of tumours. Based on morphology and immunoprofile, the diagnosis of Wilms tumour was confirmed.
Conclusion: Adult Wilms tumour is a rare but aggressive malignancy and should be considered in the differential diagnosis of renal masses in young adults. Accurate histopathological identification and prompt multimodal therapy are critical for improving outcomes.

E-PS-26-074
The discrepancy between Gleason score in prostate biopsies and radical prostatectomy specimens: predictive factors
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Background & Objectives: Prostate cancer (PCa) is one of the most common malignant tumours in men worldwide and in Tunisia. Diagnosis confirmation relies on prostate biopsy (PB) with Gleason score (GS) assessment, a key element in therapeutic decision-making. However, discrepancies in GS between PB samples and corresponding radical prostatectomy (RP) specimens have been reported. This study aimed to evaluate the concordance of GS between PB and RP specimens and identify predictive factors for these discrepancies.
Methods: A retrospective study was conducted on patients with prostate adenocarcinoma confirmed by PB and treated by RP in pathology department of Sfax University Hospital over 11 years (January 2013–December 2023). Two pathologists reevaluated GS on both PB and RP specimens. Epidemiological, clinical, biological, radiological, and histological variables were collected. GS and ISUP grade concordance was assessed using Cohen's Kappa coefficient. Logistic regression analyses identified independent predictive factors of GS discordance. ROC curves determined optimal thresholds for significant quantitative variables. Statistical significance was set at $p \leq 0.05$.
Results: Forty-nine patients were included. Concordance rates for GS and ISUP grade between PB and RP were 69.39% and 57.14%, respectively, with weak agreement (Kappa = 0.39 and 0.29 respectively). PB underestimated GS in 30.61% of cases, without overestimation. Univariate analysis showed that a low percentage of grade 4 on PB and low-risk D'Amico classification were significantly associated with GS discordance ($p < 0.001$ and $p = 0.004$). The optimal threshold for grade 4 percentage was 2.5%, with 73.5% sensitivity and 93.3% specificity. Multivariate analysis identified the percentage of grade 4 on PB as the only independent predictor of GS discordance between PB and RP ($p = 0.021$; OR = 1.608; 95% CI [1.073–2.411]).

Conclusion: The concordance of GS between PB and RP is crucial in PCa management. Identifying predictive factors of GS discordance enhances prognostic accuracy and therapeutic strategy.

E-PS-26-075

Molecular subtyping of non-muscle invasive urothelial carcinoma by immunohistochemical analysis

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Background & Objectives: Non-muscle invasive urothelial carcinoma (NMIUC) has a heterogenous outcome and is a challenge to treat. The aim of this study was to categorize NMIUC's into basal, luminal and p53 like categories, using surrogate immunohistochemical (IHC) markers and to correlate with prognosis.
Methods: A retrospective study with a sample size of 100 NMIUC's (Ta,Tis,T1). Tissue microarray slides were stained with nine markers. Tumour cell scores (TCS) for each antibody was evaluated either as intensity of staining or percentage of positive cells or both as designed by Hardy et al. After obtaining TCS normalised scores, Hardy et al's IHC Classifier tree algorithms were applied.
Results: Only three IHC markers ie Gata3 (cutoff 0.21), CK5/6 (cutoff 0.09) and P16 (cutoff 0.42) were found useful in the molecular subtyping. In cohort A (all cases), Gata 3 was positive (value > 0.21) in **94 cases** which fell in the luminal category (Ta 64, T1-30, Rec 34) and in **3 cases** with a value of <0.21 with CK5/6 <0.09 taking it again towards the luminal category. No case fell in the basal category. Of the 94 luminal cases, p16 divided these cases with a cutoff value of < 0.42 ie the **URO group** (n=41) and >0.42 ie the **GU (genomically unstable) group** (n=49). In the URO group 16/41 cases recurred and one case upstaged (Ta to T1). In the GU group , 18/49 recurred and 3 cases upstaged (T1 to T2). No case upgraded.
Conclusion: By using three antibodies (GATA3, CK5/6 and p16), NMIUC's can be divided into luminal (URO &GU) and basal groups on a routine basis. More cases upstaged in the GU group concluding that GU group performs worse than the URO group. DFS was more in the URO group.

E-PS-26-076

Bilateral epididymal papillary cystadenoma and metastatic clear cell renal cell carcinoma: differential diagnosis

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Background & Objectives: Von Hippel-Lindau (VHL) syndrome is an autosomal dominant, multisystem, inherited disorder caused by germline genetic variants of the VHL gene. It is characterized by the occurrence of highly vascularized tumours such as hemangioblastomas of the central nervous system and retina, visceral tumours such as clear cell renal carcinoma, pheochromocytoma, epididymal cystadenomas, pancreatic neuroendocrine tumours, and cysts.
Methods: We present a case report of von Hippel-Lindau disease associated with multiple cerebellar hemangioblastomas, clear cell renal cell carcinoma, pancreatic cysts, ocular disturbances and the presence of a bilateral epididymal mass. A 57-year-old man presented with hard, painless lumps in the area of both testicles, measuring up to 2 cm. Ultrasonography and radiographic examinations showed multilocular tumours in the bilateral epididymis, which were surgically resected.
Results: Histopathological examination revealed cystadenomas in both epididymides. In the right epididymis, in addition to the cystadenoma, there was a relatively well-circumscribed nodule with morphological and immunohistochemical characteristics of metastasis of clear cell renal cell carcinoma (CCRCC). Cystadenocarcinoma of the epididymis was also considered in the differential diagnosis. The patient has not received adjuvant therapy and is continuing to experience further complications related to VHL syndrome.
Conclusion: In this case, based on the immunohistochemical expression of markers for CCRCC, we cannot rule out epididymal metastasis from this carcinoma.

E-PS-26-077

Pathological challenges in frozen section examination for excisional biopsy of testicular masses: insights from a large retrospective cohort study

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Background & Objectives: Frozen section examination for excisional biopsy (FSEB) of testicular lesions is an underused pathological & surgical approach considering the increasing number small testicular lesions that are found to be benign on radical orchidectomy specimens. This study aims to address existing gaps in the literature regarding pathology issues that may discourage practicing pathologists from performing FSEB for testicular masses.
Methods: We describe a large retrospective cohort of FSEB in our academic institution to assess its accuracy and discuss its pathological challenges and pitfalls. The algorithm determined by FSEB diagnosis was that radical orchidectomy would be carried out for malignant diagnoses only.
Results: From 2005 to 2024, 137 FSEB (median of 10 FSEB per year) were performed in 133 patients with a median tumour size of 0.9 cm (range 0.2-4 cm). The most common diagnoses on FSEB were Leydig cell hyperplasia/tumour and seminoma, both diagnosed in 37 (27%) and 37 (27%) cases. On FSEB, benign diagnoses represented 58% of cases which allowed 79 testis to remain in situ. The sensitivity and specificity of FSEB for malignancy were 100% and 96.3%, respectively. There were no false negatives and no delayed radical orchidectomy was required. One cause of false positive was the impossibility of immediate ancillary testing for mature teratomas without germ cell neoplasia in situ. Some histological pitfalls including regression changes and morphological changes of Leydig cell tumours became particularly challenging for non-uropathologists on FSEB. Immunohistochemistry was mostly unaffected by previously frozen tissue with the exception of the less precise, but still positive OCT3/4.
Conclusion: Our experience has proven that FSEB is accurate and safe for distinguishing benign from malignant testicular lesions if one is aware of the common pitfalls of testicular pathology. We hope this study will help pathologists become more familiar with testicular frozen sections and serve as a useful resource for routine practice.

E-PS-26-078

Survivin and Ki-67 co-expression: a potential prognostic indicator in urothelial cancer

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Background & Objectives: Urothelial carcinoma is one of the most common malignancies in Europe, with invasive urothelial carcinoma ranking as the fourth most prevalent cancer. Non-invasive forms are notable for their high recurrence rates, highlighting the need for reliable prognostic markers. Survivin, an anti-apoptotic protein, and Ki-67, a cell proliferation marker, are associated with tumour progression across various cancer types. This study evaluates the correlation between these markers in urothelial carcinoma, providing insights into tumour behaviour and potential prognostic significance.
Methods: We analysed 145 formalin-fixed, paraffin-embedded tissue samples from patients with low-grade and high-grade papillary urothelial carcinoma. Following deparaffinization, immunohistochemical staining was performed to detect nuclear expression of Survivin (rabbit monoclonal antibody) and Ki-67 (mouse monoclonal antibody). Immunofluorescence microscopy was conducted to confirm co-localization of these markers. Statistical analyses (Pearson correlation coefficient, Spearman's correlation coefficient) were performed to assess their correlation.
Results: Statistical analyses revealed a significant correlation between Ki-67 and Survivin expression across all 145 urothelial carcinoma samples ($p < 0,01$). Immunofluorescence confirmed the presence of both markers within the identical cell nuclei, with differences in expression patterns corresponding to the degree of cytological atypia.
Conclusion: The significant correlation between Survivin and Ki-67 expression underscores their potential as combined prognostic markers in urothelial carcinoma. Elevated levels of these proteins have been individually associated with poor clinical outcomes, including reduced survival rates and increased recurrence. Their combined assessment may offer valuable insights into tumour aggressiveness and therapeutic targeting strategies, aiding in identifying high-risk patients.

Funding: „Funded by the EU NextGenerationEU through the Recovery and Resilience Plan for Slovakia under the project No. 09I03-03-V03-00046"

E-PS-26-082

HER2 expression in urothelial neoplasms

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Background & Objectives: The clinical significance of HER2 expression in urothelial cancer is increasing in line with the application of antibody-drug conjugates in advanced or metastatic urothelial cancer. In this study we aimed to define the clinicopathologic significance of HER2 expression in non-muscle invasive (NMIBC) and muscle-invasive urothelial carcinomas (MIBC) using immunohistochemical stain and silver in situ hybridization.
Methods: A cohort of 60 non-invasive papillary urothelial carcinoma and 54 muscle-invasive urothelial carcinoma was used. They were immunostained with HER2 using the whole section. HER2 protein expression was interpreted using FDA criteria (0,1+, 2+, 3+), and categorized into negative (0, 1+) and positive (3+). When the HER2 expression was 2+, we underwent silver in situ hybridization and interpreted using FDA criteria. Clinicopathologic features were also investigated.
Results: HER2 expression is observed in 6/60 NMIBC (10%), whereas MIBC showed positive results in 23/54 (43%). There is a significant regional heterogeneity of positive area in both NMIBC and MIBC. HER2 expression was found to be associated with progression-free survival in MIBC, and was associated with recurrent free survival in NMIBC.
Conclusion: It is suggested that HER2 expression is associated with tumour progression or recurrence. The HER2 expression rate is higher than in other studies, which is thought to be the result of staining of whole sections rather than tissue microarray to overcome regional heterogeneity.

Funding: This work was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Minist (2022R1A2C1011889 for KHL, 2021R1F1A1062783 for SSK)

E-PS-26-083

Clinicopathological features of Testicular Sex-cord Stromal Tumours (TSCSTs) - Institutional experience

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Background & Objectives: Testicular sex-cord stromal tumours (TSCSTs) represent a group of rare primary testicular tumours, originating in the supporting tissue of the testis. TSCSTs are neoplasms mostly with benign clinical behaviour. We analysed clinicopathological features of TSCSTs diagnosed in our Institute.
Methods: A surgical pathology archive from 2009 to 2024 has been searched for cases of TSCSTs in the final diagnosis. Patients' age, tumour subtype, tumour size, lymphovascular invasion, mitosis, necrosis, and immunophenotype were analysed. In cases with the presence of clinicopathological characteristics suggestive of malignancy, patients' follow-up were analysed.
Results: Radical inguinal orchiectomy as a surgical treatment of testicular tumours was performed in 384 patients. TSCST was diagnosed in 10 patients (2.6%) with an average age of 35.60 ± 10.55. The mean tumour size was 19.80 ± 9.41mm. Benign Leydig-cell tumour was the most common, and diagnosed in seven patients (70%). In one case each, a malignant Leydig cell tumour, malignant TSCST not otherwise specified and Large cell calcifying Sertoli cell tumour with uncertain behaviour were diagnosed. None of the patients disclose disease progression during follow-ups from 15 to 120 months. In each TSCST, immunopositivity for at least two of the following antibodies: Melan A, Calretinin, Inhibin A, and Vimentin was detected.
Conclusion: TSCSTs are a rare group of neoplasms, most commonly comprised of cells resembling nonneoplastic Leydig cells. It is a heterogeneous group of tumours with diverse morphology, cell origin and biological behaviour. Some cases occur only sporadically or disclose unspecific morphology and immunophenotype. Correct recognition of morphology, knowledge of diagnostic criteria, and immunohistochemical analysis are required for tumour typing and determination of its malignant potential. All of our malignant TSCTs revealed favourable clinical outcomes.

E-PS-26-085

Loss of glutamine synthetase expression may support a diagnosis of urothelial carcinoma in situ

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Background & Objectives: Glutamine synthetase (GS) is a critical enzyme that is responsible for the synthesis of glutamine from glutamate and ammonia and hence is involved in glutamine metabolism. Glutamine plays an important role in maintaining the function of many cells as a nucleotide and a main source of energy for rapidly dividing cells. The aim of this study was to investigate the immunohistochemical expression of GS in the flat urothelial lesions of the bladder posing a diagnostic challenge (Urothelial carcinoma in situ? /Non-tumoral urothelium?)
Methods: This study included 50 patients diagnosed with urothelial carcinoma in situ (UCAIS) between 2022 and 2025 in our department. Paraffin blocks containing UCAIS areas with surrounding non-neoplastic urothelium were selected from the H&E-stained sections of the patients. Immunohistochemical staining was performed with GS antibody. The presence or absence of cytoplasmic expression in UCAIS and non-neoplastic urothelium were noted and results were statistically compared.
Results: 6 cases were excluded from the study because of sub-optimal staining results. Non-tumoral epithelium was not observed in the immunohistochemically stained sections of 18 patients. However, GS was not expressed in the UCAIS areas in these cases. In the remaining 26 cases, which included both UCAIS and non-tumoral urothelium, we observed that GS expression was maintained in non-tumoral urothelial areas, however it was lost in UCAIS areas. This difference was statistically significant ($p<0.001$).
Conclusion: To the best of our knowledge, this is the first study to evaluate GS expression in urothelial tumours, in which we showed that GS expression is maintained in non-tumoral urothelium, however its expression is lost in UCAISs. This difference may aid in the differential diagnosis of UCAIS in routine pathology work up. However, the molecular mechanisms underlying GS homeostasis and glutamine metabolism in UCAIS and other urothelial tumours need further effort to be discovered in the future.

E-PS-26-086
Tumour heterogeneity and prognostic significance of PD-L1 expression according to the durvalumab companion VENTANA (SP263) assay in metastasizing urothelial bladder carcinoma
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Background & Objectives: To determine the distribution of the therapeutic target programmed cell death 1 ligand 1 (PD-L1) in metastasizing muscle-invasive urothelial bladder carcinoma and assess its impact on overall survival (OS).
Methods: A total of 124 patients without any neoadjuvant therapy underwent radical surgery with curative intent and were followed prospectively. We constructed tissue microarrays with multiple samples from their primary tumours (PTs) and 1–3 corresponding lymph node metastases (LNMs; $n = 241$) and determined PD-L1 expression in all samples using the VENTANA (SP263) Assay. Differences in PD-L1 expression between various tumour components and OS were assessed using appropriate statistical tests.
Results: On average, 2.9 tumour foci per patient were analysed. The mean PD-L1 staining rate was significantly higher in tumour cells (TCs) than in immune cells (ICs) in the PTs (12.5% vs. 6.4%, $p < 0.05$) but not in the metastasizing tumour components (MTCs; 10.3% vs. 9.3%, $p = 0.67$). The frequency of high PD-L1 scores (TC/IC25%) was similar in PTs and MTCs (16.9% vs. 21.0%, $p = 0.23$). Additionally, 10.5% of patients presented with homogeneously high PD-L1 scores in all tumour foci, while 20.2% presented with high and low scores. Intermetastatic heterogeneity in PD-L1 scores was observed in 20.3% of the 69 patients with multiple LNMs. A high PD-L1 score in the PT independently predicted a favourable OS.

Conclusion: Primary-to-metastatic conversion of the PD-L1 score occurred in 20.2% of patients, and testing both components might improve patient selection for immune checkpoint therapies. A favourable OS for patients with high PD-L1 scores is compatible with tumour suppressive effects, as recently described for this biomarker.

Funding: Thurgauische Krebsliga, Stiftung für klinisch-experimentelle Tumorforschung (SKET) and a Protected Research Time Grant (University of Bern)

E-PS-26-087
Paratesticular well-differentiated liposarcoma with osseous metaplasia presenting as in indirect inguinal hernia: a case report
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Background & Objectives: Liposarcomas are the most common type of spermatic cord sarcomas in adults. We report on a case of well-differentiated liposarcoma with metaplastic ossification, an unusual finding within these tumours.
Methods: We report on a case of a 77-year-old male patient, presenting with an inguinal mass, initially diagnosed as an indirect inguinal hernia. During follow-up, the mass showed rapid growth and with the onset of pain, hernioplasty was performed. During the procedure, a large multinodular spermatic cord mass was identified and partially resected. A CT scan also revealed extensive areas of fat tissue and calcifications. The patient subsequently underwent radical orchiectomy.
Results: Gross examination of the specimen revealed an extensive spermatic cord mass, measuring 10x6x4,5cm, composed of large areas of adipose tissue with multifocal haemorrhagic tissue and hard consistency areas. Microscopic evaluation showed a heterogeneous proliferative lesion composed of mature adipocytes containing fibroblastic bands and extensive areas of osseous metaplasia. In the fibrotic component, spindle-shaped, atypical, and pleomorphic cells with hyperchromatic nuclei were observed. Among the mature adipocytes, rare lipoblasts were noted. Immunohistochemical study for MDM2 and p16 was positive, and a diagnosis of a well-differentiated liposarcoma/ atypical lipomatous tumour was made.
Conclusion: Liposarcomas of the spermatic cord can be clinically asymptomatic in the absence of rapid growth and may mimic indirect inguinal hernias. Surgical resection with widely negative margins is generally curative, although late recurrence can occur. Excluding benign lipomatous tumours, as well as differentiating well-differentiated from dedifferentiated tumours, is important as it affects prognosis — the latter being associated with a risk of metastatic disease. We highlight the importance of maintaining a high level of clinical suspicion for malignant disease in the presence of a painful inguinoscrotal mass, as well as the relevance of the pathological examination of these specimens.

E-PS-26-088
Comparative analysis of the efficacy between MRI lesion-targeted or combined versus standard prostate needle core biopsies in detecting prostatic adenocarcinoma
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Background & Objectives: Prostate needle core biopsies (PNBs) are the gold standard for diagnosing prostatic adenocarcinoma, the most prevalent malignancies in men in North America. The NSH Central Zone processes a high volume of prostate biopsies. Recently, the integration of MRI in detecting prostate nodules into the diagnostic workflow has led to more lesion-targeted biopsies. This study compares the performance indicators of PNBs obtained in 2016 (pre-MRI era) and in 2022/23 (post-MRI era) to assess the impact of MRI-targeted biopsies on the diagnostic yield and quality control benchmarks.
Methods: We retrospectively analysed 1,345 PNB cases during the two years. Biopsy cases were classified into systematic, MRI lesion-targeted, or combined biopsy (MRI lesion-targeted and systematic) types. The cases were further broken down by diagnoses and grade group (GG) if the results were positive for prostatic adenocarcinoma. Statistical analyses using chi-square tests were performed to compare trends in biopsy usage, positive detection rates, and quality control markers such as atypical small acini proliferation (ASAP) diagnoses.
Results: Chi-square analysis ($p < .00001$) revealed a significant increase in MRI-targeted and combined biopsies from 2016 to 2022/23. However, the positive case rates between the systematic and MRI-targeted/combined biopsies were not significantly different ($p \approx 0.12$). The rate of atypical gland diagnoses was 4.98% (67/1345), meeting the established quality benchmark of <5%. Notably, no ASAP cases were identified in MRI-targeted or combined biopsy groups.
Conclusion: The number of MRI lesion-targeted and combined biopsies for diagnosing prostate cancer has significantly increased in NSH Central Zone. Despite this shift, positive case rates remain comparable between systematic and MRI-targeted/combined biopsy approaches. Additionally, the atypical gland diagnosis rate remains within the accepted <5% benchmark, reinforcing the region's consistency and quality of diagnostic practices. These findings highlight the growing role of MRI in biopsy guidance while maintaining diagnostic reliability.

E-PS-26-089

A rare case of low-grade oncocytic fumarate hydratase-deficient renal cell carcinoma

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Background & Objectives: Fumarate hydratase (FH)-deficient renal cell carcinoma (FH-deficient RCC) is a rare and typically high-grade, aggressive subtype of renal cell carcinoma (RCC) characterized by alterations in the FH gene.
The 2022 World Health Organization (WHO) classification introduced a subset of FH-deficient RCC cases exhibiting low-grade eosinophilic oncocytic morphology, which appears to be associated with a relatively favourable prognosis. However, such cases remain exceedingly rare, with only a limited number reported in the literature.
Methods: Herein, we present a case of FH-deficient RCC with rare low-grade eosinophilic cytology. The patient was a 21-year-old male who was admitted to the hospital with abdominal pain. Abdominal computed tomography (CT) revealed a mass located in the lower and medial poles of the right kidney. Histopathological and immunohistochemical analyses confirmed FH deficiency, with findings consistent with low-grade eosinophilic morphology.
Results: In macroscopic examination the focus in the mid-pole of the kidney appeared solid and gray-white in colour, whereas the focus in the lower pole was dark brown and contained cystic areas.
Histopathological evaluation revealed tumour cells are composed of oncocytic cells with, prominent nucleoli, and occasional perinuclear halos. The cystic component, tubulucystic component is also observed in the lower pole focus, Importantly, no evidence of necrosis, mitotic activity, or high-grade morphological features was identified.
Tumour cells were negative for CK7, CK20, Carbonic Anhydrase IX (Ca-IX), and TFE3. In contrast, AMACR and SDHB showed positive immunoreactivity. Loss of FH expression was confirmed by immunohistochemical analysis, with FH staining being negative in both distinct foci of the tumour.
These findings support the diagnosis of FH-deficient renal cell carcinoma with low-grade eosinophilic morphology.
Conclusion: This case contributes to the understanding of the clinicopathological spectrum of FH-deficient RCC and highlights the importance of recognizing this rare morphological variant in clinical practice.

E-PS-26-090

Leydig tumour microenvironment induces T-lymphocyte recruitment and tubular epithelial testicular atrophy

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Background & Objectives: We report a patient, a 56-year-old male, with right testicular atrophy with a simultaneous occurrence of Leydig cell hyperplasia (LCH) and Leydig cell tumour (LCT).
The objective of the presented study was to explore both lesions' morphology and their contribution to atrophy and fibrosis.
Methods: Immunohistochemical analysis was performed, including a standard diagnostic antibody panel (PLAP, inhibin, WT-1, calretinin, Melan-A/MART-1, vimentin, and Ki-67). Immunophenotyping of the inflammatory cells differentiated between mononuclear cells, using primary antibodies for macrophages (CD68 and CD163) and B- and T-lymphocyte subgroups (CD20, CD8, CD5, CD4, and CD3).
Results: Physical examination revealed an above-average size of the left testicle, bilateral gynecomastia, and normal routine blood tests. Testicular ultrasonography showed an atrophic right testicle with hypoechoic masses measuring up to 6×9 mm. The right orchiectomy specimen appeared inconspicuous, with a single whitish nodule measuring 9 mm in diameter.
Leydig cell hyperplasia and atypical Leydig cell tumour with different morphology were diagnosed. Both LCH and LCT displayed the same immunoprofile. Additional immunophenotyping of the inflammatory cells was performed. Decreased spermatogenesis was observed, with sclerotic and hyalinized tubules. Lymphocytic aggregates were visible in the peritubular interstitium, and focal intraepithelial lymphocytes were noted. Peritubular lymphocytic cuffing was observed, indicating the early phase of a chronic inflammatory process with consequent destruction of the epithelium.
Conclusion: The B-lymphocyte cell population resided in areas surrounding the LCT, accompanied by the remaining mononuclear cells identified as macrophages. T-lymphocyte distribution suggested epithelial tropism and pronounced both peritubular and pericapillary cuffing. Based on these observations, the testis affected by LCH and LCT shows progressive germ cell epithelial destruction mediated by T-lymphocyte recruitment. Therefore, a mechanism of inflammatory mononuclear immune cell recruitment mediated by Leydig cell paracrine and endocrine stimulation has been proposed as a testicular microenvironment milieu shifter.

E-PS-26-091

Primary ASPS of kidney mimicking translocation RCC: a diagnostic conundrum

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Background & Objectives: **Background:** Alveolar soft part sarcoma (ASPS) is an uncommon and unique tumour, typically affecting

young individuals. It has been sparsely reported to affect kidney with only 3 cases reported in published literature. ASPS shares the molecular and immunohistochemical overlap with Translocation associated RCC and distinction of the two can be a diagnostic challenge.
Objective: To present the morphological, immunohistochemical and ultra structural features of primary ASPS of kidney.
Methods: Here we report a case of a 19-year-old female who presented with discomfort in the left flank region since last one year. On examination, a firm mass of 10*10 cm was palpated in the left hypochondrium with indistinct upper margins, CECT of the same showing mass arising from the kidney, pushing the pancreas anteriorly and abutting the spleen. With a clinical diagnosis of RCC, a left radical nephrectomy was performed. We performed histological, immunohistochemical and ultrastructural analysis on the primary tumour of kidney.
Results: Sections from the mass showed a tumour arranged predominantly in nested and alveolar pattern comprising of large, polygonal, highly pleomorphic tumour cells having abundant granular eosinophilic cytoplasm, vesicular chromatin, and prominent nucleoli. Necrosis, haemorrhage, tumour giant cell reaction and foci of dystrophic calcification were also noted.
On immunohistochemistry these tumour cells were immunopositive for TFE3 and Cathepsin K. SDH-B was retained. PAS positive diastase resistant intracytoplasmic needle shaped granules were seen.
Ultrastructural examination showed numerous intracytoplasmic needle to rhomboid shaped crystals. Based on the histological, immunochemical and ultrastructural findings a diagnosis of ASPS was rendered.
Conclusion: ASPS has morphological and molecular similarity to translocation associated RCC and poses diagnostic difficulty in kidney. Awareness and recognition of ASPS as one of primary renal sarcoma is important to avoid this pitfall. Ultrastructural examination is helpful for definitive diagnosis.

E-PS-26-092
Prostatic elastosis: a morphological feature to distinguish atrophy from adenocarcinoma in prostate needle biopsies
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Background & Objectives: Prostatic atrophy is a frequent mimic of adenocarcinoma, making their distinction in needle biopsies challenging. Atrophy incidence increases with age, and ischemia appears to be important in its pathogenesis. A correlation has been described between local prostatic arteriosclerosis and atrophy.
Elastosis has been found in 65–85% of prostates at autopsy and, like atrophy, is linked to ischemia and arteriosclerosis. Despite its frequency, its significance remains unclear and is often overlooked. Some morphological features help rule out adenocarcinoma in benign glands, known as "features against cancer," including atrophic cytoplasm, corpora amylacea, merging with benign glands, and inflammation. Elastosis may serve as an additional morphological feature supporting benignity, as an inverse correlation has been observed between elastosis and neoplastic lesions.
We aimed to determine the frequency of elastosis in prostate needle biopsies, assess its association with atrophy and cancer, and evaluate its potential as a histopathological marker.
Methods: We conducted a retrospective observational study at Médica Sur's Department of Anatomic Pathology, reviewing all prostate needle biopsies from January 1st to July 31st, 2024. Two residents and one senior pathologist reviewed each case, recording elastosis and the gland type it surrounded (atrophic or malignant). Atrophy was subclassified into hyperplastic, simple, cystic, sclerotic, and partial. In difficult cases, p63 immunohistochemistry confirmed basal cells.
Results: We reviewed 92 biopsies: 90.0% (80/92) showed atrophy, 56.5% (52/92) adenocarcinoma, and 35.9% (33/92) elastosis. Elastosis was exclusively observed around atrophic glands. Among atrophy cases, 41.3% (33/80) had elastosis, while none of the adenocarcinoma glands exhibited elastosis (0/52). Fisher's exact test showed a significant association between elastosis and atrophy ($p = 0.0036$), and a strong inverse association with carcinoma ($p < 0.00001$).
Conclusion: Elastosis correlates strongly with benign atrophic glands and may aid in ruling out carcinoma in prostate biopsies, as only atrophic glands exhibited elastosis.

E-PS-26-093
Spatial transcriptomics in bladder cancer: insights into tumour heterogeneity
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Background & Objectives: Urinary bladder carcinoma is a common malignancy with increasing incidence, occurring six times more often in high-income countries. It exhibits significant intratumoral heterogeneity, posing diagnostic challenges and contributing to variability in grading. Accurate differentiation of dysplastic changes and understanding their genetic basis are essential, alongside the clinical distinction between low- and high-grade lesions and analysis of mutational, transcriptomic, and proteomic profiles. Research in this field represents an important challenge for the future.
Methods: Using the 10X Visium Spatial Gene Expression technology, we focused on molecular profiling of selected urinary bladder tumours. This technology enables effective spatial analysis and visualization of the whole transcriptome within the morphological context of FFPE samples. We analysed bladder tumour specimens with low-grade and high-grade dysplasia, including cases without signs of invasion as well as tumours exhibiting invasive growth patterns, aiming to better understand the spatial transcriptomic landscape associated with tumour progression.
Results: In our analysis, we identified transcriptomic changes in genes involved in cell signalling and growth regulation (P2RY2, KIAA1324), extracellular matrix remodelling and cell adhesion (FBLN1, CLIC3), and epithelial cell differentiation and development (MAL, MALL), specifically within tumour areas with and without invasive growth. Spatial analysis provided new insights into tumour heterogeneity, including the ability to detect cells artificially damaged during sampling, which exhibited altered transcriptomic profiles.
Conclusion: Spatial transcriptomics has proven to be an effective approach for identifying distinct cell populations, particularly in the context of tumour heterogeneity. Through this method, we have identified potential transcriptomic alterations linked to the diverse biological behaviour of tumour cells. Interestingly, noteworthy changes were also observed in the transcriptomic profiles of surrounding non-epithelial supportive tissues. Moreover, the ability to reliably distinguish potentially false transcriptomic changes caused by sampling artifacts is of significant importance for ensuring accurate data interpretation and clinical relevance in cancer research.

Funding: Funded by the EU NextGenerationEU through the Recovery and Resilience Plan for Slovakia under the project No. 09I03-03-V03-00046

E-PS-26-094
p53 mutation phenotype and its correlation with ki67 and Her2 in metastasizing urothelial bladder carcinoma
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Background & Objectives: To assess the Ki67 proliferation marker and the Her2 amplification status in urothelial bladder carcinoma with and without p53 mutational phenotype.

Methods: Tissue microarrays with 978 samples of 1 mm in diameter from 124 primary tumours (PTs) and corresponding lymph node metastases (LNMs) were evaluated for p53 immunophenotype, Ki67 expression and Her2 gene status (VENTANA HER2 Dual ISH DNA Probe Cocktail).

Results: Of the evaluated tumour samples, 434 reveal a p53 mutational phenotype, 455 a p53 wild type and 30 could not be assigned to a category. In spot-by-spot analyses, tissues with p53 mutational phenotype have a significantly higher mean Ki67 staining than p53 wild type tissues (39.7% vs. 25.2%; $p < 0.05$). In addition, the frequency of Her2 amplification was significantly higher in tissues with p53 mutational phenotype (15.1% vs. 8.7 %; $p < 0.05$). The p53 phenotype of the PT is highly conserved in the LNM.

Conclusion: The increased Ki67 proliferation and Her2 amplification rate in urothelial carcinoma samples with p53 mutational phenotype are in line with a loss of tumour suppressor function and genomic stability. p53 status in the PT is highly conserved in the LNMs facilitating tissue testing for drugs targeting p53 mutations.

E-PS-26-095

p63 and HER2 expression patterns in plasmacytoid variant of urothelial carcinoma: immunohistochemical analysis and comparison with literature

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Background & Objectives: Plasmacytoid urothelial carcinoma (PUC) is a rare and aggressive variant of urothelial carcinoma characterized by discohesive tumour cell. It harbours CDH1 mutations, resulting in loss of e-cadherin expression, similar to lobular breast carcinoma or signet ring gastric cancer. Immunohistochemical (IHC) markers such as p63 and GATA3 may assist in confirming the diagnosis, while HER2 overexpression by IHC may provide potential therapeutic targets, particularly in the emerging era of antibody-drug conjugates.

Methods: A retrospective analysis was conducted on PUC diagnosed between 2015 and 2024. Tissue specimens were evaluated using IHC for p63 (clone BC4A4, Dako) and HER2 (clone SP3, Cell Marque). Staining intensity and proportion were scored using standard criteria; HER2 interpretation was performed using accepted guidelines on gastrointestinal system malignancies. Clinical and demographic data, including age, gender, metastasis status, and follow-up outcomes, were analysed.

Results: The study included 16 cases of PUC, with a male predominance (75%) and a mean age of 68 years (range: 50–83 years). 62.5% (10/16) of the cases presented with advanced-stage tumours (pT3/pT4), and metastasis was detected in 43.7% (7/16), primarily involving the liver and peritoneum. The average follow-up period was 18 months (range: 7–28 months), and 56.2% (9/16) of the patients died during follow-up. p63 expression was observed in only 50% (8/16) of the cases. HER2 overexpression (3+) was detected in 37.5% (6/16) of the cases. Cases with HER2 positivity were associated with higher stages (pT3/pT4) and worse outcomes. E-cadherin loss was noted in 70% of cases.

Conclusion: Lack of p63 expression may be challenging in the diagnosis of PUC, since it is expected to be negative in top differential diagnoses. Increased HER2 overexpression may provide alternative therapeutic options in patients with PUC.

E-PS-26-096

Urothelial carcinoma with chordoid features: a rare diagnostic pitfall illustrated by three cases

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Background & Objectives: Urothelial carcinoma (UC) with chordoid features is an exceptionally rare histological subtype that shows significant morphological overlap with various myxoid neoplasms, posing diagnostic challenges. We present three cases to highlight the clinicopathological and immunohistochemical features of this subtype and to emphasize the difficulties in differential diagnosis.

Methods: The patients included a 58-year-old woman and two men aged 55 and 65, all presented with macroscopic haematuria. In two of the cases, tumours were located in the left ureteral orifice region of the bladder and measured 4 cm and 6 cm in diameter. All tumours were sampled by transurethral resection. Histologically, each tumour showed conventional urothelial carcinoma with variable proportions of chordoid features characterized by tumour cells arranged in reticular or cord-like patterns within a myxoid stroma. All cases displayed extensive and deep lamina propria invasion. In the female patient, tumour also exhibited extensive muscularis propria invasion, widespread lymphovascular invasion, and areas of sarcomatoid differentiation. Immunohistochemical markers of urothelial lineage showed variable expression in the chordoid areas.

Results: All tumours demonstrated deep lamina propria invasion and adverse prognostic features such as lymphovascular and perineural invasion. Notably, one case revealed a clear morphological transition between chordoid areas and sarcomatoid differentiation, suggesting that this pattern may represent a precursor or transitional stage toward sarcomatoid transformation—a hypothesis previously proposed in the literature.

Conclusion: Only a limited number of cases of this histological subtype have been reported. Greater awareness is essential for pathologists—primarily to avoid misdiagnosis due to its morphological overlap with various tumour types, and secondarily to understand its potential prognostic relevance. Further multicentre studies are required to clarify the clinical implications of chordoid features in urothelial carcinoma.

E-PS-MD-01 E-Posters Molecular Diagnostics Pathology Symposium (MD)

E-PS-MD-01-001

A methylation-based diagnosis of an intracranial MPNST with unusual morphological and immunophenotypical features case report

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Background & Objectives: Malignant peripheral nerve sheath tumour (MPNST) is a rare, aggressive spindle-cell tumour that seldom develops intracranially. This study aims to report a case of this rare location and provide new insights into its clinical presentation in various stages.
Methods: We integrated clinical and imaging data with histopathology and molecular analysis. Retrospective DNA methylation profiling of the first three biopsies was performed using EPICv2 BeadChip arrays and classified by the Heidelberg classifier v12.8. Therapy targets were assessed with the TruSight Oncology 500 panel.
Results: The primary tumour did not align with any known peripheral sheath tumour by immunophenotype, nor did it correspond to any methylation category defined by the Heidelberg classifier with a sufficiently high classification score. On the contrary, its further recurrences were all classified as MPNST by accepted histopathological criteria and methylation profiling. Additionally, the tumour harboured the same NRAS gain-of-function variant in all the tumour samples strongly supporting its shared origin.
Conclusion: We present a rare case of intracranial MPNST with abundant myxoid stroma, broadening the recognized morphological spectrum of these tumours. Moreover, this case provides evidence for a potentially novel precursor lesion of intracranial MPNST, a finding not previously described in the literature. In routine diagnostic practice, MPNST should be considered in the differential diagnosis of myxoid tumours, regardless the proximity to a peripheral nerve.

Funding: This work was supported by Masaryk University in Brno, Czech Republic, under Grant MUNI/A/1559/2023 and MUNI/A/1621/2024, the Ministry of Health, Czech Republic, grant project no. NU23-03-00100 and by an internal grant from St. Anne's University Hospital Brno. Supported by the project National Institute for Cancer Research (Programme EXCELES, ID Project No. LX22NPO5102) - Funded by the European Union – Next Generation EU

E-PS-MD-01-002
Revolutionizing sepsis diagnosis: assessing the Genes2Me 'Sepsis-Q' Point-of-Care Test for rapid detection of 32 sepsis pathogens from whole blood in just 90 minutes
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Background & Objectives: Traditional sepsis detection via blood cultures is slow, delaying treatment. The Genes2Me Sepsis-Q RT-PCR Kit enables rapid, accurate detection of 32 pathogens (bacteria, viruses, fungi) directly from whole blood. Using multiplex PCR with five fluorescence channels, it delivers results within 90 minutes (total ~2 hours). Optimized for OnePCR POCT & Rapi-Q POCT platforms.
Methods: 1. OnePCR POCT – A compact, sample-in-result-out platform designed for single-sample rapid testing. Using a four-tube assay and five fluorescence channels, it detects 20 high-priority sepsis pathogens, covering 94% of sepsis cases. Fully automated from extraction to results, it's ideal for point-of-care settings requiring quick clinical decisions.
2. Rapi-Q POCT with Rapi-X16 – A high-throughput system integrating the Rapi-X16 automated extraction unit, capable of processing 1 to 16 samples simultaneously. The eight-tube assay ensures comprehensive detection of 32 sepsis pathogens (100% prevalence coverage), making it ideal for batch processing in labs without compromising accuracy.
Both platforms use Genes2Me's Direct Blood Kit, featuring CellCrack Buffer & GeneErase Enzyme for efficient nucleic acid extraction directly from whole blood. These solutions provide high sensitivity, streamlined workflows, and rapid turnaround times, improving sepsis detection and patient outcomes in both POC and high-throughput settings.
Results: The Sepsis-Q Kit demonstrated analytical sensitivity at 100 copies/reaction and achieved 100% specificity, with no cross-reactivity observed with pathogens such as Chlamydia pneumoniae and Mycoplasma pneumoniae. Interference testing with human DNA, haemoglobin, NaCl, and BSA confirmed no impact on assay performance. Precision testing showed CV < 2%, and the kit exhibited an overall accuracy of 98%.
Conclusion: The Sepsis-Q Real-Time RT-PCR Kit offers a reliable, rapid solution for sepsis detection, with high sensitivity and specificity. Its integration with OnePCR and Rapi-Q platforms provides end-to-end automation for both point-of-care and high-throughput settings, significantly improving diagnostic speed and enabling timely, targeted treatment, ultimately reducing sepsis-related mortality.

E-PS-MD-01-003
Equivalence of laboratory-developed test and PD-L1 IHC 22C3 pharmDx in the pan-tumour and gastric cancer settings
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Background & Objectives: Previously, a 22C3 antibody-based LDT protocol was validated on the Ventana BenchMark XT and BenchMark ULTRA platforms, showing high concordance between the LDT and the FDA-approved, CE-marked, PD-L1 IHC 22C3 pharmDx (Agilent) in several solid tumour types, except for gastric cancer (GC) (Vainer G. *PLOS One*. 2023). Here, we report on the correlation between the previously validated 22C3 antibody-based LDT and PD-L1 IHC 22C3 pharmDx in GC and an updated pan-tumour analysis.
Methods: PD-L1 expression by continuous combined positive score (CPS) was analysed in tumour samples obtained from participants with multiple tumour types, including GC, using both the 22C3 antibody-based LDT on Ventana BenchMark XT or BenchMark ULTRA and PD-L1 IHC 22C3 pharmDx, which served as the gold standard. Correlation between assays by CPS was assessed using interclass correlation coefficient (ICC) and Spearman correlation coefficient (ρ) in the GC samples and in a pan-tumour cohort including GC samples. Assay agreement rates at prespecified cutoffs (CPS ≥1 or ≥10) were reported as overall percentage agreement (OPA), positive percentage agreement (PPA), and negative percentage agreement (NPA).
Results: PD-L1 expression was evaluable in 129 GC samples by LDT and PD-L1 IHC 22C3 pharmDx. ICC was 0.93 (95% CI, 0.91-0.95) and ρ was 0.95 in GC. For PD-L1 CPS ≥1, OPA was 98% (95% CI, 93-100), PPA was 96% (87-100), and NPA was 99% (93-100). For PD-L1 CPS ≥10, OPA was 98% (95% CI, 95-100), PPA was 93% (66-100), and NPA was 99% (95-100). In 681 pan-tumour samples, ICC was 0.96 (95% CI, 0.95-0.96) and ρ was 0.94.
Conclusion: In GC samples, a 22C3 antibody-based LDT on the Ventana BenchMark XT or BenchMark ULTRA platforms yielded comparable results to PD-L1 IHC 22C3 pharmDx. In the updated pan-tumour analysis, a strong correlation was observed between the two assays.

E-PS-MD-01-004
Improved L252P *MYD88* mutation detection by Droplet Digital™ PCR
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Background & Objectives: The L252P (formerly L265P) mutation in the *MYD88* gene is a characteristic alteration of lymphoplasmacytic lymphoma (LPL), making its detection essential for differential diagnosis with other lymphomas. This mutation is frequently analysed in formalin-fixed paraffin-embedded (FFPE) biopsies including bone marrow samples, often with a low percentage of neoplastic cells or with degraded DNA. Therefore, it is crucial to have a highly sensitive method. In our laboratory, pyrosequencing is routinely used to detect this mutation, with a limit of detection (LOD) of 3.5%. To increase sensitivity, droplet digital PCR (ddPCR) was set up, and its sensitivity was compared to pyrosequencing by analysing cases with prior wild-type (WT) results.
Methods: The L252P *MYD88* mutation was detected by ddPCR (Bio-Rad) in 21 FFPE samples with *MYD88* mutations previously characterized by pyrosequencing. Additionally, 16 normal tissue samples were analysed to establish the cut-off for the technique. A total of 17 samples with lymphoproliferative processes requiring a differential diagnosis of plasmacytic lymphoma and WT by pyrosequencing were also analysed. Furthermore, the sensitivity (LOD) of ddPCR was established in the wt cases taking in account that this value is experiment and sample depenent. Variant allele frequency (VAF) was also evaluated in the mutated cases.
Results: The L265P mutation was confirmed by ddPCR in all 21 *MYD88* mutated cases detected by pyrosequencing once the ddPCR cut-off was established using normal tissues. Additionally, *MYD88* mutation was detected by ddPCR in 5 of the 17 wt cases by pyrosequencing, with VAFs ranging from 0.4% to 3.11%. Negative results were confirmed with an sensitivity ranging from 0.09% to 0.89%.
Conclusion: The results of this study confirm that ddPCR offers greater sensitivity than pyrosequencing for detecting the L252P *MYD88* mutation, making it a highly valuable tool in the diagnosis of LPL, particularly in cases with low neoplastic cell representation and degraded genetic material.