



Abstract Book

2026 Fall Meeting

October 14-18, 2026

I. Platform Presentations

II. Posters



Platform Presentations

Platform 1: Pediatric (I)

2496558

Profound Endothelial Identity Disruption Characterizes Dysplastic Capillaries in Alveolar Capillary Dysplasia

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Background: Alveolar capillary dysplasia (ACD) is a rare and often fatal developmental lung disorder presenting with refractory neonatal respiratory failure followed by early postnatal death. Histologically, ACD is characterized by severe alveolar dysplasia, impaired vascular development, and dysplastic alveolar capillaries (DACs). Although the structural abnormalities of DACs are well established, the endothelial cell (EC) identities within these aberrant vascular networks and the molecular mechanisms underlying impaired alveolar–capillary gas exchange remain poorly understood.

Methods: We investigated EC phenotype distribution within alveolar–capillary regions of ACD lung biopsies (N=5) and control lungs (n=4). Histopathologic assessment was integrated with high-resolution spatial EC mapping (Polaris) and spatial transcriptomics (GeoMx Digital Spatial Profiler). EC phenotype distributions and spatial gene-expression profiles were evaluated using mixed-effects models and pathway enrichment analyses, with comparisons between typical and atypical ACD cases and controls.

Results: ACD lungs exhibited a disorganized, densely packed, multilayered alveolar capillary network accompanied by profound alterations in EC phenotype composition. General capillary (gCap) ECs were nearly completely absent, with a marked reduction in aerocyte ECs and expansion of EC populations exhibiting pulmonary venous-, lymphatic-, and systemic venous-like phenotypes. These alterations were accompanied by coordinated enrichment of translational and ribosomal pathways and increased expression of integrated stress-response markers. The immune regulatory gene CCL14 was significantly upregulated, whereas genes involved in vascular homeostasis, including TMEM100 and SFTPA2, showed strong trends toward downregulation. Notably, the atypical ACD case, characterized by later presentation, milder clinical symptoms, and a more favorable outcome, demonstrated partial preservation of mature endothelial phenotypes and attenuated stress-response signatures. These findings suggest that the degree of EC identity disruption may contribute to clinical severity and outcome in ACD.

Conclusion: ACD is characterized by profound disruption of endothelial identity and

specialization within the alveolar–capillary unit, accompanied by dysregulation of stress, inflammatory, and vascular homeostasis pathways. These findings expand the pathobiologic framework of ACD beyond alveolar growth impairment and vascular remodeling to include abnormal endothelial fate specification and reprogramming. The identified molecular alterations provide new avenues for mechanistic and therapeutic investigation, while novel endothelial markers may have potential utility as diagnostic biomarkers in pediatric pulmonary pathology.

Platform 1: Pediatric (II)

2496613

Vascular Anomalies of The Female Genital Tract in Children and Young Adults: A Clinicopathologic Study of 85 Cases

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Background: Vascular anomalies involving the female genital tract encompass a broad spectrum of conditions that can pose significant diagnostic and surgical challenges. Historically, pathologic terminology has not always aligned with contemporary vascular anomaly nomenclature. In this study, we reviewed gynecologic vascular anomalies occurring in children and young adults evaluated at our multidisciplinary vascular anomalies center and reclassified them according to the 2025 International Society for the Study of Vascular Anomalies (ISSVA) classification

Methods: We retrospectively reviewed 85 specimens from 62 patients with gynecologic vascular anomalies collected from 1997 through 2024. Cases were stratified by age < 18 versus ≥ 18 years. Diagnoses were reclassified according to the 2025 ISSVA framework. Demographics, anatomic location, genetic and syndromic associations, multifocality, and extragenital involvement were recorded

Results: Of 85 specimens, 60 (70.6%) involved patients < 18 years and 25 (29.4%) patients ≥ 18 years, with the vulva being the most affected site (84.7%). Vascular malformations accounted for 71/85 (83.5%) cases, while vascular tumors/neoplasms occurred in 14/85 (16.5%). Slow-flow malformations were most commonly encountered with 74.1%, including venous malformation (VM 43.5%) and lymphatic malformation (LM; 30.6%). Other anomalies were: arteriovenous malformation (2.4%), intramuscular fast-flow vascular anomalies (4.7%), infantile hemangiomas (9.4%), and other benign vascular tumors (7.1%). 2.4% thought to fit with potentially unique vascular anomalies. Syndromic associations were documented in 24 patients (28.2%), with Klippel-Trenaunay syndrome being the most frequent association (15.3%), followed by Bockenheimer venous malformation (3.5%), Blue Rubber Bleb Nevus syndrome (2.4%), and Parkes-Weber syndrome, Proteus syndrome, CLOVES syndrome, PTEN/Cowden syndrome, and a venous anomaly associated with Landau-Kleffner syndrome (each 1.2%). Other molecular alterations included PIK3CA variants (7.1%, 2 VM, 4 LM) and TEK variants (2.4%, 2 VM).

Conclusion: Gynecologic vascular anomalies in children and young adults comprise a diverse and clinically complex spectrum, predominantly consisting of slow-flow vascular malformations and frequently occurring in the setting of multisite, genetic, or syndromic disease. Accurate classification using contemporary ISSVA criteria, together with recognition of associated

molecular and syndromic features, is critical for establishing the correct diagnosis and guiding multidisciplinary, individualized management of these potentially morbid conditions.

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Platform 1: Pediatric (III)

2494819

Exploring the Significance of Lenticulostriate Vasculopathy: Radiologic-Pathologic Correlations and Histologic Evidence of Associated Brain Injury

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Background: Lenticulostriate vasculopathy (LSV) is a cranial ultrasound (US) finding in infants characterized by branching/punctate hyperechogenicities in the basal ganglia and/or thalamus, corresponding to the lenticulostriate branches of the middle cerebral arteries. These vessels are normally indistinct on US in healthy infants while LSV is seen in ~20% of very preterm neonates. The clinical significance of LSV is uncertain though it has been associated with adverse neurodevelopmental outcomes and may be a risk factor for thrombosis/infarction. Some authors suggest mild cases may not represent true pathology, unlike moderate and severe cases. Rare pathology reports of LSV exist. The underlying pathophysiology is presumed to be mineralization of vessel walls and/or perivascular mineralized globular deposits. Our aims were to investigate associations between histologic and US findings and to look for co-occurring histologic abnormalities in brains with LSV.

Methods: Subjects who underwent brain autopsy between 2016-2025 with microscopic examination of the basal ganglia and/or thalamus and brain US < 1 month prior to death were included. Clinical data was collected for all cases. Two radiologists independently classified LSV as none, mild, moderate, or severe. A neuropathologist reviewed all brain autopsies and classified vascular mineralization as absent, focal/scattered, numerous, or extensive. All other histologic abnormalities were documented. A Fisher's Exact test was used to investigate associations between histopathology and US findings.

Results: Thirty subjects were included in the study (median adjusted age: 3.5 weeks; M:F=1.5:1). The median interval between US and death was 5 days. 43% of subjects were born preterm, and 56% had genetic abnormalities. On US, LSV was seen in 69% of cases; 50% mild, 25% moderate, and 25% severe. Deep gray matter vascular mineralization was seen in 55% of cases; 25% focal/scattered, 44% numerous, and 31% extensive. All cases with mineralization had other histologic abnormalities (100%). When mineralization was present on histology, LSV was seen on US in 82% of cases. There was a significant association between US LSV and histologically abnormal lenticulostriate vessels ($p=0.042$) though in not all instances were abnormal vessels mineralized. There was moderate agreement between US and histology grading of LSV/vascular mineralization ($p=0.036$).

Conclusion: Associations between histology and US were present; however, the findings

indicate that not only vessel mineralization, but vascular congestion and proliferation may also contribute to the LSV seen on US. Understanding radiologic-pathologic correlations for LSV will allow better understanding of the long-term clinical significance of these imaging and histologic abnormalities.

Platform 1: Pediatric (IV)

2493256

Frequency and outcomes of allograft steatosis in Progressive Familial Intrahepatic Cholestasis type 1 patients following liver transplantation: A mono-institutional retrospective cohort study

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Background: Progressive familial intrahepatic cholestasis type 1 is a rare genetic disorder caused by defects in the ATP8B1 gene that codes for the FIC1 protein, leading to impaired bile salt secretion. It is characterized by hepatocellular cholestasis. Many of these patients progress to end-stage liver disease and require liver transplantation (LT). Steatosis following LT has been reported, however the mechanism remains incompletely understood. We aimed to evaluate the frequency of hepatic steatosis following LT in our cohort and assess the outcome of these patients.

Methods: With a retrospective cohort study, we identified patients with genetically confirmed PFIC1 who received a liver transplant between 2003 and 2025. We re-reviewed their allograft liver biopsies and separated them into three discrete time intervals: the first post-transplant biopsy, 5 months to 1.5 years after transplant, and their most recent biopsy (37 days – 16 years 8 months post-transplant). Histologic slides were analyzed at the time of diagnosis by applying the Banff criteria for rejection, the nonalcoholic steatohepatitis histologic scoring system, and the liver allograft fibrosis semiquantitative score (LAFSc). When lobular inflammation was reported, it was described as none, mild, or present without further description. We recorded T-cell mediated rejection as “Y” (yes, present), “N” (no, absent) or “Ind” (indeterminant) without further classification.

Results: Our cohort included 5 males and 8 females, and the median age at transplant was 5 years old (range 2 – 13 years). The mean duration of follow-up was 3 years and 3 months (range 37 days – 16 years and 8 months). This range is represented by the “most recent” biopsies. Ten of 13 patients had some degree of steatosis in their first allograft biopsy (range 5 days – 7 months 1

week post-transplant). 6 out of 13 patients had an additional biopsy within the 5 months – 1.5 years post-transplant timeframe. All six patients had at least 33% steatosis. Of the 12 patients with a “most recent” biopsy, one had no steatosis per the reporting institution, one had 1-33% steatosis, one had 33-66% steatosis, and 9 had greater than 66% steatosis. All six of these patients had either stable or worsening steatosis from the first allograft biopsy. No biopsy at any time interval from any patient had lobular inflammation greater than mild. No patient developed fibrosis greater than 4/9. The patient/graft survival is currently 100%.

Conclusion: Steatosis without accompanying lobular inflammation or development of significant fibrosis is a common finding in the allograft livers of PFIC1 patients in our cohort. This is in contrast to previous studies that have reported progression to cirrhosis. Future studies are needed to elucidate the underlying pathophysiology behind this finding.

Patient	First post-transplant biopsy				5 months - 1.5 years post-transplant				Most recent biopsy			
	% Steatosis	Lobular Inflammation	tCMR (Y/N/Ind)	Fibrosis (/9)	% Steatosis	Lobular Inflammation	tCMR (Y/N/Ind)	Fibrosis (/9)	% Steatosis	Lobular Inflammation	tCMR (Y/N/Ind)	Fibrosis (/9)
Patient 1	1-33%	None	N	0/9	>66%	Mild	Y	0/9	1-33%	Mild	Ind	0/9
Patient 2	>66%	Mild	N	0/9	>66%	Mild	Y	0/9	>66%	Mild	N	4/9
Patient 3	0	Mild	Y (mild)	0/9					>66%	None	N	0/9
Patient 4	0	None	Ind	1/9					>66%	Mild	Ind	1/9
Patient 5	0	Mild	Y (mod)	0/9					None per scanned in report from outside facility	None	Y	0/9
Patient 6	>66%	Mild	N	0/9	>66%	Mild	Ind	2/9	>66%	Mild	N	2/9
Patient 7	>66%	N/A	Ind	0/9	>66%	N/A	N	0/9	>66%	Mild	N	1/9
Patient 8	1-33%	Mild	Y	0/9	>66%	Mild	N	0/9	33-66%	None	N	0/9
Patient 9	1-33%	Mild	Y	0/9					>66%	None	N	0/9
Patient 10	1-33%	None	N	1/9	>66%	None	N	0/9	>66%	None	N	0/9
Patient 11	33-66%	None	N	0/9	>66%	Present (NOS)	N	Not scored	>66%	None	N	1/9
Patient 12	33-66%	None	N	1/9								
Patient 13	33-66%	None	N	0/9					>66%	None	N	0/9

Platform 1: Pediatric (V)

2492001

Cyclic Vomiting Syndrome: Is there anything to see?

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Background: Cyclic vomiting syndrome (CVS) is characterized by the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition as repeated episodes of acute onset, repetitive vomiting with ≥ 4 discrete episodes in the prior 12 months, lasting 2 hours to 7 days. Episodes should occur at least 1 week apart with a period of normalcy between them. The disorder is one considered one of brain gut interaction with autonomic dysfunction currently considered the culprit. The diagnosis does not require endoscopy and only a urinalysis and basic metabolic panel during a vomiting episode along with an upper gastrointestinal contrast series are recommended. The purpose of our study was to determine what, if any, upper endoscopy histologic findings are typical in patients with a diagnosis of cyclic vomiting syndrome.

Methods: A natural language search was performed of pathology reports which included the words “cyclic vomiting” between April 1, 2021, and March 31, 2026. The electronic medical record was then searched, documenting at the time of biopsy if the criteria for cyclic vomiting syndrome were met, age of onset, medication history, personal and/or family history of migraine, select laboratory results, barium imaging results, and age at biopsy were noted. The biopsy specimens from the patients’ upper endoscopy were reviewed by two pathologists and consensus findings were recorded.

Results: A total of 57 pathology reports were identified for potential inclusion, of these, 6 were excluded. A total of 46 patients and 51 cases were included. The age at biopsy ranged from 1.7 – 23.3 y with an average of 12.4 y with no sex predominance (male: female 12:11). 28 patients had documentation of 4 episodes within one year which met criteria for cyclic vomiting syndrome, while others did not have episode number and period clearly noted in the chart. A total of 48 duodenal, 47 gastric, 50 distal esophageal, and 39 proximal esophageal biopsies were evaluated histologically. 32 duodenal, 35 gastric, 35 distal esophageal, and 30 proximal esophageal biopsies showed no significant changes. Many patients had mild changes noted. However, 6 patients had moderate to severe active esophagitis. In patients who had special stains and immunostaining performed, no fungal organisms, cytomegalovirus, or herpes simplex virus was detected. 4 of these patients had documentation verifying they met criteria of number and frequency of episodes. The average age of patients in this was slightly higher than the cohort overall, 14.2 years.

Conclusion: A subset of patients with CVS had biopsies with moderate to severe active esophagitis. This is significant as these patients may present with more severe symptoms, require endoscopy, and benefit from different therapies than most patients with the diagnosis.

Platform 1: Pediatric (VI)

2496211

Fetal Programming of Sex Specific Cancer Microenvironment and Epigenetic Burden

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Background: Oxidative stress in maternal vascular malperfusion (MVM) leads to accelerated tissue aging, which has been well-described as an underlying pathology in the placenta and various fetal organs associated with the developmental origins of adult-onset disease. For example, placental telomeres are shorter (older) in MVM cases compared with gestational-age matched controls. Architecture is accelerated. Epigenetic burden is increased, especially, when the baby is male. This is also true for other organs like the kidney and pancreas. Our group recently showed that pancreas microenvironment response to injected pancreatic cancer (PDAC) cells is different in males vs females +/- castration and +/- fetal growth restriction. The largest tumors were in males and the smallest in ovariectomized females. In this study we investigated pancreas tissue composition, tumor associated endothelial cell growth, and epigenetic burden in these six phenotypic groups.

Methods: Genetically identical black 6 mice were used to study the impact of fetal growth restriction and fetal sex +/- castration on pancreas composition, tumor induced angiogenesis and pancreatic epigenetic variance. One cohort (n=36 mice) were injected with murine KPC PDAC cells and harvested after 10 days. Tumor associated angiogenesis was measured using CD31 stained histologic sections of the pancreatic tumors scoring 3 regions of interest in the periphery and then again centrally for complete vascular cross-sections. A separate cohort of adults at 12 weeks of age (n=36) without tumor injections were used to characterize pancreatic tissue composition and analyze whole genome bisulfite sequencing (WGBS) of epigenetic burden.

Results: The adult pancreas from FGR progeny had fewer beta islet cells (66%) than their normal birthweight and castrated cousins. Therefore, subsequent pancreas epigenetic studies compensated for this variance in tissue composition. WGBS showed significant differences in males compared with females, including the PDX-1 gene known to be involved in the pathogenesis of PDAC, in a pattern suggestive of advanced tissue "aging". We observed less angiogenesis both peripherally and centrally in PDAC tumors from FGR males and females with

values very similar to ovariectomized females.

Conclusion: Decreased beta islet cell numbers in FGR has been described previously, suggesting our model of FGR is similar. Taking pancreas composition into account revealed a number of epigenetic changes in the female pancreas related to tissue aging. Both male and female FGR showed less tumor associated angiogenesis in our model, which may explain the surprising observation that castrated and FGR progeny had smaller PDAC tumors than normal birthweight male and female controls.

Platform 2: Practice (I)

2489284

Stain-Scan-Share: A Histology-Led Digital Pathology Model to Address Pediatric Pathology Workforce Shortages and Enable International Collaboration

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Background: Pediatric pathology faces persistent shortages of both pathologists and lab personnel. Although digital pathology (DP) can expand access to expertise and enable remote practice, implementation may be challenging in already resource-constrained laboratories because scanning introduces additional workflow steps. We evaluated a histology-led DP implementation designed to support prospective scanning, remote sign-out, and international subspecialty consultation.

Methods: An automated hematoxylin and eosin staining and cover slipping workflow was integrated with two whole-slide imaging scanners at a pediatric hospital. Scanning responsibilities were incorporated into a redesigned histology assistant position, with three histotechnologists providing backup and on-call scanning support. Four pediatric pathologists validated dual-monitor office and home workstations with high-resolution diagnostic displays and secure high-speed network access. An internationally based pediatric pathologist was credentialed at the institution who provided subspecialty consultation using a validated remote workstation. De-identified whole-slide images were additionally used for regular inter-institutional case conferences, consensus review, and trainee education. Operational metrics from May through July 2026 were evaluated using laboratory analytics dashboards.

Results: During the initial 3-month period, 3,085 patient accessions comprised 9,007 blocks, generating 13,306 digital images. Prospective scanning increased from 72.6% in May to 94.2% in June and 94.7% in July, demonstrating rapid transition to near-comprehensive prospective digitization. Median prospective scanning time was 1.45 hours. Histology workflow optimization included consolidation of tissue placement and implementation of single-slide gastrointestinal biopsy protocols. Following this change, monthly slide production volume decreased by 10.6%, while prospective scanning increased. More than 50 cases were also reviewed through international pediatric pathology consultation, supplemented by recurring multidisciplinary educational and consensus conferences.

Conclusion: A histology-led integrated DP model achieved >94% prospective scanning while preserving diagnostic subspecialty care in a resource-constrained pediatric pathology setting. Reducing unnecessary slide production decreased scanning workload, highlighting the value of redesigning histology processes rather than simply adding digitization to existing workflows. Validated remote workstations and international consultation expanded workforce flexibility and access to subspecialty expertise. Together, lab automation, workflow optimization, and remote digital practice can mitigate pediatric pathology workforce limitations while supporting clinical care, consultation, and education.

Platform 2: Practice (II)

2495127

A Deep Learning Model to Predict Hepatocellular Neoplasm-Not Otherwise Specified (HCN-NOS).

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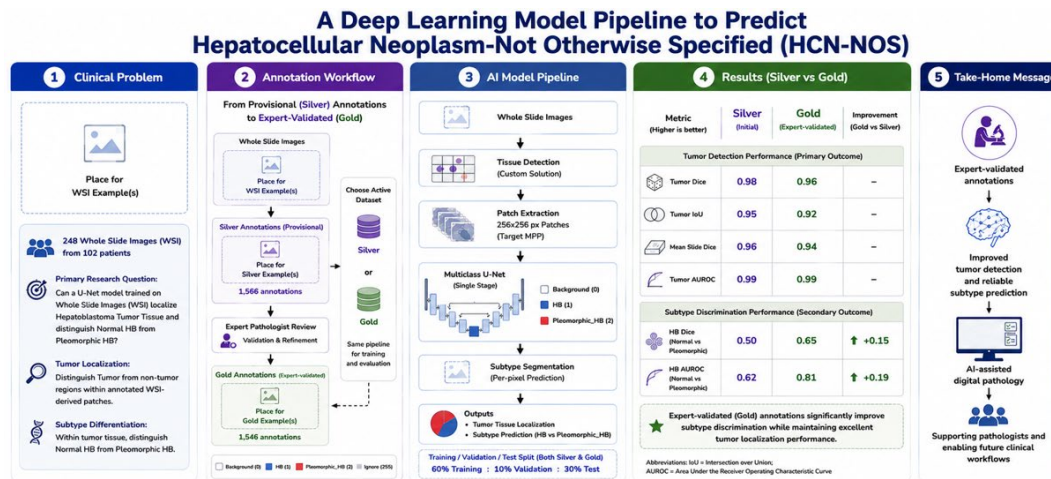
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Background: Hepatocellular neoplasm-not otherwise specified (HCN-NOS) is increasingly recognized as a subset of hepatoblastoma (HB) with poor prognosis, characterized by pleomorphism and/or hepatocellular carcinoma-like features. Identifying morphologic features of HCN-NOS is a challenge and subject to inter-observer variability. We present a deep learning (DL) model to predict HCN-NOS using hematoxylin-eosin-stained (H&E) whole-slide images (WSIs) of pre-therapy tumor samples (biopsies or upfront resections).

Methods: With IRB approval, pediatric liver tumor patients were identified from the pathology and surgery databases. Those with digitally scanned H&E-stained slides from pre-therapy samples were included in the study. The U-Net model was selected based on its data efficiency and precise capability for pixel-level tumor localization. The PyTorch package (version 2.13.0+cu126) through Python (version 3.11.3) was used for model development, and OpenSlide (version 4.0.1) was used for WSI processing. QuPath (version 0.7.0) was used to read and annotate the WSIs in the .svs and .qpdata file formats respectively. Image preprocessing, model training and evaluation of metrics was performed on a High-Performance Computing (HPC) cluster operated by the Cincinnati Children's Biomedical Informatics Center with 24 CPU cores assigned, 128 GB random access memory (RAM), and a gpu-a100 queue was used. WSIs were annotated for "conventional HB" (fetal or embryonal differentiation) and "pleomorphic HB" (areas of pleomorphism or carcinoma-like features) by a trained student (silver-standard) and revised by an expert-pathologist (gold-standard). Patients were divided into train/validation/test sets (60:10:30 ratio). The performance of the model was quantified using dice score (predicted area matching with ground truth), intersection over union (IoU), and area under the ROC curve (AUROC), with slide level bootstrap confidence intervals. (Fig 1)

Results: We included a total of 248 WSIs on 102 patients with 1566 and 1546 annotations in the silver and gold sets respectively. Model performance for the silver/gold sets was as follows: tumor dice 0.98/0.96, tumor IOU 0.95/0.92, mean slide dice 0.96/0.94, tumor AUROC 0.99/0.99, HCN-NOS dice 0.5/0.65, HCN-NOS AUROC 0.62/0.81.

Conclusion: Our results show that a U-Net-based DL model can be highly accurate for HB tumor identification when trained on H&E WSIs. We also show that expert annotations can increase the accuracy for sub-group specific prediction of HCN-NOS. This work lays the foundation for the construction of a multi-modal risk stratification algorithm for pediatric liver tumors, including artificial intelligence-based features.



Platform 2: Practice (III)

2475812

A Novel Semi-Automated Pipeline for Autopsy Data Standardization for the Use or Development of Large Language Models

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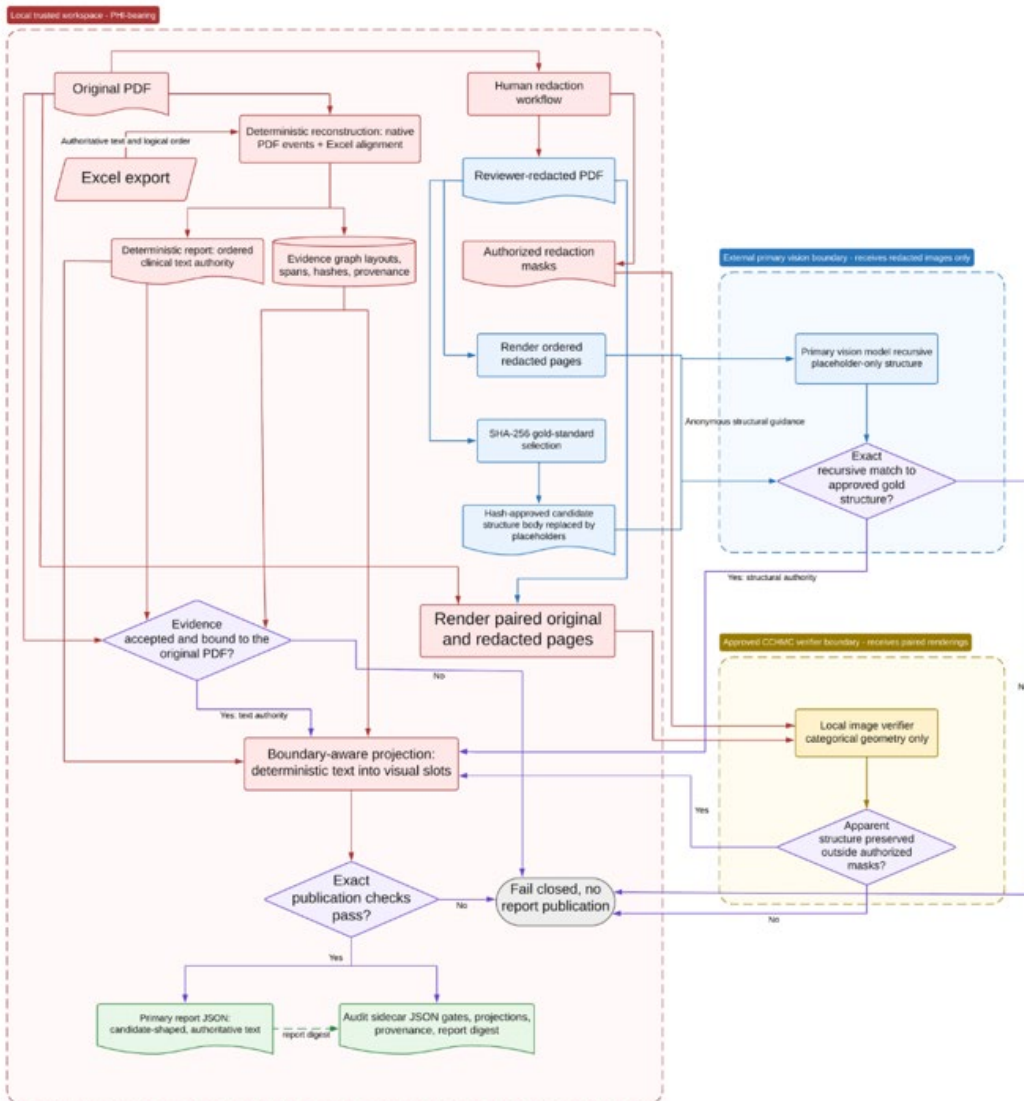
Background: Large language models (LLMs) can increase the accuracy and efficiency of autopsy reporting. However, preparing autopsy reports for LLM training is challenging because exports from the laboratory information system (LIS) strip formatting, resulting in loss of information conveyed through indentation, nested lists, and tables. Variability in section organization and the placement of protected health information (PHI) further limits the automated report processing and preparation.

Methods: Stillbirth autopsy reports from 2024-2025 were queried and exported to Microsoft Excel along with corresponding PDF files of preliminary and final reports. Since PDF files primarily preserve visual layout rather than explicit document structure, report organization had to be inferred, while unformatted text exports were used to verify word order. Redaction was a semimanual process. A JavaScript Object Notation (JSON) schema was developed to differentiate subsections, paragraphs, lists, tables, and redactions. Structured JSON reports were manually reviewed for PHI leakage and structural accuracy. (Fig 1)

Results: Formatting-dependent elements, including list hierarchies and tables, were lost in MS Excel exports for all the reports (n=98). Text from MS excel exports was combined with PDF-derived structure to generate JSON files for model input. Gross description measurements were recorded as tables in 24 (24.5%) reports, paragraph text in 72 (73.5%), and were absent in 2 (2%). Additional variability in headings, list conventions, page breaks, and PHI placement complicated extraction and deidentification. Automated PHI detection identified 97.6% of PHI instances, but 31.7% of reviewed reports contained at least one missed instance. A revised semi-manual workflow combining automated detection with manual review achieved complete redaction. After a 3-month development period, reconstruction of report structure into JSON averaged 1 minute 45 seconds per report, while semi-manual redaction averaged approximately 7 minutes per report.

Conclusion: Preparation of autopsy reports for LLM applications is limited by formatting dependent structure not retained in databases and the variability of PHI type and placement.

Inconsistent report structure was a major barrier to reliable automated processing for large data. In its current form, autopsy reports are not suitable for machine processing. Standardization of document structure, hierarchy, and PHI placement would substantially improve the accuracy and efficiency of converting reports into structured data.



Platform 2: Practice (IV)

2494910

Machine Learning Techniques to Understand Placental Pathology Associations with Adverse Pregnancy Outcomes

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Background: Placental pathology has potential to provide information about adverse pregnancy outcomes such as preterm birth (PTB), fetal growth restriction and stillbirth, but its value has been called into question recently, in part because of the complexity of understanding the numerous placental lesions that can be identified. Our aim was to utilize machine learning for multivariable analysis in a large cohort of placentas and present the most highly associated placental lesions in PTB, small for gestational age (SGA) infant, and stillbirth identified by these prediction models.

Methods: This was a retrospective, single institution, cohort study of maternal-placenta dyads collected between 2017-2024, including pregnancies with liveborn and stillborn babies [9783 liveborn (PTB n=2086 and SGA infant n=1145) and 149 stillborn]. Placental lesions were categorized using a validated text search algorithm and divided into 87 raw variables (obtained from direct exam of the placenta) or 52 derived variables (requiring grade/stage/score). Pregnancy outcomes evaluated were: 1) stillbirth, 2) PTB (< 37 weeks) and 3) SGA infant (birthweight < 10th %ile). The raw data were chosen to train least absolute shrinkage selection operator (LASSO) logistic regression models for each outcome. The LASSO regression was performed using glmnet ten-fold cross-validation in R version 4.4.1. The predictive power of each model was analyzed using the area under the curve (AUC) of the receiver operator characteristic (ROC) and precision recall (PR) curves.

Results: The top 5 raw variables in each outcome model are presented in Table 1. Raw placental variables performed better than derived in predicting stillbirth (raw ROC AUCs 0.93 vs derived 0.77 and raw PR AUCs 0.40 vs derived 0.16). The PTB models showed similar ROC AUCs with raw 0.82 vs derived 0.79, as well as the PR AUCs raw 0.62 vs derived 0.57. The SGA models performed similarly too with ROC AUCs raw 0.88 vs derived 0.87 and PR AUCs raw 0.56 vs derived 0.53. Including gestational age (GA) in the model had an effect on the stillbirth ROC AUC for the derived variables only (ROC AUC with GA 0.90 vs without GA 0.77), but AUCs for raw variables in stillbirth and all variables in SGA infant were relatively unchanged.

Conclusion: Using machine learning techniques, we show that several placental variables are important predictors of stillbirth, PTB, and SGA infant. The stillbirth model had the best

predictive value, and the raw variables alone had good predictive value for all 3 outcomes. Inclusion of variables that had component of grade/stage/score did not significantly improve the models, particularly in stillbirth. This data may help pathologists to understand the importance of accurate recording of placental lesions for clinical correlations and for research studies.

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Platform 2: Practice (V)

2491660

The Value of Subspecialty Placental Review in Intrauterine Fetal Demise

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Background: Placental analysis offers valuable information about both the mother and the infant. In cases of intrauterine fetal demise (IUFD), the cause of death is often found in the placental exam and not necessarily within the fetal autopsy. Some placental lesions may also have implications for recurrence, making their accurate recognition and clear communication important for counseling and management of future pregnancies. Placental specimens are often evaluated in general surgical pathology practices, where access to specialized training in perinatal pathology and dedicated time may vary. The complexity of placental findings, varied terminology and varied reporting practices can make clinically significant lesions more difficult to recognize and consistently interpret. Thus, there is a growing push for report standardization through the Amsterdam guidelines, as well as specialized review by a perinatal pathologist, especially in cases of IUFD.

Methods: A review of fetal autopsies performed in consult at an academic pediatric hospital was undertaken. Of these cases, those in which a placental report was generated at both the outside (referring) hospital and the pediatric hospital were selected. Reports were assessed for adherence to the Amsterdam Consensus guidelines and for diagnostic discrepancies. Discrepancies were categorized by severity according to their relevance to the cause of death, recurrence risk, and critical value reporting guidelines. Additionally, the credentials of the finalizing pathologist for each report were reviewed to determine whether the pathologist was board certified in pediatric pathology.

Results: Among the 78 placental cases reviewed, 9 (11.5%) outside reports fully adhered to Amsterdam diagnostic terminology, compared with 62 (79.5%) internal reports. Diagnostic discrepancies occurred in most cases, with outside reports often lacking placental lesions, failing to classify lesions using Amsterdam terminology, or incompletely grading or staging inflammatory processes. Approximately one-third of discrepancies were considered critical. Pediatric pathologist review yielded more comprehensive placental diagnoses and identified clinically significant lesions that were absent or incompletely characterized in the original reports.

Conclusion: Dedicated pediatric pathologist review identified substantially more clinically significant placental lesions and showed markedly greater adherence to Amsterdam consensus

terminology. These findings support subspecialty placental evaluation in cases of intrauterine fetal demise and highlight the importance of standardized Amsterdam-compliant reporting to both improve diagnostic accuracy and identify lesions with potential relevance to the cause of death, recurrence risk, and management of future pregnancies.

Platform 2: Practice (VI)

2496643

Global Practice Patterns in Placental Pathology: Deviations Despite a Decade of the Amsterdam Criteria

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Background: The Amsterdam Placental Workshop Group Consensus Statement (“the Amsterdam Criteria”; Khong TY, et al, 2016) and the Classification and reporting guidelines for the pathology diagnosis of placental accreta spectrum (PAS) disorders (“the PAS guidelines”; Hecht JL, et al, 2020) have resulted in standardization of the placental pathology literature and investigation. However, the degree to which these recommendations have been adapted in the daily practice of laboratories across the globe is uncertain.

Methods: We distributed a 42-question web-based survey to placental pathologists listed on the member directories of the Society for Pediatric Pathology and PathologyOutlines.com (n=300), which included the assessment of 21 potential deviations from consensus guidelines.

Results: 88 pathologists responded (29%), representing 18 countries (66% United States). Most were from large academic medical centers (n=58; 65.9%), with additional representation from 7 (7.9%) small academic centers, 8 (9.1%) community practices, 10 (11.4%) private practices, 1 (1.14%) Veterans Association, and 4 (4.55%) listed as ‘Other.’ Annual case volumes ranged from less than 500 (n=25; 28.7%), 500-1000 (n=21; 24.1%), 1000-3000 (n=23; 26.4%), to greater than 3000 (n=18; 20.7%). Of the 88 respondents, 83 (94.3%) reported at least one deviation from consensus recommendations. A total of 406 deviations were reported, with deviations per respondent ranging from 0-20 (mean 4.6, median 4). These included differences in gross examination and sampling, use of diagnostic criteria, and reporting practices (Table 1; red text). In a comparison of the practice patterns between academic medical centers (AMCs) and non-AMCs, only the subspecification of maternal inflammatory response in amniotic fluid infection (p=0.021) and the staging of basal plate myometrial fibers (p=0.042) were statistically significantly and reported more by AMCs.

Conclusion: Even though the Amsterdam Criteria have been available for over a decade, variation persists in the routine practice of placental pathology. Section submission, histopathologic diagnosis, and reporting differs from institution to institution despite available consensus guidelines. Additional investigation is needed to determine the driving factors for these deviations.

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Platform 3: Perinatal (I)

2493825

Elevated Maternal Serum Cytokine Levels and Reduced Extracellular Vesicle Concentrations Associated with Placental Chronic Villitis: A Matched Case-Control Study

L Ernst¹, A Freedman², M Morita³, A Franklin¹, L Keenan-Devlin¹, A Borders⁴, G Miller², T Morgan³; ¹ Endeavor Health, ² Northwestern University, ³ Oregon Health Sciences University, ⁴ Endeavor

Background: Chronic villitis is characterized by maternal T-cell recognition of chorionic villi with stromal infiltration and tissue destruction usually seen in 3rd trimester placentas. However, the etiology and timing of the disease process are not well-understood. We hypothesized that placental and maternal immune cell-specific extracellular vesicles (EVs) and inflammatory cytokines in maternal serum in the 2nd and 3rd trimesters may provide insights into the mechanisms and timing of disease progression.

Methods: This is a matched case-control study of banked maternal serum samples from patients with high grade chronic villitis (cases, n=33) and negative controls (n=66) matched on sex and gestational age at delivery. Serum samples were from late 2nd trimester (mean 24 weeks) and third trimester (mean 33 weeks). Cytokines were measured in triplicate for the 2nd trimester samples using a multiplex immunoassay protocol on an automated microfluidic platform (Simple Plex, Protein Simple). Maternal platelet, endothelial, CD4, and CD8 T-cell, placental syncytiotrophoblast (STB) and extravillous trophoblast (EVT) specific EVs were measured in triplicate using our validated NanoFACS-based approach. Data were analyzed by conditional logistic regression.

Results: In the matched analysis, mothers of chronic villitis cases were older (35.3 years $\pm$ 5.4 vs. 32.6 years $\pm$ 4.9; p=.02) and more likely to be Hispanic (36.4% vs. 15.2%; p<.01), which were subsequently included as covariates in adjusted models. A 1 standard deviation (SD) higher 2nd trimester serum IL-6 was associated with 2-fold higher odds of being a chronic villitis case (OR: 2.1 [95% CI: 1.1-4.1], adjusted p-value = .03, See Table). In 2nd trimester samples, one SD increases in maternal CD4 T-cell EV, STB EV, and platelet EV counts were significantly associated with lower odds of chronic villitis (CD4 T-cell OR: 0.36, 95% CI: 0.15, 0.91, p=.03; STB OR: 0.42, 95% CI: 0.19, 0.93, p=.03, platelet OR: 0.42, 95% CI: 0.19, 0.91, p=.03). In 3rd trimester samples, the association was consistent for CD4 T-cell EVs but not STB or platelet EVs. In 3rd trimester samples, but not 2nd trimester samples, higher EVT EV count was associated with lower odds of chronic villitis.

Conclusion: Elevated IL-6 levels and reduced immune cell and trophoblast cell EVs in both the 2nd and 3rd trimester in chronic villitis compared to controls suggests that inflammatory and immunomodulatory processes may begin to be altered early in pregnancy, and these alterations may be detectable in the midtrimester. The reasons for lower EVs in chronic villitis is currently unclear, and further research is need to determine if lower EVs are the result of placental injury in chronic villitis or if the lower EVs contribute to abnormal immune tolerance and promote chronic villitis.

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Platform 3: Perinatal (II)

2495871

Maternal Inflammatory Markers and Microbiological Findings in Histological Chorioamnionitis and Funisitis: A Retrospective Study

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Background: Chorioamnionitis (CA) and funisitis (F) are associated with maternal and perinatal morbidity. This study investigates the associations between maternal clinical and laboratory parameters, the stage and grade of maternal and fetal inflammatory responses, microbiological findings, and neonatal outcomes.

Methods: We retrospectively analyzed 220 pathology reports from 2024–2025 documenting chorioamnionitis (CA) and funisitis (F). Data included the stage and grade of CA and F; maternal demographic, clinical, and inflammatory parameters; obstetric variables; and neonatal outcomes, including birth weight and Apgar scores at 1 and 5 minutes. We also evaluated differences between microbiological samples collected in the delivery room and those obtained in the Pathology laboratory, as well as the association between time from collection to microbiological analysis and test results. Statistical analyses were performed to assess associations between histopathological findings and clinical variables.

Results: F was associated with elevated maternal CRP (10.09 mg/dL; $p = 0.001$), maximum temperature (37.54 °C; $p = 0.005$), and WBC count ($18.71 \times 10^3/\mu\text{L}$; $p = 0.006$). Maternal inflammatory response was associated with higher WBC counts (18.34 vs $15.46 \times 10^3/\mu\text{L}$; $p = 0.005$), whereas CA/F stage and grade showed no significant associations. Among 106 operative deliveries, non-reassuring CTG alone occurred in 44 cases (41.5%) and with arrest of labor progression in 5 (4.7%). Chorionic vasculitis was more frequent in NICU-admitted newborns (10/31; 32.3%) and operative deliveries for non-reassuring CTG (10/44; 22.7%; $p = 0.033$); the combined CTG/arrest indication was associated with maternal inflammatory response stage and grade. Among 121 singleton pregnancies, placental cultures were positive in 19/109 cases (17.4%) and subamniotic swabs in 38/120 (31.7%). Placental culture positivity correlated with higher maternal temperature (37.95 °C; $p = 0.015$). In 40 paired subamniotic cultures, delivery-room sampling yielded more positive results than Pathology sampling (15/40; 37.5% vs 6/40; 15.0%), while processing delay was not associated with culture negativity.

Conclusion: Funisitis and maternal inflammatory response were associated with elevated maternal inflammatory markers, while chorionic vasculitis correlated with NICU admission and

non-reassuring CTG. Placental culture positivity was associated with higher maternal temperature. Delivery-room subamniotic sampling improved culture yield, whereas processing delay did not affect negativity.

Platform 3: Perinatal Organ (III)

2494449

Basal Plate Myometrial Fibers in the Delivered Placenta Associate with Increased Prevalence of Postpartum Hemorrhage

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Background: Basal plate myometrial fibers (BPMF) in the delivered placenta have been associated with maternal hemorrhagic morbidity and an increased risk for placenta accreta spectrum in a subsequent pregnancy; however, these findings are not universally reported, leading to confusion about the clinical significance of BPMF. Our aim was to explore the prevalence of hemorrhagic morbidity in patients with BPMF.

Methods: This was a retrospective, single institution, cohort study of mother-placenta dyads with delivery of a liveborn infant and placenta sent to pathology between 2020-2024, when examination for BPMF was routinely performed and reported. BPMF was identified in the pathology report text via a validated text searching algorithm (R version 4.4). BPMF was staged as either Stage 1 (decidua present) or Stage 2 (decidua absent), and in this analysis presence of either Stage 1 or 2 was considered BPMF present. We used automated electronic medical record searches to identify hemorrhagic maternal outcomes. Postpartum hemorrhage (PPH) was the primary outcome and defined as quantitative blood loss (QBL) $\geq 1000\text{mL}$. Other outcomes collected included QBL as a continuous variable, use of uterotonic medication outside of routine postpartum pitocin (misoprostol, hemabate, methergine, tranexamic acid), intrauterine mechanical interventions (JADA system and/or Bakri), and need for blood transfusion. Analyses were performed using R version 4.4.

Results: Among 6,073 placentas from singleton live births, 1304 (21.5%) had BPMF. Patients with BPMF were more likely to be older, multiparous, Caucasian, and to have delivered by cesarean section in the current pregnancy compared to those without BPMF. Pre-existing diabetes mellitus, gestational diabetes mellitus, hypertensive disorders of pregnancy, and chronic hypertension, were not significantly associated with the presence of BPMF. Patients with BPMF had a higher prevalence of PPH (213 [16.3%] with BPMF vs 514 [10.8%] without BPMF) along

with higher mean QBL, and higher prevalence of uterotonic medication, JADA and Bakri use, and blood transfusion (Table 1). In an analysis adjusted for covariates (maternal age, race, parity and mode of delivery), patients with BPMF were 55% more likely to have PPH (aOR=1.55 (95% CI 1.29-1.85), $p<.001$).

Conclusion: BPMF was present in 21.5% of the study population and was associated with greater postpartum blood loss and increased need for blood transfusion. The results from this large cohort suggest that BPMF is associated with increased risk for PPH and maternal hemorrhagic morbidity. While the exact factors leading to BPMF are poorly understood, these results could help obstetricians use the placental pathology report to understand the potential factors contributing to PPH.

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Platform 3: Perinatal (IV)

2495839

Maternal Vascular Malperfusion and Clinical Outcomes- Implications for Neonate, Subsequent Pregnancy and Long-term Maternal Health: a Retrospective Cohort Analysis

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Background: Maternal vascular malperfusion (MVM) has been associated with preeclampsia, fetal growth restriction and future maternal cardiovascular disease. Multiple grading systems have been proposed to identify MVM placentas most associated with clinical severity, but the outcomes studied differ. We sought to identify risk factors common to index pregnancy clinical severity, neonatal illness, subsequent pregnancy outcomes and maternal cardiovascular (CV) risk factors in a cohort of placentas with features of MVM.

Methods: Retrospective cohort study from 296 sequential singleton placentas with features of MVM in 2015. Maternal and infant data were obtained from the medical record. Individual MVM features were studied for significant relation to outcomes with Chi-square test, Fisher's exact test, Wilcoxon rank-sum and the Kruskal-Wallis test as appropriate. A summative MVM score weighted similarly to prior studies was analyzed by receiver operating characteristic (ROC), with sensitivity, specificity, positive and negative predictive values for binary outcomes.

Results: Significant associations (Table 1) were observed with several maternal and neonatal outcomes supporting inclusion in a grading system. Features more heavily weighted in prior studies showed: Placenta weight < 3rd percentile more commonly seen in index SGA, subsequent SGA births and dyslipidemia at last follow-up. Fibrinoid necrosis/acute atheromatous change more commonly seen in all the outcomes depicted in the table over hypertrophic/persistent SM in basal plate (hyp/PSM) with exception of hyp/PSM being more often associated with obesity. None of the ordinal features associated with elevated pulsatility index on Doppler, Apgar score < 7 at 5 minutes, subsequent pregnancy loss or chronic/end-stage kidney disease at last follow-up. ROC characteristics of the summative MVM score showed fair or good discrimination for birthweight < 10th percentile (area under curve, AUC=0.83), GA < 32 weeks (AUC=0.8), absent/reversed end-diastolic flow (AUC=0.77), NICU admission (AUC=0.71), hypertension in pregnancy (AUC=0.71), and subsequent hypertension in pregnancy (AUC=0.7). Predictive performance was poor or no better than chance for most maternal CV health outcomes (AUC range: 0.51-0.61). Optimal MVM score cutoff values were not consistent across outcomes, and thresholds identified by the Youden Index and sensitivity-specificity equality methods frequently differed.

Conclusion: No single feature associates with all measures of clinical severity in the index pregnancy, neonatal course, subsequent pregnancy or maternal cardiovascular risk at last follow-up. A composite of multiple features suggests a more complete risk profile for both mother and neonate. Use of statistics to derive the best scoring system for outcome association is ongoing.

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Platform 3: Perinatal (V)

2495896

Placental Erythroblastosis and Normoblastemia: Correlation with Neonatal Disease.

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Background: NRBC elevation in fetal blood may be an indicator of fetal stress, anemia, or rarely a myeloproliferative disorder. Elevated NRBC have been defined as >10 NRBC in the fetal circulation in 10 hpf of terminal villi at term. We explore cases of increased NRBC to determine if the range of elevation correlates with neonatal conditions.

Methods: IRB approval was obtained for this study. The pathology database was queried for placentas with diagnoses including “erythroblastosis” and “normoblastemia” from 2015-2025. Data including the number of NRBC in 10 sequential 40x fields (hpf) of chorionic villi was extracted from the report. For cases where a count was not specified in the microscopic description, slides were pulled and a count performed. Only placentas associated with live birth were included. The maternal and neonatal medical record was queried for evidence of neonatal anemia from: 1) elevated fetal MCA doppler in utero, 2) Fetal hemoglobin or hematocrit < 5% for gestational age, 3) neonatal diagnosis of anemia, and 4) neonatal transfusion given. NRBC/10hpf counts were categorized as low (11-29), medium (30-49), high (50-99), and massive (>100) elevation.

Results: 45 placentas were identified, 44 singleton and 1 dichorionic/diamniotic twin. The average GA was 35 wks 6 days (range 26w0d to 41w4d), including 20 preterm, 10 of which were early preterm (< 32 weeks). Cases included 25 low, 7 medium, 7 high and 6 massive elevations in NRBC. The NRBC count ranged from 11-800. In 6 cases the diagnosis of fetal anemia was made in utero including 2 low, 2 medium, 1 high, and 1 massively elevated NRBC; 2 of these cases received in utero transfusion. Data for neonatal anemia by category of elevation are presented in Table 1. 31 patients were admitted to the NICU. 16 had an Apgar score at 5 minutes < 7. 16 had a diagnosis of multiple congenital anomalies, cardiac anomalies, Trisomy 21 or Rasopathy. 2 had a diagnosis of hemolytic anemia (immune-mediated, KLF-1).

Conclusion: Enumeration of NRBC is an important component of placental examination when they are appreciated to be increased. No specific level of NRBC elevation was associated with the diagnosis of anemia. Patients with hypoxic/ischemic conditions (neonatal encephalopathy, metabolic acidosis) more often had low level elevation (11-29 NRBC/10 hpf). Pathologists should consider alerting the pediatrician about the possibility of anemia when NRBC are elevated, for cases without an already recognized clinical cause.

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Platform 3: Perinatal (VI)

2496517

Fetal Sex Impacts Postpartum Placental Syncytiotrophoblastic Extracellular Vesicles

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Background: Placental syncytium releases multinucleated syncytiotrophoblastic (STB) "buds" into the maternal circulation throughout pregnancy. These circulating STB buds express placental alkaline phosphatase (PLAP) and lodge in the maternal lungs and persist for months after placental delivery. In this study we tested banked maternal plasma from 3 months, 6 months, 1 year, 1.5 years, and 2 years postpartum for STB EVs and compared levels with perinatal metrics including fetal sex and maternal complications.

Methods: Archived platelet poor plasma collected in EDTA tubes spun at 2x 15 minutes and banked at -80 were thawed only once and immunolabeled for STB-specific EVs (PLAP+/HLA-Gneg/CD63+) using 30 postpartum samples from primiparous women collected from 3 months to 2 years after vaginal deliveries at term. STB EVs were imaged and quantified by NanoFACS using published methods from our laboratory. Fetal and maternal metrics were extracted from the EMR. We compared STB EV counts/ml of plasma by maternal race, age, fetal sex, birthweight, and perinatal complications.

Results: Placental STB EVs peaked at 6 months postpartum subsequently decreasing by 50% every 6 months thereafter reaching non-detectable levels by 2 years after delivery. Levels were significantly increased when the delivered baby was a female compared with males. Cases of late onset preeclampsia and fetal growth restriction were associated with an INCREASED level of STB EVs at 3 months postpartum in both males and females ($p < 0.01$). Notably, extravillous trophoblast (EVT) EV signal defined as strong HLA-G and weak PLAP/CD63+ was identified in only 3 cases at 3 months.

Conclusion: Placental STB EVs are circulating at relatively high levels (10^6 /ml) months to years after delivery. The cargo and function of these postpartum placental EVs is currently unknown, but further study is warranted.



Posters

Poster 1

2486227

Detection of Blasts in Placentas of Down Syndrome Associated Transient Abnormal Myelopoiesis: Unusual Scenarios in Reviewing Placental Cases

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Background: Transient abnormal myelopoiesis (TAM) is a hematopoietic disorder in approximately 10% of newborns with Down syndrome. It is characterized by peripheral leukocytosis, thrombocytopenia or thrombocytosis, and increased megakaryoblasts with N-terminal truncating mutations in the GATA1 gene encoding a transcription factor essential for erythropoiesis and megakaryopoiesis. Symptomatic patients can manifest as early as the first week of life and may be noticed up to 2 months of age. Severe cases affect the liver, spleen, pleura, pericardium, and peritoneum. About 20% to 30% of the patients will progress into myeloid leukemia associated with Down syndrome (ML-DS)", most commonly acute megakaryoblastic leukemia before 4 years old. Identification of TAM at the earliest time is imperative to monitor the progression to a potentially critical condition. Routine hematologic evaluation after the occurrence of symptoms may be slower than histologic examination of placentas, thus, the instantaneous postpartum placental examination may enable early diagnosis of TAM.

Methods: Cases of TAM were searched retrospectively from Epic Beaker at our institution from 2010 to 2025. Cases with placenta tissue available were included in this study. Morphology of these placentas with CD34 and CD61 immunohistochemical stainings were examined by two pathologists who confirmed the diagnosis of TAM with positive CD34 and CD61 staining in blast cells. Clinical characteristics were obtained from pathology reports and the electronic medical record. Molecular studies and cytogenetic studies for karyotyping were also performed.

Results: Four cases of TAM with placenta examined were identified. All patients were symptomatic and had blasts in fetal vessels of their placentas. The features of the blasts in placentas were large size with megakaryoblastic differentiation demonstrated by CD61. All cases showed positive GATA1 truncating mutations with the karyotype as 47,XY,+21 or 47,XX,+21.

Conclusion: Blast detection in placenta can be more prompt if routine complete blood counts and peripheral smears are not performed or delayed for silent Down syndrome neonates. Placenta evaluation can provide ample tissue for comprehensive laboratory testing and tissue bank for future test development and research. In case of fetal demise without the authorization of autopsy, examination of placenta could potentially aid in determining the cause of death if there

is Down syndrome associated TAM of the fetus.

Poster 2

2496682

Mediastinal Soft Tissue Histopathologic Findings in Pediatric Pulmonary Vein Stenosis

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Background: Pulmonary vein stenosis (PVS) in infants and children affects large (extrapulmonary) pulmonary veins (PV); it causes impaired PV return and severe pulmonary hypertension, with limited treatment efficacy and high morbidity. Prior histologic investigations have focused on intimal and medial changes, with little attention to surrounding structures. Recent multidetector computed tomography studies have demonstrated that pediatric PVS is consistently associated with an ill-defined, mildly heterogeneously enhancing, noncalcified soft tissue mass following contours of affected veins in the mediastinum. We aim to identify the histologic correlate for this mass as a next step to understanding this novel finding.

Methods: Following institutional review board approval, autopsy specimens containing PV from pediatric patients with PVS were identified through a pathology database search covering 1994-2026. Clinical records were reviewed. Histologic evaluation of archival H&E- and elastic von Gieson-stained sections focused on the surrounding mediastinal tissue. Ten control PV from 4 pediatric autopsy patients (uninvolved PV from 1 patient with PVS, 2 patients with congenital heart disease, and 1 patient with pneumonia/sepsis) were examined.

Results: Twenty-eight PVS-affected PV from fourteen patients (8 males, 6 females) with available autopsy material were identified. Mean age at autopsy was 15 months (range, 2-32 months). PV with PVS showed intimal hyperplasia and variable medial disruption/scarring. Median maximum adventitial thickness was 2514 μm (range, 1089–12,000 μm); controls: median, 2653; range, 513– 6906 μm). Adventitial/perivascular tissue was variably composed of fibrous tissue rich in elastic fibers, slips of cardiomyocyte-like cells (most prominent at the PV atrial aspect), adipose tissue, small vessels, and nerves. Extracellular matrix was subtly myxoid. A subset of PVS adventitia showed reactive fibroblasts, macrophages, hemosiderosis and lymphocytes; one case showed extensive postoperative scarring with giant-cell reaction to foreign material. No appreciable collateral vasculature or edema was noted. No distinct or consistent qualitative differences in adventitial histopathologic features were observed between PVS and control veins.

Conclusion: Histologic evaluation of mediastinal perivascular soft tissue in PVS and controls is limited by scant attached tissue in autopsy samples. Targeted histologic examination reveals no

discernable anatomic cause for the mediastinal “mass” that is consistently observed radiologically. The cellular composition of these mediastinal changes, and whether they may represent a cause, consequence, or combination thereof in relation to PVS and/or its therapy, remains unclear.

Poster 3

2491829

A Retrospective Review of Factors Affecting Clinical-Pathologic Discordance in Acute Placental Abruptio; A Single Hospital Experience

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Background: Placental abruptio is primarily a clinical diagnosis, but placental examination may provide gross or microscopic supporting evidence.

Methods: We performed a retrospective clinicopathologic correlation study of sequential singleton placentas submitted for pathologic examination. Two groups were evaluated: placentas submitted with a clinical diagnosis or suspicion of acute abruptio (n=78), and placentas diagnosed pathologically as abruptio without clinical suspicion (n=14). Clinical signs were abstracted from admission and delivery records. Gross and microscopic placental findings were obtained from pathology reports with slide review when necessary.

Results: Pathology examination confirmed abruptio in 14/78 (17.9%) of clinically suspected cases. Among confirmed cases, clinical signs occurred only on admission in 28.6%, only at delivery in 21.4%, and at both time points in 50.0%, compared with 17.2%, 43.8%, and 29.7%, respectively, among unconfirmed cases (p=0.18). Admission bleeding was more frequent in confirmed than unconfirmed cases (71.4% vs 43.8%, p=0.06), while intrapartum bleeding was similar (71.4% vs 65.3%, p=0.76). NICU admission was significantly more frequent in confirmed cases (78.6% vs 29.7%, p=0.003). Among 28 pathologically diagnosed abruptios, half were clinically suspected and half were identified by pathology alone. Pathology-only cases frequently lacked documented clinical signs of abruptio (64.3%); 14.3% had signs at both admission and delivery. Pathologic evidence was heterogeneous. Among clinically suspected/pathology-confirmed cases, 14.3% had gross findings only, 14.3% microscopic findings only, and 71.4% both; corresponding proportions among pathology-only cases were 21.4%, 7.1%, and 71.4%. Evidence of older changes were seen more often in pathology-only cases. There was no significant effect of cesarean delivery. On chart review, clinical features were present in only 35.7% of pathology-only cases. These findings suggest inconsistency in clinical diagnosis. Among unconfirmed cases, clinical signs at delivery were more common than at admission (43.8% vs 17.2%) compared to confirmed cases (21.4% vs 28.6%) suggesting that these might represent more acute abruptio without fully developed pathology.

Conclusion: Clinical suspicion of acute placental abruptio had a low rate of pathologic confirmation, favoring cases with more established clinical features. The lack of standardized

documentation of clinical diagnostic criteria should also be investigated.

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Poster 4

2495370

Expanding the Molecular Landscape of Pediatric Mesothelioma

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Southwestern/Children's Medical Center Dallas, ² University of Texas Southwestern/Children's Medical Center Dallas

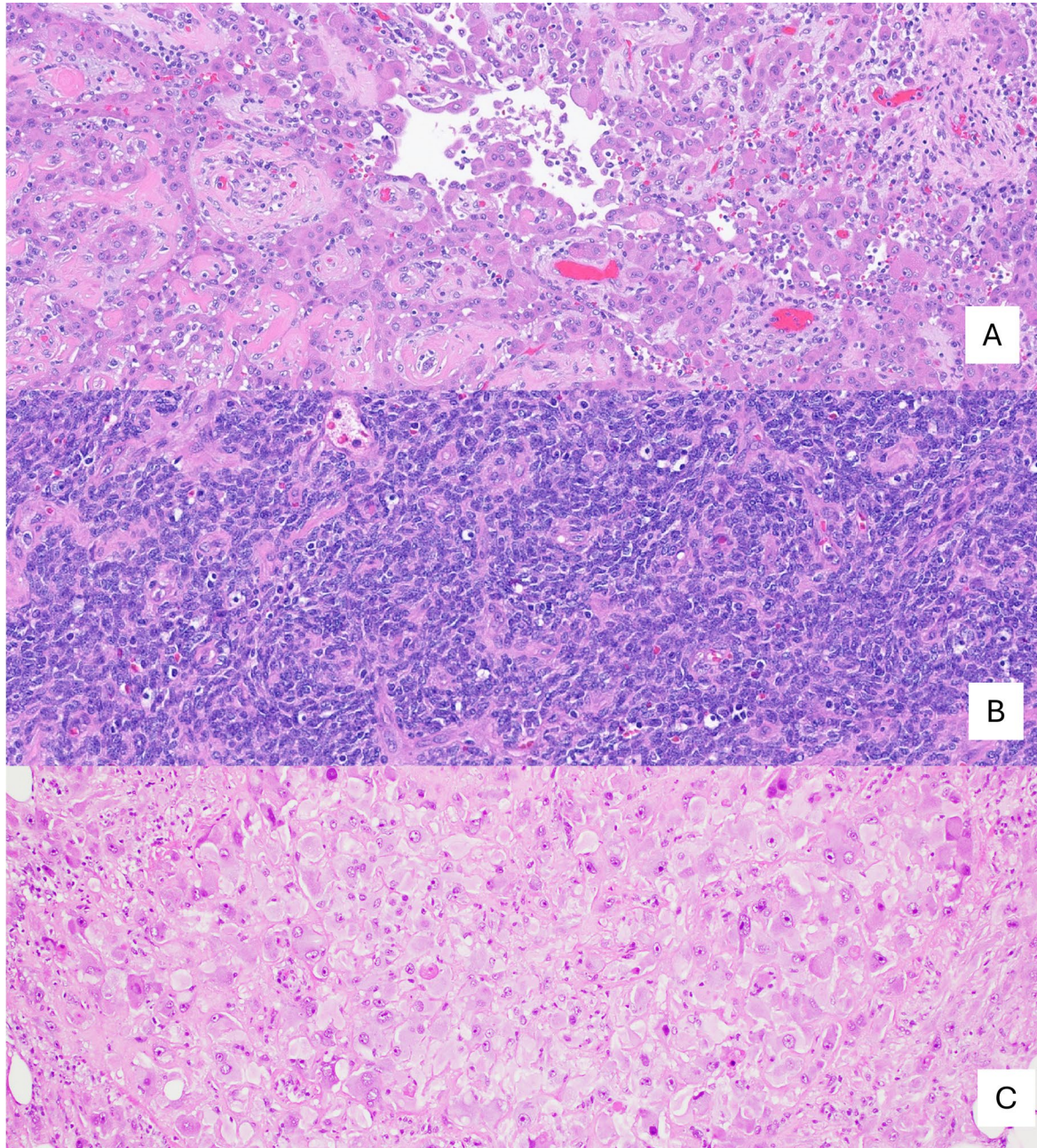
Background: Malignant mesothelioma is exceedingly rare in the pediatric population, with an estimated incidence of 0.5–1 case per 10 million children per year, and mesothelioma of the peritoneum represents only a fifth of those cases. While previous reports have found rearrangements involving EWSR1 or ALK genes in pediatric mesotheliomas, overall the molecular features of pediatric peritoneal mesothelioma remain poorly characterized. Herein, we present a series of three pediatric peritoneal mesothelioma cases to characterize the spectrum of histopathologic morphology and examine their associated immunohistochemical and molecular profiles.

Methods: Institutional pathology records were retrospectively reviewed to identify cases of pediatric peritoneal mesothelioma with unique morphologic and molecular findings. Three cases were identified, with patients ranging in age from 10 to 16 years at diagnosis; all three patients were male. Clinical history, gross and histopathologic findings, immunohistochemical profile, and molecular testing results were reviewed for each case.

Results: All three cases presented with peritoneal masses. None of the patients had a documented history of asbestos exposure. The morphology of each case differed, described as epithelioid mesothelioma, small cell mesothelioma, and deciduoid mesothelioma. None of the cases showed anaplasia, brisk mitotic activity, or extensive necrosis. All cases demonstrated immunoreactivity for mesothelial markers and were negative for desmin. In the cases where testing was performed, BAP1 expression was retained and rearrangement of ALK was negative. The case of deciduoid mesothelioma was found to have an EWSR1::TEAD3 fusion by next generation sequencing (reported in a previous case series). The small cell mesothelioma occurred in the youngest patient and harbored an EWSR1::YY1 gene fusion; this represents a rare fusion that has been reported in association with epithelioid mesothelioma of adults but, to our knowledge, has not previously been described in a pediatric peritoneal mesothelioma. The third case was found to have a RAD51B::SH3KBP1 gene fusion, a novel fusion which has not been previously reported in any tumor.

Conclusion: Pediatric peritoneal mesothelioma can demonstrate substantial morphologic and molecular heterogeneity, including unusual small cell morphology and gene rearrangements. As

next generation sequencing becomes more widely adopted, novel gene fusions such as the RAD51B::SH3KBP1 described here may be more frequently identified in these rare pediatric tumors.



Poster 5

2495442

Aneurysmal Fibrous Histiocytoma Associated with Langerhans Cell Histiocytosis: a Collision Tumor?

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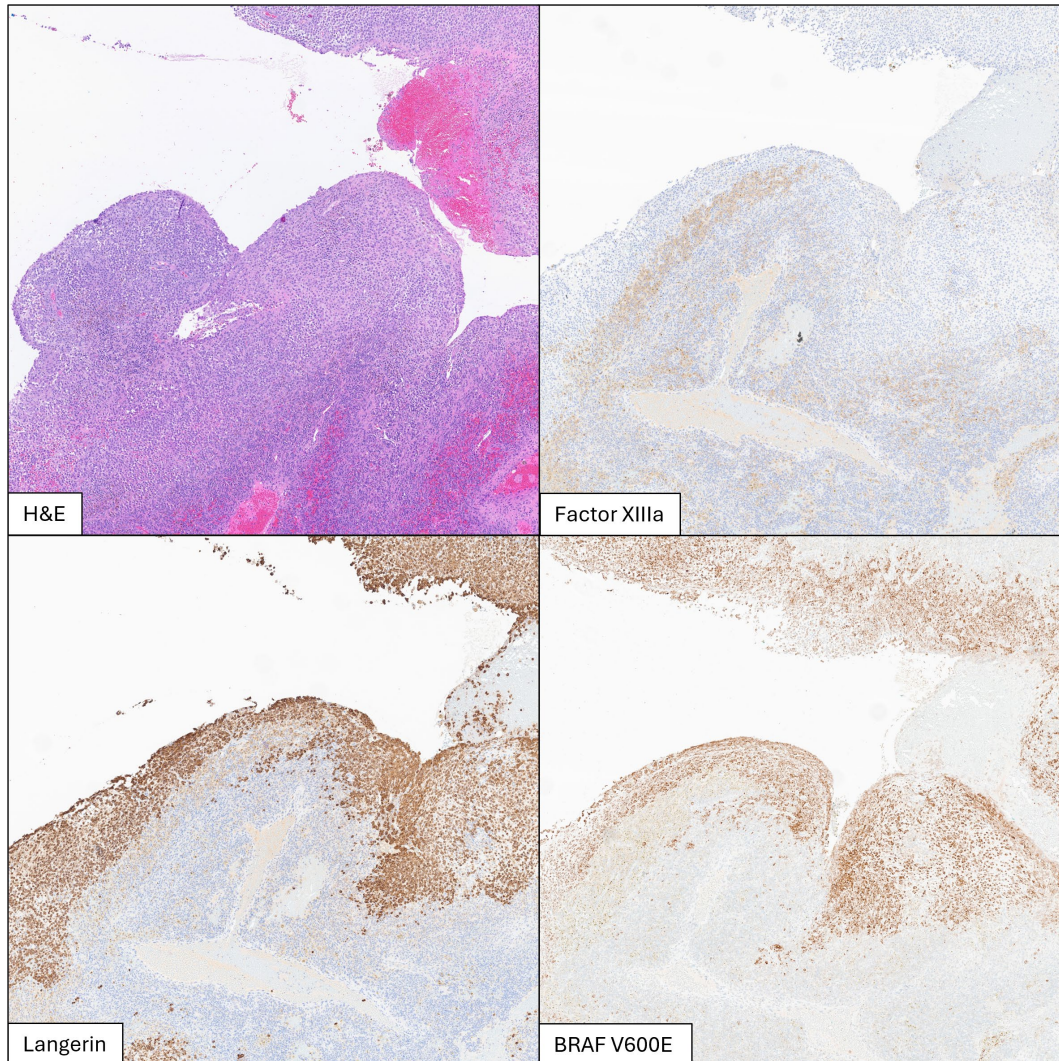
Background: Langerhans cell histiocytosis (LCH)-like proliferations have been reported in association with a variety of neoplastic and inflammatory conditions, often representing an exuberant inflammatory response. When present in cases of fibrous histiocytoma (FH), some authors have proposed other possible pathogenetic mechanisms, including a collision tumor, divergent differentiation arising from a common progenitor, or an indeterminate cell histiocytosis with involutional fibrosing changes.

Methods: An 18-year-old female presented with a 5 cm mass on her back near the scapula that had been present for one year. Imaging revealed a multilobulated and septate subcutaneous mass with fluid levels. The lesion was surgically excised and described as a dermal-based lesion with hemorrhagic contents. It was submitted for further examination, including histology, immunohistochemistry, and molecular testing.

Results: Histologic examination revealed a hemorrhagic dermal lesion with vaguely cystic architecture and composed of two different populations of cells. One population formed the "outer portion" of the cystic space, composed of spindled-to-epithelioid cells with an infiltrative pattern that surrounded peripheral bundles of dermal collagen and associated with hemosiderin deposition; these cells showed patchy positivity for CD163 and factor XIIIa by IHC, consistent with aneurysmal fibrous histiocytoma. The second population of cells formed the "inner wall" of the cystic components, composed of plump histiocytoid cells with ovoid-to-convoluted nuclei that had frequent nuclear grooves, occasional multinucleate cells, and an associated inflammatory infiltrate of lymphocytes, eosinophils, rare neutrophils and plasma cells. This second population was positive for langerin, CD1a, S100, PU.1, and BRAF V600E by IHC, consistent with Langerhans cell histiocytosis. Molecular studies confirmed a BRAF V600E mutation and also identified a LAMTOR1::PRKCD gene fusion.

Conclusion: Aneurysmal fibrous histiocytoma is a rare dermatofibroma variant that typically presents as a solitary pigmented nodule on the extremities or trunk. Histologically, it is a poorly circumscribed dermal proliferation of spindle to epithelioid cells in a storiform pattern, with prominent blood-filled pseudovascular spaces, hemosiderin, and hemosiderophages. LAMTOR1::PRKCD gene fusions have been described in aneurysmal FHs, supporting this

diagnosis. Concurrently, a positive BRAF V600E mutation by PCR in combination with a population of atypical histiocytoid cells confirms a neoplastic process consistent with LCH. This lesion likely represents a collision tumor of Langerhans cell histiocytosis, a relatively common entity, arising within a rare aneurysmal FH. Three months after excision the patient is without recurrence or secondary lesions.



Poster 6

2473135

Pulmonary Vasculopathy in Restrictive Allograft Syndrome - An Underrecognized Component of Chronic Lung Allograft Dysfunction

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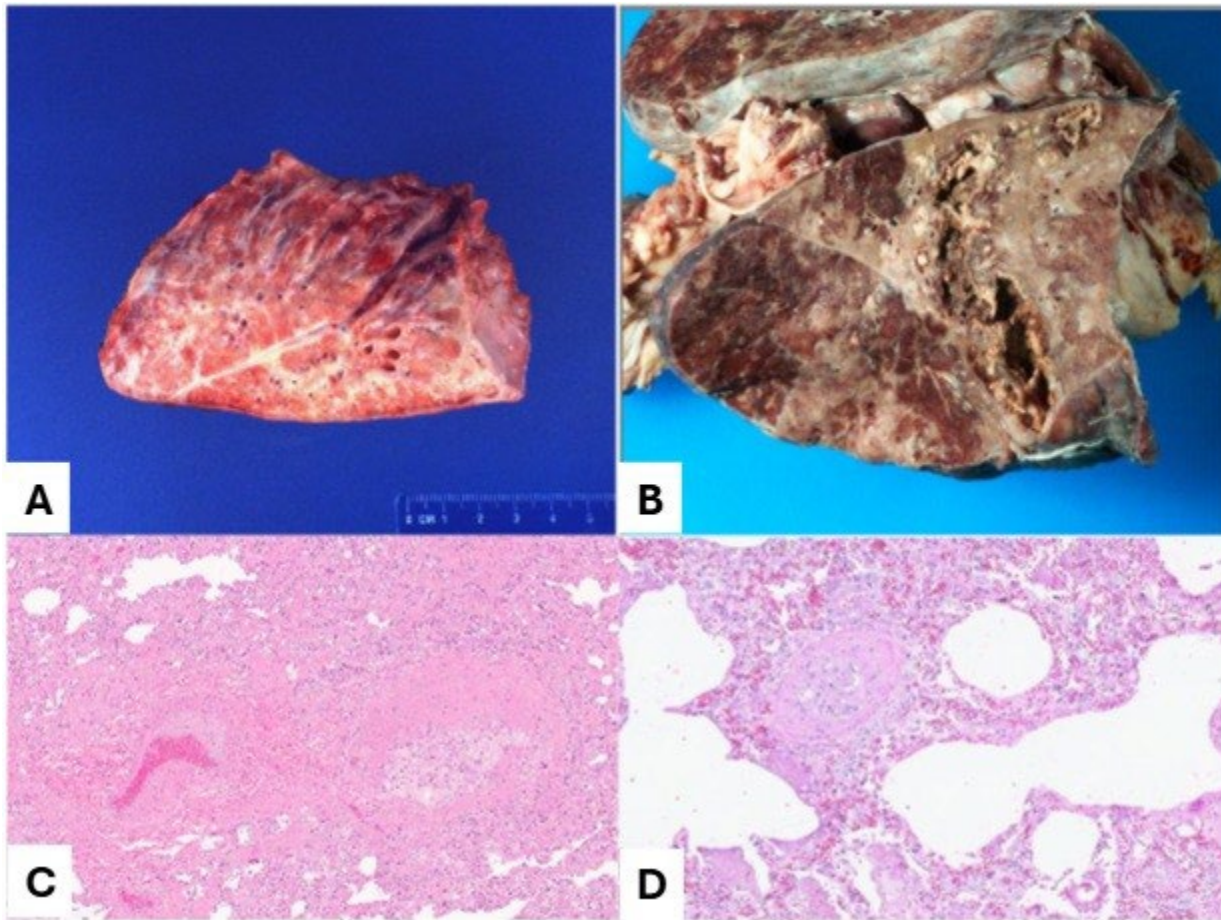
Background: Restrictive allograft syndrome (RAS) affects 30% of patients with chronic lung allograft dysfunction (CLAD), with median survival of 1-2 years. While pleuroparenchymal fibroelastosis and obliterative bronchiolitis are recognized as histopathological hallmarks, the pulmonary vascular compartment has received limited evaluation despite evidence of higher vascular fibrosis scores in RAS compared to bronchiolitis obliterans syndrome. The presence and significance of pulmonary vasculopathy in RAS was underrecognized as a core pathological feature in current classification systems.

Methods: We present two RAS patients with Cystic Fibrosis. Patient 1, a 12-year-old male, underwent double lung transplant due to cystic fibrosis. He had class I and class II DSA detected beginning the same month of his initial transplantation with biopsy suspicious for antibody mediated rejection (AMR) but no acute cellular rejection (ACR) was documented. Over four years after transplantation, he developed progressive respiratory decline with restrictive pulmonary function test (PFT), diagnosed as RAS, and underwent bilateral re-transplantation. The explanted allografts were evaluated. Patient 2, a 16-year-old female, underwent double lung transplant secondary to cystic fibrosis. Biopsy at five months after transplantation showed probable high-grade rejection with graft vasculopathy, focal C4d deposition, acute lymphocytic bronchiolitis, and acute lung injury. She had class II DSA detected 5 months after transplantation and received appropriate treatment. Her course was complicated by multiorgan failure and death. The allograft lungs were evaluated at autopsy.

Results: We present two RAS cases, an explanted lung allograft, and an autopsy lung allograft. Both cases demonstrated concurrent pleuroparenchymal fibroelastosis, obliterative bronchiolitis, and prominent pulmonary vasculopathy. Detailed histopathological examination revealed extensive vascular remodeling affecting both arterial and venous compartments, including medial hypertrophy, intimal fibrosis, and luminal narrowing.

Conclusion: These cases draw attention to pulmonary vasculopathy as a potentially important, yet underrecognized, histopathological feature of RAS. Systematic evaluation of pulmonary vascular changes in RAS is necessary to better understand the pathogenesis and develop new

management strategies.



Differential Diagnosis of Pulmonary Alveolar Proteinosis in Pediatric Bronchoalveolar Lavage Specimens

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Background: Pulmonary alveolar proteinosis (PAP) is a nonneoplastic condition characterized by filling of the lung alveolar spaces with proteinaceous material that is most frequently treated by whole lung lavage. Primary PAP is caused by disruption of GM-CSF signaling due to anti-GM-CSF autoantibodies or GM-CSF receptor mutations, whereas secondary PAP is due to an underlying disease that reduces the numbers or function of alveolar macrophages. PAP can be diagnosed on bronchoalveolar lavage (BAL) specimens but there is limited literature on the cytologic differential diagnosis of PAP in BAL specimens, particularly in the pediatric age group.

Methods: We sought to better understand the cytological differential diagnosis of PAP in BAL specimens in our pediatric center, which performs over 2,000 BALs each year. We searched our archive for cases which morphologically resemble PAP to compare the cytologic findings. We reviewed cases of PAP (3), diffuse alveolar damage (3), acute hemorrhage (3), plastic bronchitis(1), pneumocystis pneumonia (2), and acute aspiration (1).

Results: Cytologic preparations of PAP cases contained granular and amorphous PAS positive globular eosinophilic material in the background. The macrophages were markedly enlarged with vacuolated cytoplasm and Oil Red O positive lipid droplets. Diffuse alveolar damage samples contained diffuse eosinophilic material, but the material was often fibrillary and more irregularly shaped, sometimes having a linear appearance resembling hyaline membranes. Acute hemorrhage was associated with eosinophilic debris that was more fibrillary in nature within a background of blood. Fibrillary eosinophilic material was also seen in cases of plastic bronchitis. Acute aspiration was characterized by granular debris that was more diffuse and not associated with globules. Cases with Pneumocystis infection had fluffy appearing eosinophilic material that was not associated with globules and demonstrated positivity on GMS stain. These findings are illustrated in Figure 1.

Conclusion: PAP can be diagnosed by BAL in the appropriate clinical context. Several pulmonary conditions can mimic PAP in cytology specimens due to the presence of overlapping eosinophilic extracellular material. However, recognition of key cytomorphologic features, including the characteristic PAS-positive globules, granular background, and lipid-laden macrophages, can aid in distinguishing PAP from its mimics. Awareness of these differential

diagnostic features, together with clinical correlation and ancillary studies, is essential to arriving at an accurate diagnosis.

Poster 8

2496397

Tissue Stewardship in Pediatric CNS Tumor Specimens: Maximizing Precision Diagnosis and Research

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Background: Pediatric CNS specimens increasingly must support histologic diagnosis, molecular classification, future clinical needs, and research, creating competing demands when tissue is limited. We evaluated whether deliberate tissue stewardship can maximize both precise diagnosis and research allocation.

Methods: We retrospectively reviewed 178 pediatric and young-adult CNS tumor specimens from 2024 to 2025, recording procedure type, number of blocks, frozen and fresh research allocation, DNA sequencing, RNA fusion testing, methylation profiling, and other molecular studies. Cases without molecular testing were reviewed to determine whether testing was required for precise classification or had been performed previously. Findings were used to develop a practical triage framework prioritizing diagnostic adequacy, clinically necessary molecular testing, preservation of clinical reserve, and consented research, supported by tissue-sparing handling and coordinated ancillary testing.

Results: The cohort included 142 resections, 29 biopsies, and 7 combined procedures. Molecular testing was performed on the current specimen in 146/178 cases (82.0%). Of 32 untested cases, 22 had diagnoses not requiring molecular testing for precise classification and 8 recurrent/residual tumors had been molecularly characterized at an earlier resection; only 2 lacked potentially useful characterization. Thus, 176/178 cases (98.9%) achieved appropriate diagnostic characterization. Overall, 148/178 cases (83.1%) contributed frozen and/or fresh tissue to research. Among biopsies, which generated fewer blocks than resections (median 3 vs 4.5; $P=.0018$), 24/25 (96.0%) cases requiring molecular characterization underwent testing, while 18/29 (62.1%) contributed research tissue; 15/18 of these research-contributing biopsies also underwent molecular testing.

Conclusion: Careful stewardship of limited pediatric CNS tissue can support both contemporary precision diagnosis and meaningful research banking. The resulting practical triage approach emphasizes advance communication, adequacy-directed intraoperative assessment, minimal tissue manipulation, separation of small fragments/cores across blocks, shallow/no-waste facing, coordinated hypothesis-driven ancillary testing, preservation of a clinical reserve, and a pause before block exhaustion. This workflow provides a reproducible strategy to maximize diagnostic

and research value, including from small biopsies.

Poster 9

2496550

Identification of placental Barr bodies using H3K27me3 immunohistochemical stain: a potential diagnostic adjunct in Turner syndrome mosaicism

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Background: Turner syndrome is a congenital genetic condition seen in females, characterized by loss of one X-chromosome (45X). In rare cases, the loss may not impact all cells of the embryo, resulting in an eventual fetus with a mosaic expression of Turner syndrome(45X/46XX). Mosaicism can also be confined to the placenta. Maternal mosaicism can be clinically inapparent and result in false positive prenatal fetal screening. In cells with two X-chromosomes (46XX), one copy is randomly inactivated, resulting in condensed heterochromatin known as a “Barr Body”. The immunohistochemical stain H3K27me3 can identify these Barr bodies, but its diagnostic utility in placenta is largely unknown.

Methods: Clinical, imaging, histologic, immunohistochemical, and molecular findings were reviewed in 3 cases.

Results: Case 1 had two positive (45X) cell-free DNA screens followed by negative amniocentesis (46XX). H3K27me3 staining of the placenta showed numerous putative Barr bodies were identified in maternal (decidual) and fetal cells (villous stromal and endothelial cells, amniocytes, and subamniotic stroma). Baby shows no stigmata of Turner syndrome. Maternal chromosome analysis was ordered but not performed. The etiology of the positive result was not definitively established. Case 2 had a positive cell-free DNA screen (45X). H3K27me3 staining of the placenta showed numerous putative Barr bodies were identified in maternal (decidual) and fetal cells (villous stromal and endothelial cells, amniocytes, and subamniotic stroma). Baby showed no stigmata of Turner syndrome. Maternal chromosome analysis confirmed low-level maternal mosaicism 45,X[5]/46,XX[42]. Case 3 had a positive cell-free DNA screen (45X). H3K27me3 staining of the placenta showed numerous putative Barr bodies were identified in maternal (decidual) and fetal cells (villous stromal and endothelial cells, amniocytes, and subamniotic stroma). Baby showed no stigmata of Turner syndrome and had a normal karyotype (46XX). Maternal chromosome analysis confirmed low-level maternal mosaicism 45,X[6]/46,XX[41].

Conclusion: Herein we present 3 cases in which the H3K27me3 immunohistochemical stain was used to identify Barr bodies in maternal and fetal cells in cases with positive cell-free DNA screens, suggesting at least some maternal and fetal cells contained two X-chromosomes in all cases. Two cases were confirmed to be low-level maternal mosaics, while the third was lost to

follow-up. These cases suggest a possible utility of H3K27me3 in the investigation of a potential Turner syndrome mosaicism.

Poster 10

2496559

A male infant with metastatic YWHAE::NUTM2B fusion-positive undifferentiated sarcoma with novel morphologic and immunohistochemical features

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Background: YWHAE::NUTM2B -rearranged sarcoma is a unique tumor of infancy that affects axial soft tissues and involve genes in the MAD transcription family, rather than the BRD fusions seen in NUT carcinoma. They are aggressive, with over half of reported cases dying of disease, and have an unusual predilection for CNS metastases. Primitive monomorphic small round blue cells and prominent arborizing vasculature are the recurrent histologic findings. Optimal treatment regimens need to be established.

Methods: Clinical, imaging, histologic, immunohistochemical, and molecular findings were reviewed.

Results: A 3-week-old male infant presented with a palpable left lumbosacral soft tissue mass. Infantile hemangioma was favored. After 2 [DP1.1]months of continued rapid growth (from 1.9 to 7 cm) on treatment (six weeks of propranolol therapy followed by prednisone and sirolimus given concern for other vascular anomalies), and largely non-diagnostic superficial biopsy attempt, a decision was made to pursue surgical resection. Histologic examination demonstrated a well-circumscribed hypercellular tumor surrounded by a fibrous pseudocapsule, predominantly comprised of monotonous small round blue cells (~80%), with multifocal rhabdoid appearance (~20%; vesicular nucleoli, prominent central eosinophilic nucleoli, and abundant eosinophilic cytoplasm). Multiple staghorn vessels, blood-filled pseudoangiomatoid spaces, numerous mitoses(>10 per 10 HPF), and patchy necrosis (~20%) were also noted. Given the non-specific morphology an extensive immunohistochemical panel was performed. This showed patchy positivity for EMA, DUX4 (cytoplasmic), CD99 (variable cytoplasmic and membranous staining in ~80%), Beta-catenin (wild type), and pan-TRK (strong and diffuse cytoplasmic/membranous expression). INI1 and SMARCA4 were retained. Ki-67 was elevated (~70%). The tumor was negative for NUT, CD43, AE1/AE3, ERG, GATA3, MyoD1, desmin, myogenin, SSX/SSX-SS18, ALK, STAT6, PHOX2B, S100, SALL4, and WT-1. A sarcoma fusion panel allowed diagnosis as YWHAE::NUTM2B fusion-positive undifferentiated sarcoma. An enlarged left inguinal lymph node was biopsied and contained metastatic sarcoma. There is no evidence of CNS involvement and he is receiving sarcoma chemotherapy modeled on ARST1321.

Conclusion: We report a male infant with a rapidly growing YWHAE::NUTM2B fusion-positive

undifferentiated sarcoma. This case confirms the potential for lymph node metastases, expands the pathologic spectrum to include prominent rhabdoid differentiation and strong NTRK-immunohistochemical expression, and highlights how they can mimic common tumors of infancy.

Poster 11

2496588

A novel variant of aggressive rhabdomyosarcoma with a unique RBPJ::NCOA2 fusion

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Background: Pediatric rhabdomyosarcoma has traditionally been subclassified into embryonal, alveolar, and spindle-cell subtypes. PAX3/7::FOXO1 gene fusions occur in 80% of alveolar subtypes and are strongly predictive of outcome. However, novel variants have recently been described that do not align with any of the 3 major subtypes. These can have distinctive histologic and immunohistochemical findings, harbor novel molecular alterations of potential predictive and prognostic significance and have unique clinical behavior.

Methods: Clinical, imaging, histologic, immunohistochemical, and molecular findings were reviewed.

Results: A 2-year-old male presented with a several month history of an enlarging non-tender right parotid mass following a recent household-wide influenza-like illness and positive EBV swab. After imaging, a biopsy was performed which identified a malignant spindle cell and epithelioid neoplasm with abundant myxoid stroma and prominent plexiform vasculature. No definite anaplasia, rhabdomyoblastic differentiation, or atypical mitoses were seen. Numerous mitoses were present throughout. Given the nonspecific and unusual morphology, an extensive immunohistochemical characterization was performed. The tumor cells were positive for myo D1 (patchy; < 50%), diffusely expressed desmin, smooth muscle actin (patchy; ~50%), CD99 (patchy; < 30%), pan-TRK (patchy; < 30%), S100 (patchy; < 50%) and beta-catenin (membranous/cytoplasmic staining only). The tumor cells were completely negative for myogenin and many other non-myogenic markers. Ki67 was high at 70%. Overall, the findings did not allow for definitive diagnosis, but the patchy myo D1 and strong cytoplasmic expression of desmin in most tumor cells made variant rhabdomyosarcoma the leading consideration. A sarcoma fusion panel identified a RBPJ::NCOA2 gene fusion, allowing for a definitive classification as a rhabdomyosarcoma. Imaging was concerning for infiltration into the underlying mandible with possible cervical lymph node metastases. The patient underwent neoadjuvant chemotherapy for 12 weeks (vincristine, topotecan, and cyclophosphamide, modeled on COG D9803) followed by surgical resection of the mass, including a right segmental mandibulectomy and neck dissection. The resected mandible, masticator space, and infratemporal fossa demonstrated viable tumor with zero treatment effect and permeative growth through bone and to soft tissue margins. All cervical lymph nodes were uninvolved. The patient is scheduled to receive proton beam radiation.

Conclusion: Herein we present a novel RBPJ::NCOA2 fusion identified in a 2-year-old male with treatment-resistant rhabdomyosarcoma. This novel tumor has distinctive morphologic and immunohistochemical findings and has been nonresponsive to conventional rhabdomyosarcoma chemotherapy.

Poster 12

2496178

Adrenocortical Neoplasms in Children: A Three-Case Series

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Background: Adrenocortical neoplasms (ACNs) in patients younger than 20 years are rare and differ from adult tumors in clinical presentation and prognostic behavior. Although many pediatric tumors are classified as adrenocortical carcinoma (ACC), some have favorable outcomes despite aggressive histologic features. The mechanism remains unclear. We present three pediatric ACNs and correlate their histopathologic and molecular features with clinical outcomes.

Methods: Three pediatric ACNs resected at Children's Hospital Los Angeles between 2021 and 2025 were retrospectively identified. All cases underwent molecular testing; one also underwent targeted TP53 testing that confirmed the OncoKids findings. Clinical records and pathology reports were reviewed for clinical, histopathologic, molecular, and outcome data.

Results: Patients were 1, 2, and 11 years old; all were female and presented with virilization and elevated serum androgen levels. Adrenal masses measured 3.1, 11.5, and 10.5 cm, respectively, and all were surgically resected. Patient 1 was diagnosed with ACN and met one Wieneke criterion. The tumor lacked soft tissue, vascular, or capsular invasion and necrosis and showed 2 mitoses/10 HPF with rare atypical mitotic figures. Chromosomal microarray demonstrated TP53 loss. Patient 2 was diagnosed with ACC and met at least two Wieneke criteria. The 11.5-cm tumor showed necrosis and 12 mitoses/10 HPF but lacked soft tissue, vascular, and capsular invasion. Molecular testing identified a TP53 p.Arg273 mutation and losses of chromosome 11p and chromosome 17. Patient 3 was diagnosed with ACC and met at least five Wieneke criteria. The tumor showed extension into adjacent soft tissue, vascular and capsular invasion, and necrosis. Molecular testing identified a TP53 p.Ala308Thr mutation and losses involving TP53, CDKN2A/CDKN2B, chromosome 11p, chromosome 17, and NTRK3. This patient had Li-Fraumeni syndrome. At most recent follow-up, Patients 1 and 2 remained disease-free after resection, whereas Patient 3 developed pulmonary metastases and was receiving chemotherapy.

Conclusion: Pediatric ACNs show marked histopathologic and molecular heterogeneity, underscoring limitations of adult diagnostic and prognostic criteria in this population. Alterations involving TP53 and CDKN2A/CDKN2B and losses of chromosomes 11 and 17 were identified, consistent with reported genomic abnormalities in pediatric ACC. The patient with Li-Fraumeni

syndrome had a germline TP53 alteration and chromosome 17 loss and developed metastatic disease. Integrated histopathologic and molecular assessment may improve risk stratification and prognostication in pediatric ACNs. Larger studies are needed to identify clinically meaningful biomarkers.

Poster 13

2493485

First Report of a Composite Vascular Neoplasm with High-Grade Angiosarcomatous Features, Neuroendocrine Marker Expression, and PIK3CA Alteration Favoring Angiosarcoma

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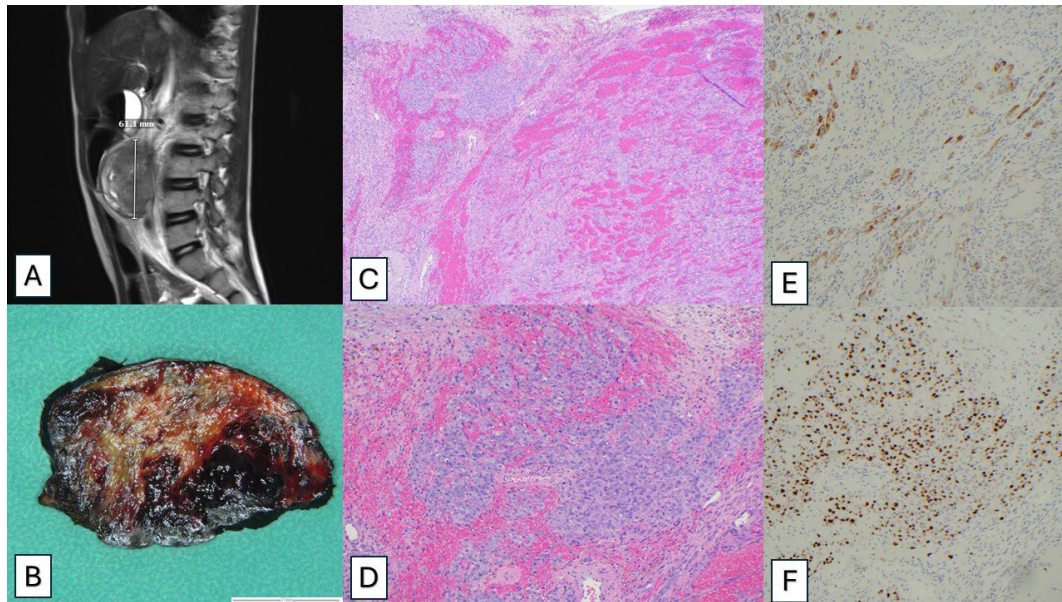
Background: Composite hemangioendothelioma (CHE) is a rare vascular neoplasm containing an admixture of distinct epithelioid and retiform hemangioendothelioma morphologies. This neoplasm has rare reports of neuroendocrine marker expression, and exceptionally uncommon examples are reported to have angiosarcomatous foci. Distinguishing CHE from conventional angiosarcoma is critical because of important differences in prognosis and management. We report a unique pediatric vascular neoplasm showing overlapping features of neuroendocrine CHE and angiosarcoma.

Methods: We evaluated the clinical, histologic, immunophenotypic, and molecular findings of a 7-year-old female presenting with a retroperitoneal tumor.

Results: A 7-year-old female with a history of 16q11.2 duplication syndrome and developmental delay presented with abdominal pain and weight loss. Magnetic resonance imaging demonstrated a 7.0 cm retroperitoneal mass with cystic and hemorrhagic components encasing the infrarenal aorta and abutting the inferior vena cava. Initial biopsy revealed an architecturally heterogeneous vascular neoplasm with retiform and epithelioid morphology with expression of neuroendocrine markers, raising consideration of CHE. Targeted next-generation sequencing identified a pathogenic PIK3CA p.E542K alteration, while testing for recurrent CHE-associated gene fusions was negative. Given the deep-seated presentation and concern for aggressive biologic behavior, the patient received chemotherapy with ifosfamide and doxorubicin as part of a clinical trial for non-rhabdomyosarcoma soft tissue sarcomas. Following three treatment cycles, repeat imaging showed approximately 16% reduction in tumor size without evidence of metastatic disease. Subsequently, resection of the mass demonstrated a malignant composite vascular neoplasm with increased mitotic activity and focal neuroendocrine marker expression as well as 20% geographic necrosis consistent with treatment effect.

Conclusion: This case represents a previously undescribed composite vascular neoplasm showing high-grade angiosarcomatous morphology, neuroendocrine marker expression, and a pathogenic PIK3CA alteration. While the initial biopsy suggested neuroendocrine CHE, the

clinical and histopathologic features, as well as the molecular findings, support its classification as angiosarcoma despite its unusual neuroendocrine phenotype. Recognition of this spectrum in composite vascular lesions is important because classification as angiosarcoma carries significant implications for prognosis and clinical management. This case also highlights the limitations of existing diagnostic categories and suggests that rare vascular neoplasms with overlapping morphologic features may require integrated molecular and clinicopathologic assessment for accurate classification.



Poster 14

2481392

Neonatal Cholestasis: A 10-Year Institutional Retrospective Review of Liver Biopsies

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Background: Neonatal cholestasis requires timely diagnosis as delayed recognition may result in progressive liver injury. The differential diagnosis is broad and includes extrahepatic biliary atresia (EBA), infection, metabolic, genetic, and total parenteral nutrition (TPN)-associated liver disease. Although liver biopsy remains an important diagnostic tool, ancillary testing is necessary to distinguish overlapping histologic patterns of injury which fall into three major categories: neonatal giant cell hepatitis (NGCH)-NOS, obstructive cholangiopathy, and bile duct paucity. To better characterize the diagnostic utility and limitations of liver biopsy, we retrospectively reviewed liver biopsies from infants aged 0–6 months over a 10-year period, correlating histopathologic findings with contemporaneous clinical data available at the time of biopsy and assessed follow-up on etiologies and clinical course.

Methods: We retrospectively reviewed liver biopsies from infants ≤ 6 months of age who underwent biopsy for evaluation of neonatal direct hyperbilirubinemia at University Hospitals Cleveland Medical Center between 2014 and 2024. Patients with a previously established diagnosis, as well as those who underwent diagnostic cholangiography or exploratory laparotomy yielding a definitive diagnosis before or at the time of biopsy, were excluded. Histologic findings, pathologic diagnoses, and clinical information available at the time of biopsy interpretation were correlated with results from subsequent molecular/genetic testing.

Results: NGCH was present in 33 of 34 cases identified. All were categorized according to the predominant histologic pattern and summarized in Table 1. The majority of cases had no available molecular/genetic data or cholangiography/nuclear imaging at the time of biopsy. However, when EBA was suggested histologically, subsequent chart review confirmed the diagnosis in all cases. Similarly, TPN-associated injury pattern was suggested and frequently confirmed with clinical improvement after withdrawal of TPN. The majority of the NOS patterns had metabolic/genetic causes.

Conclusion: NGCH is the most common histopathologic pattern of injury in patients with neonatal cholestasis and represents a nonspecific manifestation of a broad spectrum of underlying disorders. A major limitation at our institution was the lack of available radiologic, genetic, and metabolic testing with results most frequently unavailable at the time of biopsy. Liver biopsy accurately identified or suspected EBA most consistently and was frequently informative in TPN-associated cholestasis. This series highlights the continued value of liver

biopsy in the evaluation of neonatal cholestasis while emphasizing the increasingly important role of ancillary testing in achieving diagnostic precision.

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Poster 15

2496632

Mucosal Prolapse Changes in Pediatric Patients with Inflammatory Bowel Disease and Gastric Heterotopia: Case Series

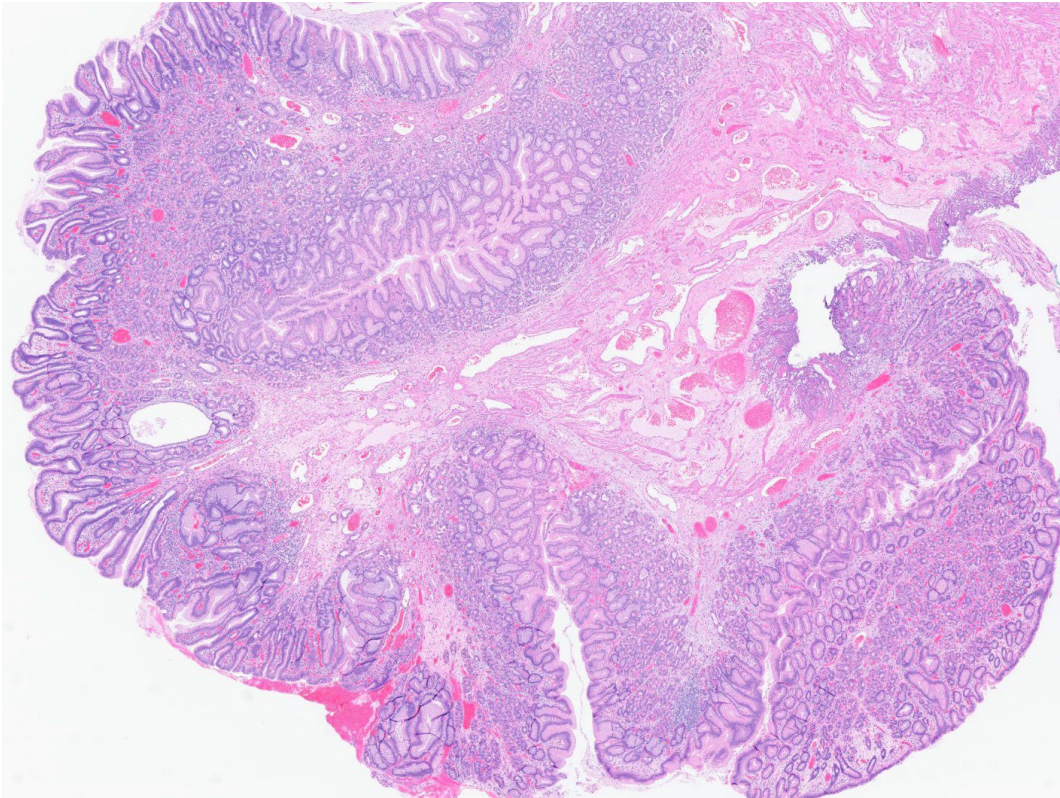
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Background: Mucosal prolapse syndrome presents with a broad spectrum of endoscopic and histologic findings, including ulceration and polyps with or without granulation tissue which frequently involves rectum and infrequently the terminal ileum adjacent to ileocecal valve. Rarely, heterotopic tissue in the rectum may present as a mucosal prolapse. In children with inflammatory bowel disease (IBD), pseudopolyps and inflammatory polyps could mimic mucosal prolapse polyp (MPP). Accurate diagnosis of MPP and its mimics is essential for successful management of the underlying conditions.

Methods: We present three cases of polypoid lesions identified following colonoscopy of children presenting with hematochezia and weight loss. All patients were males aged 15–17 years with a longstanding history of constipation. The polyps were located in the rectum (2 patients) and terminal ileum (1 patient). Two patients had previously been diagnosed with Crohn's disease (CD) and had been treated with immunotherapy and surgical intervention. Routine histopathologic examination was performed on the endoscopically removed polypoid tissue.

Results: The polyp from the terminal ileum of a patient with CD showed prominent crypt hyperplasia, villous atrophy, fibromuscular hyperplasia, and mild chronic inflammation. The polyp from the rectum of the second patient with CD showed granulation tissue, fibromuscular hyperplasia; and lymphoplasmacytic cells in lamina propria. The polyp from the rectum of the 3rd patient demonstrated gastric tissue featuring oxyntic mucosa with fibromuscular hyperplasia in lamina propria and ectatic vessels at the pedicle.

Conclusion: Mucosal prolapse changes in the rectum due to straining at stools and in ileum due to recurrent intussusception may be associated with secondary conditions such as IBD and heterotopic tissue. Crypt hyperplasia, vertically arranged myofibroblastic/smooth muscle cells (fibromuscular hyperplasia) and vascular ectasia are characteristic features seen in MPP that when correlated with location and history can lead to an accurate diagnosis. Depending on the underlying secondary condition, the management of MPP can differ significantly. In the setting of IBD, strictures causing obstruction may be the inciting event for the prolapse.



Poster 16

2496537

Explant Pathology in Hearts with Pulmonary Atresia and Intact Ventricular Septum with Right Ventricle-Dependent Coronary Circulation: Report of 2 cases

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Background: Pulmonary atresia with intact ventricular septum (PA/IVS) is a rare cyanotic congenital heart defect characterized by a hypoplastic right ventricle and, in a subset of patients, right ventricle-dependent coronary circulation (RVDCC) via myocardial sinusoids or coronary-cameral fistula (CCF). We describe the explant pathology of native hearts from two infants with PA/IVS who underwent multiple palliative procedures, followed by orthotopic heart transplantation.

Methods: Case 1: Infant was born at 36-weeks of gestation, echocardiogram on day 1 of life and showed PA/IVS, a hypoplastic tricuspid valve, severely hypoplastic right ventricle, and Doppler findings consistent with right ventricular coronary sinusoids. He underwent multiple palliative procedures including single ventricle assist device (SVAD) insertion before heart transplantation. Case 2: Infant was born at 38-weeks of gestation and was diagnosed with PA/IVS on day 1 of life. She was maintained on prostaglandin E1, followed by multiple palliative procedures including SVAD insertion before heart transplantation. Histopathologic examination of the explanted hearts was performed.

Results: Both explanted hearts revealed hypoplastic right ventricle chambers, intact ventricular septum, small tricuspid valve and absent pulmonary valve. Microscopy revealed prominent sinusoidal channels traversing the myocardium (case 1) and a grossly visible CCF in case 2 (figure 1). The epicardial coronary artery and myocardial arterioles showed intimal proliferation and fibromyxoid changes narrowing the lumina, and medial hypertrophy. Mild endocardial fibroelastosis was present. Widespread acute changes of ischemic injury were also present in case 1.

Conclusion: The 2 cases illustrate the hemodynamic changes in PA/IVS leading to development of alternate pathways of blood flow in the form of myocardial sinusoids and CCF to feed coronary vasculature during right ventricular systole. The consequences of the high pressure in the right ventricle are reflected in the vasculopathic changes of fibromyxoid alteration, intimal proliferation and medial hypertrophy in the arterial branches and arterioles.



Poster 17

2469244

Spectrum of Pediatric Liver Pathology in United Arab Emirates Only Children's' Hospital: A Year Experience

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Background: Pediatric liver disease encompasses a broad and heterogeneous spectrum of conditions that present a significant diagnostic challenge in tertiary care settings worldwide. The epidemiology of pediatric liver disease varies considerably by region. In Western countries, biliary atresia (BA), occurs at an estimated incidence of approximately 1 in 15,000–19,000 live births. By contrast, a multicenter national study from the United Arab Emirates (UAE) reported a BA incidence of 3.75 per 100,000 live births, and a national cohort from Saudi Arabia recorded 2.254 per 100,000 live births. In Arab populations, familial and inherited disorders represent up to 58% of diagnosed infantile cholestasis cases—a pattern attributed in part to elevated consanguinity rates across the region. Autoimmune and immune-mediated hepatitis, including overlap syndromes, are increasingly recognized in pediatric patients throughout the Middle East. The spectrum of pediatric liver pathology at regional tertiary centers further reflects a distinct disease distribution when compared to Western counterparts, underscoring the need for region-specific epidemiological data. This study describes the spectrum of pediatric liver pathology from a tertiary children's hospital in UAE, over a year.

Methods: We performed a search through our pathology database (CoPath software) for pediatric liver cases submitted to the centralized anatomic pathology laboratory from June, 30th, 2025 to July, 1st, 2026. The age range was 0-18 years-old.

Results: A total of 15 cases from 14 patients (7 females and 7 males) were received with age range of 2 months to 18 years. There were 3 cases of biliary atresia (1 female and 2 males), 1 case of Budd-Chiari syndrome (female), 3 cases of liver masses (3 males) including 1 focal nodular hyperplasia, 1 metastatic nasopharyngeal carcinoma, and 1 hepatocellular neoplasm not otherwise specified, 4 cases of possible autoimmune hepatitis/overlap syndrome (4 females), 1 case of biliary atresia status post liver transplant for surveillance (male), 1 case of a congenital generalized lipodystrophy with cirrhosis (male), and 1 case of mild transaminitis with normal histology (female). Table 1 summarizes the cases.

Conclusion: During this last year, our limited retrospective study demonstrates the diverse spectrum of pediatric liver diseases at a tertiary center in UAE. Autoimmune hepatitis and overlap syndromes constituted the majority of cases (4/14 patients; 28.6%). Biliary atresia and

hepatic masses each accounted for 21.4% of cases (3/14). Although only a small number of cases, these findings suggest the foundation for benchmarking the distribution of pediatric liver diseases at our center may differ from international data. Larger studies are needed to validate these findings.

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Poster 18

2496471

Inflammatory Hepatocellular Adenomas in Half-Siblings with Germline STAT3 Gain-of-Function Mutation: A Novel Phenotypic Association

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Background: Inflammatory hepatocellular adenomas (I-HCA) are driven by constitutive activation of the IL-6/JAK/STAT3 pathway. Somatic mutations in STAT3, IL6ST, GNAS, FRK, and JAK1 are frequent causes of STAT3 activation in tumor tissue. In contrast, germline STAT3 gain-of-function (GOF) mutations cause early-onset multisystem autoimmunity and lymphoproliferation, with autoimmune hepatitis being the most common hepatic manifestation. I-HCA has not, to our knowledge, been previously described in STAT3 GOF syndrome.

Methods: We report 2 half-siblings with a shared germline STAT3 GOF pathologic variant ((NM139276.3) c.454C>T, p.(Arg152Trp)) who developed I-HCAs. Patient 1 (P1), a 15-year-old female with STAT3 GOF syndrome manifesting as autoimmune hemolytic anemia and Hashimoto thyroiditis, was incidentally found to have multiple liver lesions during pulmonary nodule surveillance. Patient 2 (P2), a 20-year-old male with STAT3 GOF syndrome manifesting as Evans syndrome and interstitial lung disease, presented with elevated transaminases and multiple liver nodules. Patients share a biological mother and were raised in separate households.

Results: There was significant histologic overlap with lesional biopsies from P1 & P2 demonstrating a well differentiated hepatocellular lesion composed of eosinophilic cells with less steatosis than the background liver, scattered inflammation, glycogenated nuclei, occasional prominent nucleoli, and patchy sinusoidal dilation, compatible with I-HCA. No significant nuclear atypia or significant loss of reticulin network was present. Immunohistochemical studies demonstrated both lesions to be positive for C-reactive protein and serum amyloid A with retained liver fatty acid binding protein, and negative for nuclear β -catenin, with non-specific focal to patchy glutamine synthetase expression. Glypican-3 was negative in P1 and weakly positive in P2. Background liver of P1 & P2 showed moderate to severe steatohepatitis with nonzonal macrovesicular steatosis, prominent ballooning degeneration, and significant lobular inflammation, as well as periportal and perisinusoidal fibrosis with early bridging fibrosis. Somatic/germline comparator exome testing on P2 showed no additional somatic alterations and low tumor mutational burden. P1 shows no disease progression of liver disease 3 years after biopsy.

Conclusion: This 2-case study may represent a novel phenotypic expansion of STAT3 GOF

syndrome. The absence of somatic alterations in P2's I-HCA suggests the germline variant alone may be sufficient for tumorigenesis. The concordant phenotype across half-siblings with partially distinct genetic backgrounds and differing environments strengthens this genotype-phenotype association and supports consideration of I-HCA as a potential hepatic manifestation of STAT3 GOF syndrome.

Poster 19

2492441

Molecular Detection of *Ureaplasma parvum* in Congenital Pneumonia Associated with Infant Death

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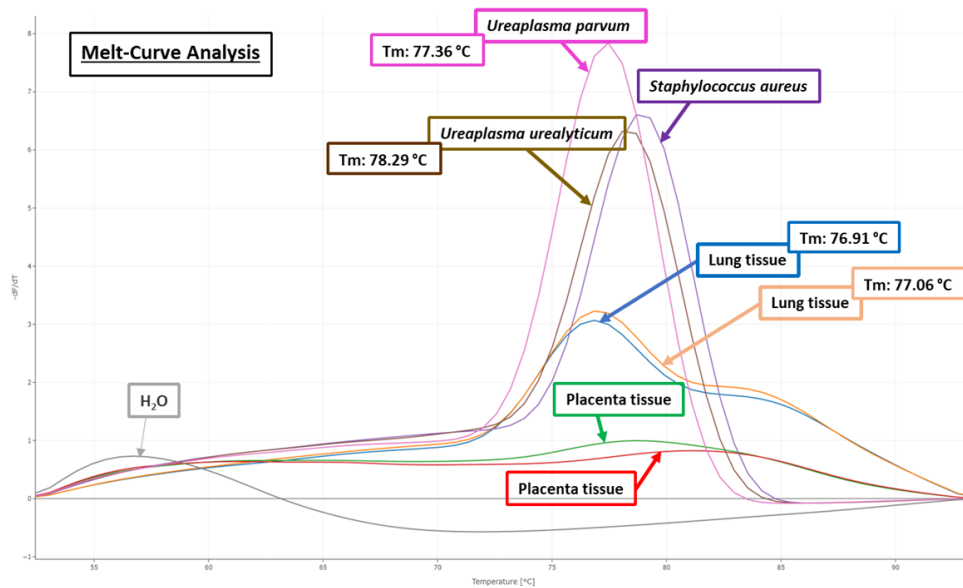
Background: Most cases of amniotic fluid infection (AFI) are caused by microorganisms found in the maternal genitourinary tract that ascend into the uterus during pregnancy. This can include bacterial and fungal organisms, most commonly group B streptococcus and *Escherichia coli*. Inhalation of infected amniotic fluid can lead to congenital pneumonia and in severe cases can be associated with neonatal death. Detection of bacteria can be difficult postmortem, and we present a case where molecular analysis was required to identify the pathogen associated with a fatal pneumonia.

Methods: A 1-day-old full term female neonate was born to a 19-year-old G3P1 Group B Streptococcus positive female who presented for induction of labor, where her membranes were artificially ruptured and meconium was noted. Upon delivery, Apgar scores were 1 and 1 at 1 and 5 minutes and respiratory distress was noted. Despite invasive mechanical ventilation, the infant did not survive and was pronounced dead. An autopsy was performed with review of the hematoxylin and eosin stains, histochemical stains, and immunohistochemical stains. Untargeted metagenomic sequencing and confirmatory species-specific PCR were performed on DNA extracted from the placental tissue and lung for pathogen detection.

Results: Autopsy revealed evidence of AFI with maternal (stage 1) and fetal (stage 2) acute inflammatory responses in the placenta and congenital pneumonia in the infant lungs. Gram and Grocott methenamine silver stains performed on lung tissue were negative. No postmortem cultures were performed on lung tissue. Untargeted metagenomic sequencing of the lung tissue revealed bacterial DNA sequences from *Cutibacterium acnes* and *modestum*, *Streptococcus thermophilus*, *Staphylococcus epidermidis*, and *Ureaplasma parvum* above a minimum threshold of 100 sequences. Species-specific PCR revealed *Ureaplasma parvum* in the lung tissue, but not the extraplacental membranes. The other visceral organs showed evidence of stress likely related to infection and hemodynamic instability, including hemorrhage in the adrenal glands and kidneys, hepatic steatosis and increased extramedullary hematopoiesis, and moderate thymic involutional changes. The brain also showed hypoxic-ischemic damage in the white matter.

Conclusion: Congenital pneumonia can sometimes be caused by atypical bacteria, such as

Ureaplasma spp. and lead to neonatal death. Postmortem molecular analysis may be needed to detect these unusual bacteria and better understand their pathogenic factors. Furthermore, Ureaplasma infection may be important to detect in liveborn infants with suspected pneumonia and has been shown to play a role in neonatal neuroinflammation.



Poster 20

2469240

Fetal Demise Associated with Umbilical Cord Ulceration-Intestinal Atresia Syndrome: A Case Report and Literature Review

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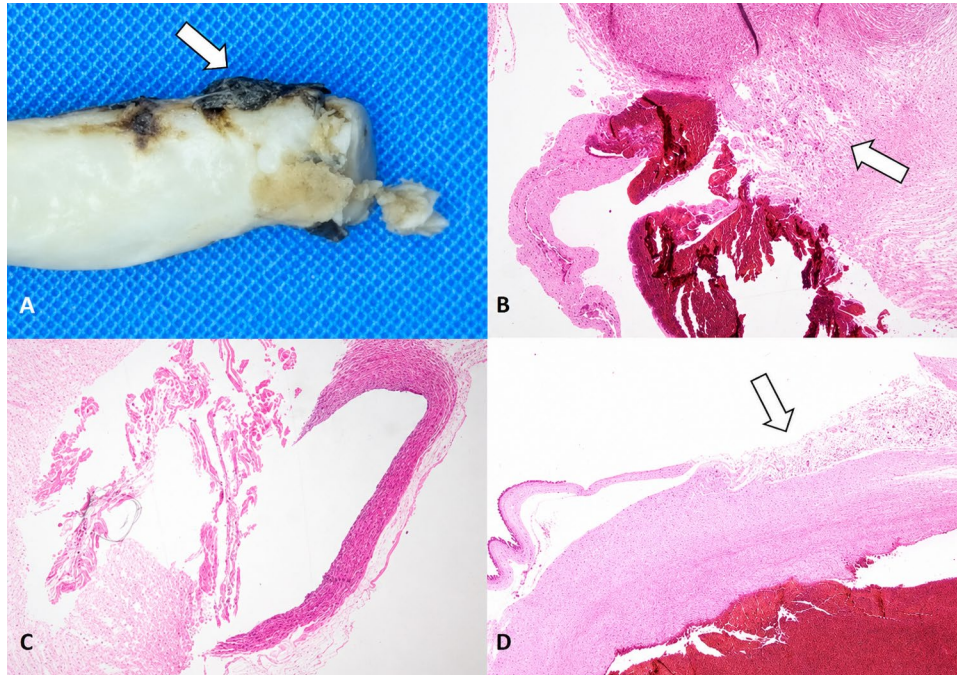
Background: Umbilical cord ulceration-intestinal atresia syndrome (UCIA) is a clinicopathologic entity associated with poor perinatal outcomes, including high risk for neonatal and intrauterine fetal demise (IUFD). It can be challenging to recognize both prenatally and at the autopsy bench. We present an autopsy case of a 30-week 5-day gestational age stillborn male fetus, delivered vaginally to a 27-year-old G3P1 female, in order to highlight the pathologic findings.

Methods: Full autopsy and placental examination were performed on the presented case. Findings from a comprehensive literature review are summarized.

Results: Autopsy showed a mildly macerated male fetus with measurements appropriate for gestational age. Jejunal atresia (type IIIa) involving the proximal jejunum was identified during the autopsy gross examination. Other anomalies included intestinal malrotation and a short pancreas. There were findings suggestive of fetal anemia including cutaneous pallor, erythroid hyperplasia of bone marrow, and increased hepatic extramedullary hematopoiesis. The placenta (231 g) had notably pale parenchyma. Gross examination showed focal hemorrhage firmly attached to the umbilical cord (Fig. 1A). Histology showed umbilical cord ulceration with hemorrhage, histiocytic inflammation, loss of Wharton's jelly (Fig. 1B) and disruption of at least one superficially located vessel (Fig. 1C). Ulceration was also seen on the chorionic plate, with ulceration of the amnion extending into the fibrous chorion (Fig. 1D). Literature review revealed 25/68 reported cases of UCIA syndrome with death (10 IUFD, 5 stillborn, 10 early neonatal deaths). Cases with available hemoglobin values showed fetal anemia as low as 1.5 g/dL. Elevated amniotic bile acids were associated with umbilical cord ulceration and high-grade ulceration showed an increased risk of IUFD. The mechanism for umbilical cord ulceration is suspected to be related to bile or gastric regurgitation. These substances may cause degeneration of the Wharton's jelly. Based on the proposed mechanism, we propose that UCIA may be more appropriately called a sequence than a syndrome. The characteristic findings likely arise from a sentinel event (intestinal atresia) with downstream development of cord ulceration, vascular injury, and finally fetal hemorrhage.

Conclusion: Putting the autopsy and placental findings together with the clinical scenario, the

ultimate diagnosis was UCIA syndrome. Based on the autopsy findings of fetal anemia and clinical finding of bloody amnionic fluid, the immediate cause of the fetal demise was massive fetal hemorrhage with exsanguination into the amnionic sac.



Poster 21

2470665

A Lethal Intermediary: Case Report of an Invasive Infection by Streptococcus Intermedius

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Background: Streptococcus intermedius is part of the normal oral flora. This bacterium causes periodontitis and invasive pyogenic infections of the central nervous system. Intracranial infection is usually secondary to local spread, hematogenous spread, or due to neurosurgery or head injuries. Mortality rate is up to 20%. Co-infection by other organisms can be seen in up to two thirds of cases.

Methods: We present a case of an 18-year-old male that had complains of headache and bilateral eye swelling for approximately a week. He was taken to a local hospital where he was pronounced dead. A postmortem investigation was performed due to a possible public health threat.

Results: Postmortem investigation revealed an infection by Streptococcus intermedius that included invasive sinusitis; thrombosis; orbital cellulitis; and meningitis. Co-infection by Staphylococcus aureus and Eikenella corrodens was also identified.

Conclusion: This case represents a death that could have been prevented if the signs experienced by the patient had been recognized early and treated promptly. Death prevention involves everyone and it starts with every single individual.

Poster 22

2494600

Juvenile Xanthogranuloma in the Scrotal Hilum Mimicking a Vascular Malformation and Rhabdomyosarcoma

P Preston ¹, M Lewis ², M Malek ², J Segal ², J Picarsic ²; ¹ University of Pittsburgh Medical Center, ² UPMC Children's Hospital of Pittsburgh

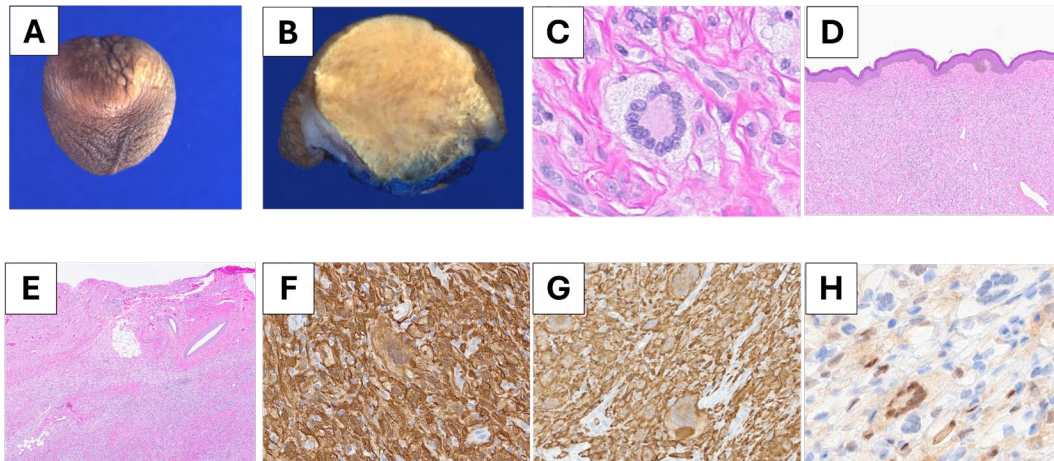
Background: Juvenile xanthogranulomas can occur in the scrotal hilum, although to date there have been few published case reports of JXGs arising in this location. We present an atypical presentation of a primary juvenile xanthogranuloma occurring solely in the scrotal hilum, with the original imaging impression consistent with a lymphatic malformation.

Methods: A 2-month-old previously full-term male with no significant medical history presented with a newly discovered scrotal mass. An ultrasound showed a well-circumscribed mixed echogenicity predominantly anechoic well-circumscribed 1.7 x 0.9 cm lesion with posterior acoustic enhancement inferior to the scrotum, separate from the testes, with areas of internal vascularity without definitive solid components, favored to represent a mixed venous lymphatic malformation. The patient was monitored clinically without intervention and was stable. On repeat ultrasound at 22 months of age there was concern for arterial waveforms within the lesion, so MRI was recommended. MRI revealed a solid, homogeneously enhancing, well-circumscribed 2.2 x 1.8 x 2.3 cm extratesticular scrotal mass with mild vascularity. The radiologic differential diagnosis was broad and included both benign and malignant entities, such as adenomatoid tumor, leiomyoma, germ cell tumor, and paratesticular rhabdomyosarcoma. Alpha-fetoprotein and beta human chorionic gonadotropin tumor markers were normal. At two years of age, the patient underwent excision of the mass without violation of the tunica vaginalis or spermatic fascia.

Results: On gross examination, the specimen had a grossly unremarkable skin surface (Figure 1A). Serial sectioning revealed a 2.5 cm well-circumscribed unencapsulated light yellow mass (Figure 1B). Touch preparation of the lesion stained with Diff-Quik showed spindled cells without other specific features, which raised the concern for a paratesticular rhabdomyosarcoma. Permanent sections revealed numerous foamy histiocytes with vacuolated cytoplasm and Touton-type giant cells (Figure 1C). The lesional cells did not involve the overlying rugated scrotal skin (Figure 1D). The cells also surrounded fat, nerves, and blood vessels (Figure 1E). The neoplastic cells were positive for CD163 (Figure 1F), factor XIIIa (Figure 1G), and cyclin D1 (Figure 1H) while negative for ALK. PanTRK showed focal, weak positivity.

Conclusion: We present one of the first published case reports of a juvenile xanthogranuloma

arising in the scrotal hilum outside the setting of dissemination. While this is an uncommon location for JXGs to arise, the entity should still be considered in a lesion in the scrotal hilum.



Poster 23

2470756

Variant of undetermined significance in a classic presentation of DICER1 syndrome: Why clinicopathologic correlation is key

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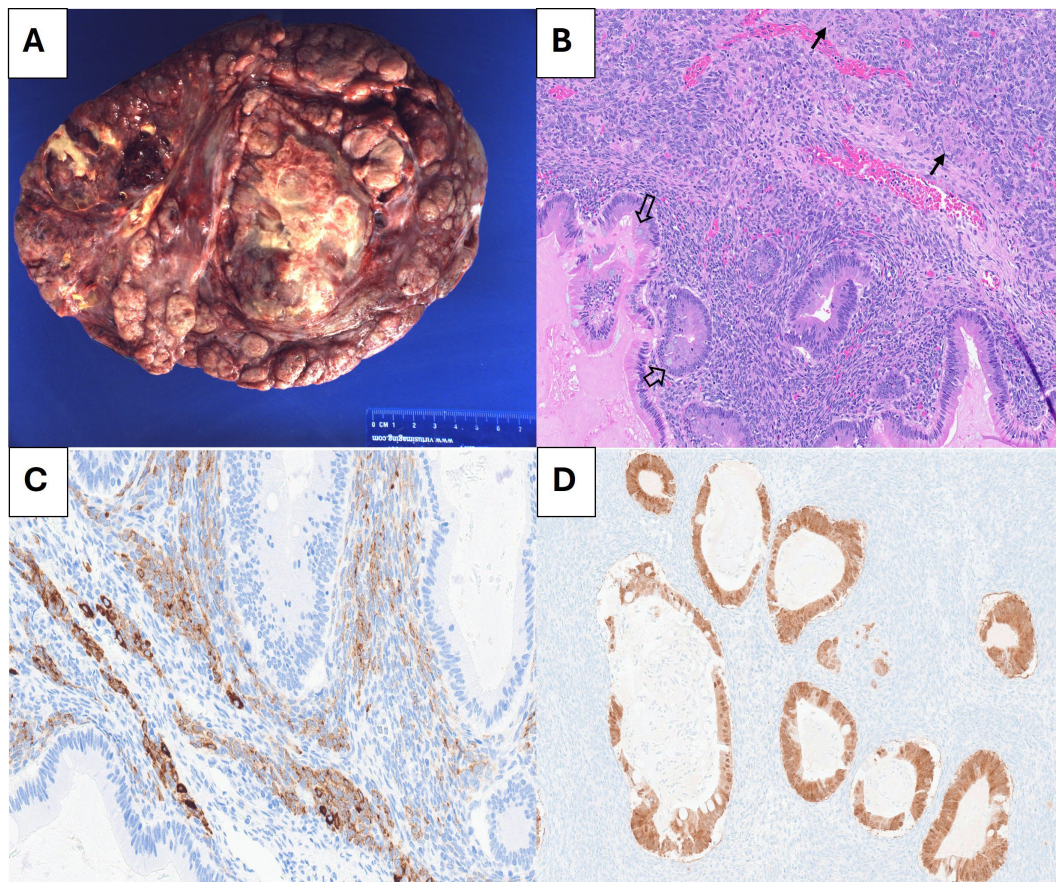
Background: Sertoli-Leydig cell tumors (SLCT) are exceedingly rare and account for less than 0.5% of all ovarian tumors. These malignant lesions represent a diagnostic challenge due to variable morphologic features particularly among poorly differentiated and retiform SLCT subtypes. Studies suggest that as many as 60% of patients with SLCT have a germline DICER1 pathogenic or likely pathogenic variant. We present a classic case of poorly differentiated SLCT with heterologous components presenting with elevated serum alpha fetoprotein (AFP) at diagnosis. Furthermore, the SLCT harbored a pathogenic somatic DICER1 mutation, and the patient harbored a germline DICER1 variant of undetermined significance (VUS). The classic histomorphologic features and clinical presentation suggest that this germline variant may represent a previously unidentified pathologic DICER1 variant.

Methods: A 17-year-old female with a multinodular thyroid goiter presented with abdominal fullness and discomfort, prompting a CT-scan. She was found to have a 22 cm ovarian mass and elevated AFP. She underwent a laparotomy with left salpingo-oophorectomy. There was no evidence of peritoneal or lymphatic spread, and the contralateral ovary was normal. Gross examination revealed a multinodular and multicystic mass. Histological examination revealed inhibin and FOXL1 positive Sertoli-like cells, rare inhibin and FOXL1 Leydig cells, and intestinal-type epithelium with goblet cells. The intestinal-type epithelium was CDX2 and CK20 positive.

Results: The final diagnosis was poorly differentiated Sertoli-Leydig cell tumor with gastrointestinal-type heterologous elements. There was no spread to the fallopian tube, omentum, or peritoneum. However, due to intraoperative adhesions, there was concern for microscopic "leakage" and localized inflammatory reaction of the pelvic peritoneum, staging this patient at FIGO IIb. Paired germline and somatic whole exome sequencing (WES) (target enrichment by hybrid capture with IDT xGen Exome Research Panel v2.0 and xGenCNV Backbone Plus Panel from Integrated DNA Technologies and sequenced using Illumina NGS) identified a somatic DICER1 p.D1709N (c.1681A>C) mutation at 31% variant allele frequency (VAF). In addition, a

germline DICER1 c.2040+4A>C (p.?) VUS was identified at 46% VAF. She received adjuvant chemotherapy with cisplatin, etoposide, and bleomycin (PEb) as per the Children's Oncology Group clinical trial AGCT1531.

Conclusion: There are numerous potential pathologic and clinical pitfalls in this case that are worth highlighting – the elevated AFP, the CDX2 positivity in the heterologous elements, and the non-specific germline variant of uncertain significance. Given the classic clinicopathologic features of this case, the VUS may represent a previously unidentified pathologic variant.



Poster 24

2485301

SS18::POU5F1 Fusion-Associated Poorly Differentiated Malignant Neoplasm with Divergent Immature Neuronal and Yolk Sac Tumor-Like Differentiation in the Youngest Reported Patient: Expanding the Spectrum of an Emerging Entity.

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Background: SS18::POU5F1 fusion-associated malignant neoplasms are very rare, with seven patients reported across six publications to date. These tumors typically present as high-grade, poorly differentiated (PD) malignancies.

Methods: We describe the youngest reported patient with this fusion, whose tumor exhibited multiphasic morphology with divergent immature neuronal and yolk sac tumor-like (YST-like) differentiation, and tabulate the clinicopathologic features of prior cases.

Results: A 5-year-old male presented with a 3-week history of a tender left posterior shoulder mass with overlying violaceous discoloration, initially interpreted clinically as abscess with cellulitis. Ultrasound showed an irregular heterogeneous hypoechoic subcutaneous lesion with skin thickening and surrounding inflammatory change; CT demonstrated two enlarged left axillary nodes. Gross exam revealed a solid tan-white mass and cystic-appearing nodes. Histologically, the tumor consisted of PD, immature neuronal, and glandular components that were sharply demarcated in some areas and intermingled in others. The glandular component exhibited YST-like differentiation, including Schiller-Duval body-like structures, while the immature neuronal component formed neuroectodermal tubules. Brisk mitotic activity and variable necrosis were present. The PD component expressed variable keratin, S100, calretinin, and synaptophysin. The neuronal component expressed SALL4, LIN28A, synaptophysin, PHOX2B, and CD56. The YST-like component expressed nuclear SALL4 and cytoplasmic glypican-3. NGS identified an SS18 exon 10::POU5F1 exon 2 fusion in all components, supported by karyotype with balanced insertion involving chromosomes 6 and 18 (long arm of chromosome 18 from band q21.3 to q11.2 inserted into the short arm of chromosome 6 at band p21.3). The patient received 7 cycles of chemotherapy per COG ARST0332 Arm D and concurrent radiotherapy was administered to the left arm and axilla. Approximately 6 weeks after completing therapy, the patient developed local recurrence and underwent resection followed by salvage nivolumab and paclitaxel.

Conclusion: SS18::POU5F1-associated neoplasms are emerging high-grade malignancies characterized by undifferentiated round-to-epithelioid morphology, brisk mitotic activity,

frequent necrosis, and a variable epithelial/S100-positive myoepithelial-like phenotype. Our case expands the morphologic spectrum as the third tumor with divergent neuronal differentiation and the first with YST-like/somatic enteroblastic differentiation, further demonstrating the broad spectrum of multilineage differentiation that may occur in this entity. Early recurrence despite multimodal ARST0332-based therapy further highlights its potentially aggressive behavior and the absence of an established treatment paradigm.

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Poster 25

2485522

Compound Heterozygous GCDH Variants and a Co-occurring De Novo CHD8 Variant Presenting as Developmental Regression and Dystonia: A Case Report

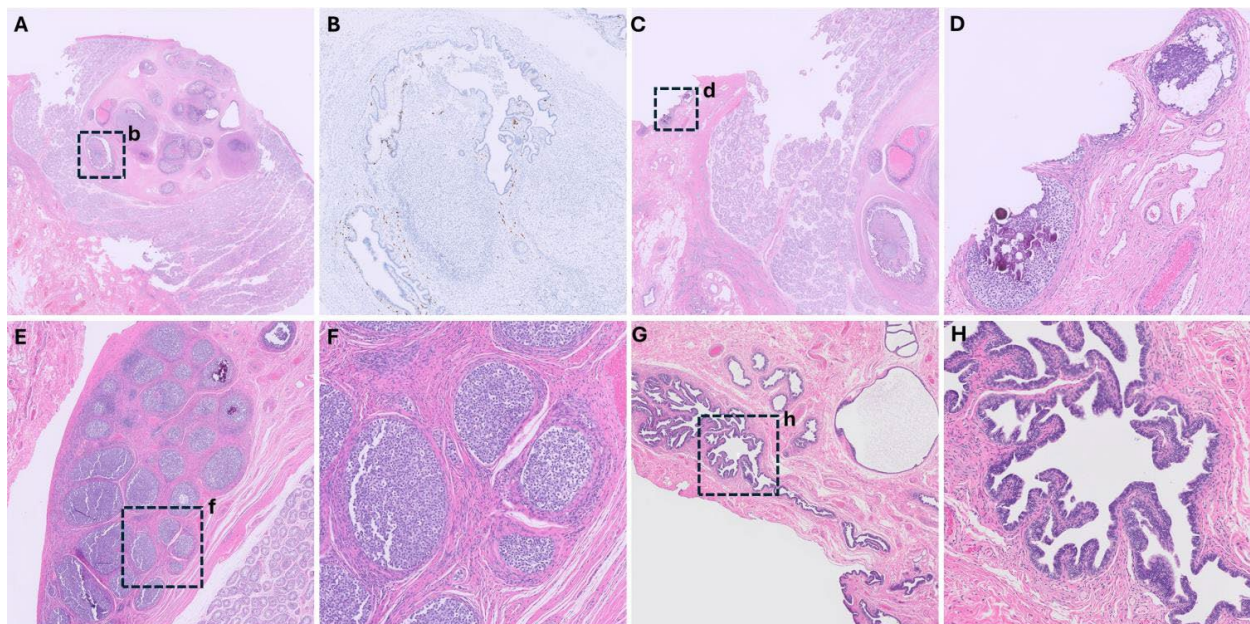
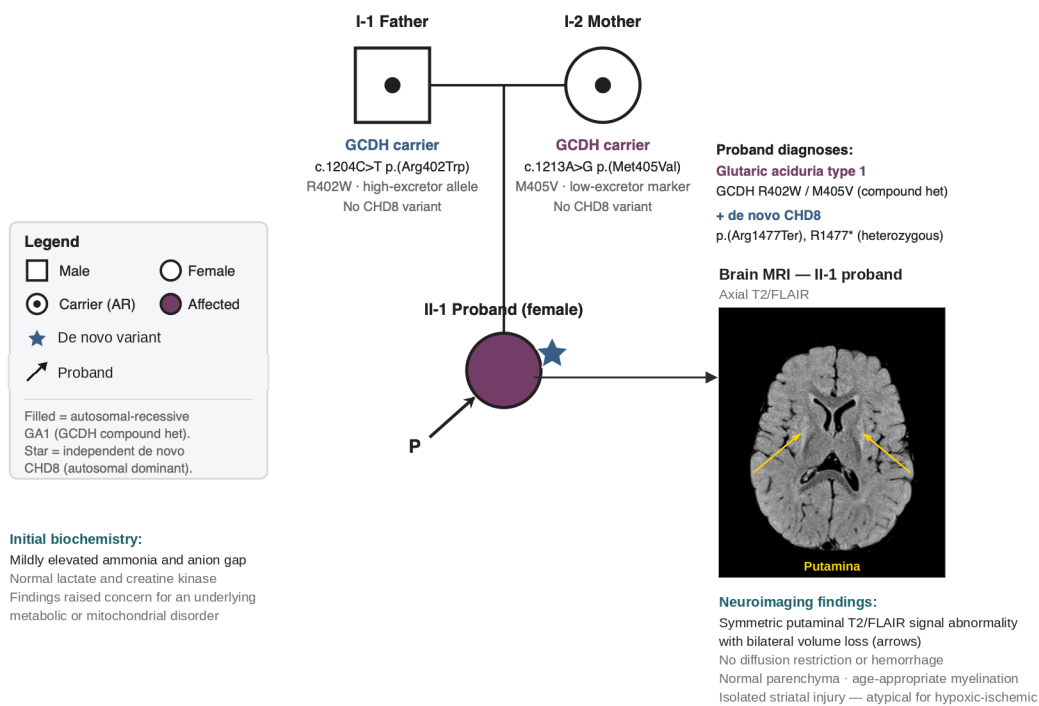
R Burchardt ¹, A Daily ¹, A Feezel ², A Potter ³; ¹ Nova Southeastern University Dr. Kiran C. Patel College of Osteopathic Medicine, ² N/A, ³ Nova Southeastern University Dr. Kiran C. Patel College of Osteopathic Medicine

Background: Glutaric aciduria type 1 (GA1) is an autosomal recessive metabolic disorder that may be missed by newborn screening in patients with the low-excretor phenotype. Concurrent monogenic disorders can further complicate diagnosis and clinical interpretation.

Methods: We report the first known case of an infant with coexisting GA1 and CHD8-related neurodevelopmental disorder. Following 8 months of normal development, the patient experienced acute neurodevelopmental regression, profound hypotonia, and progressive generalized dystonia after a febrile illness. Brain MRI demonstrated symmetric bilateral putaminal injury despite a normal newborn screening result.

Results: Trio clinical exome sequencing identified compound heterozygous GCDH variants (paternally inherited p.Arg402Trp, pathogenic; maternally inherited p.Met405Val, a likely pathogenic low-excretor allele), confirming GA1. Sequencing also identified a de novo CHD8 nonsense variant (p.Arg1477Ter), establishing a second diagnosis of CHD8-related neurodevelopmental disorder.

Conclusion: To our knowledge, this is the first reported dual molecular diagnosis of GA1 and CHD8-related neurodevelopmental disorder. This case highlights three important clinical lessons: (1) a normal newborn screen does not exclude low-excretor GA1; (2) trio exome sequencing is invaluable in infants with unexplained striatal injury and neurodevelopmental regression; and (3) dual molecular diagnoses may produce blended phenotypes that complicate clinical recognition and management.



Poster 26

2488350

Pancreatic CSF1R-Mutated Juvenile Xanthogranuloma Presenting as Obstructive Neonatal Jaundice

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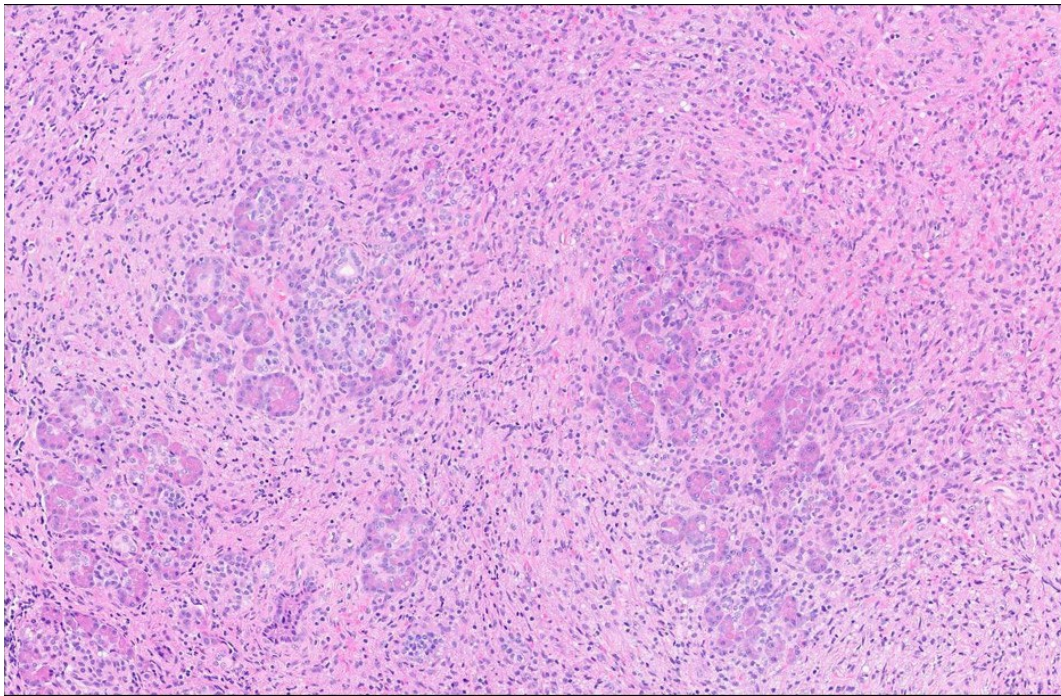
Background: Solid pancreatic masses are exceptionally rare in neonates and may raise concern for malignancy. We report a pancreatic juvenile xanthogranuloma (JXG) presenting as an obstructing pancreatic head mass, with CSF1R alterations supporting the diagnosis.

Methods: A term neonate presented at 4 weeks of age with pale stools, jaundice, and weight loss. Laboratory evaluation demonstrated direct hyperbilirubinemia with markedly elevated GGTP. Ultrasound showed hepatomegaly and common bile duct dilation. MRCP demonstrated a 1.3-cm heterogeneous pancreatic head lesion causing distal common bile duct obstruction with proximal extrahepatic and intrahepatic biliary dilation. The radiologic differential diagnosis included pancreatoblastoma and rhabdomyosarcoma. Tumor markers (AFP and beta-HCG) were normal. Following an ERCP-guided biopsy that yielded inconclusive results, exploratory laparotomy with biopsy was performed to establish a diagnosis before proceeding with more extensive surgical intervention.

Results: Biopsy revealed infiltration of pancreatic ducts and acini by sheets of histiocytes with abundant granular cytoplasm admixed with scattered chronic inflammatory cells. The lesional cells were diffusely positive for CD163 with weak Factor XIIIa expression and negative for SMA, ALK, pan-TRK, Langerin, CD1a, and S100. Special stains were negative for microorganisms. Copy-number analysis demonstrated loss of heterozygosity involving chromosome 5q. Further evaluation of genes within this region identified CSF1R alterations, including c.1631_1648del (p.P544_W550delinsR) and c.1627A>C (p.K543Q). No BRAF V600E mutations or clinically significant gene fusions were identified. The overall findings supported the diagnosis of JXG.

Conclusion: JXG is a benign non-Langerhans cell histiocytosis that most frequently involves the

skin, with visceral involvement being less common. Pancreatic JXG is rare, with fewer than 5 pediatric cases reported in the literature. These pancreatic cases have predominantly involved infants with pancreatic head masses presenting as obstructive jaundice. As in our case, these lesions may radiologically mimic malignancy, and diagnosis can be challenging, particularly in the absence of cutaneous manifestations. In some reported cases, the diagnosis was rendered only after an unnecessary Whipple procedure. CSF1R alterations have been described in JXG, including recurrent exon 12 insertion/deletions involving the intracellular autoinhibitory domain. Alterations similar to the c.1631_1648del identified in this case have been reported as activating mutations with potential therapeutic implications. Recognition of JXG as a potential cause of a pancreatic mass in neonates is important to facilitate accurate diagnosis and avoid unnecessarily aggressive surgical intervention.



Poster 27

2490616

An Unusual Superficial Presentation of Atypical Lipomatous Tumour in an 11-Year-Old Girl

A Glembocki ¹, B Ngan ², B Wehrli ¹; ¹ London Health Sciences Centre, ² The Hospital for Sick Children

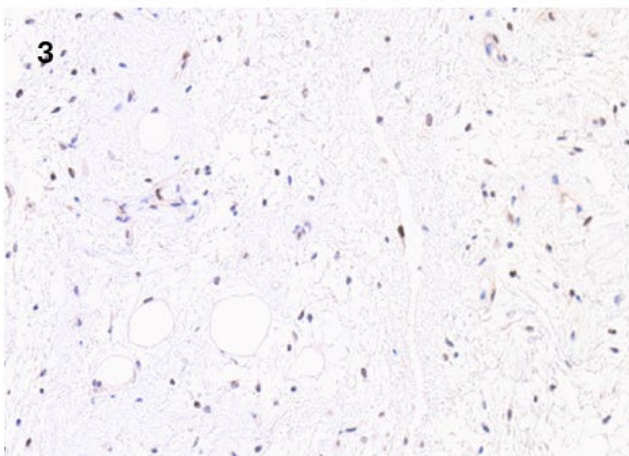
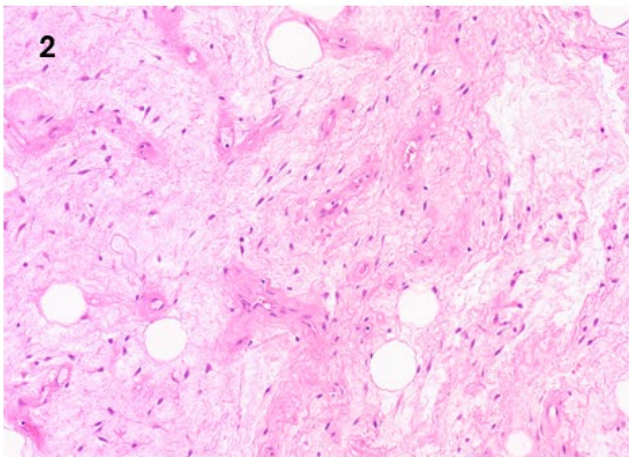
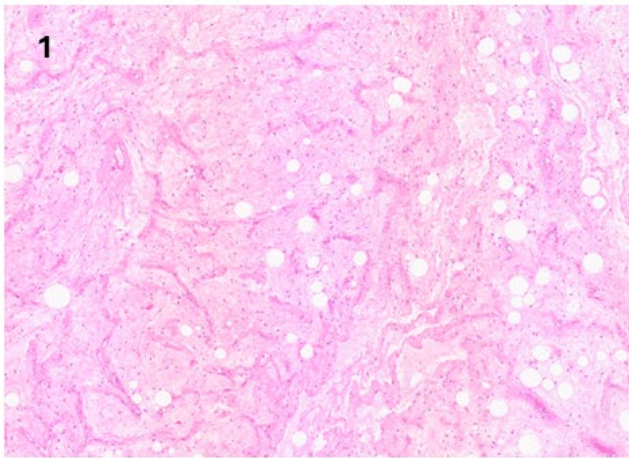
Background: Atypical lipomatous tumour (ALT) is an intermediate (locally aggressive) adipocytic neoplasm characterized by MDM2 amplification. It most commonly arises in the deep soft tissues of the proximal extremities, trunk, and retroperitoneum. While relatively common in adults, ALT is exceptionally rare in children and may pose significant diagnostic challenges, particularly when arising in superficial soft tissues and exhibiting myxoid features.

Methods: Archival material from a pediatric patient diagnosed with ALT was retrieved and reviewed, with emphasis on the clinical presentation, histologic findings, immunohistochemical profile, and molecular findings.

Results: An 11-year-old girl presented with a subcutaneous mass of the left mid-thigh. Magnetic resonance imaging demonstrated a lobulated mass centered within the subcutaneous fat along the medial aspect of the left mid-thigh, measuring $4.3 \times 2.3 \times 7.6$ cm. The lesion exhibited homogeneous T1 signal intensity similar to muscle and diffusely increased T2 signal intensity without a discernible fatty component. Histologic examination revealed a predominantly myxoid adipocytic neoplasm composed of mature adipocytes, scattered lipoblasts embedded within abundant myxoid stroma and traversed by a delicate arborizing capillary network, and hyperchromatic stromal spindle cells within fibrous septa. Focal nuclear atypia in both adipocytes and stromal cells was present (Figures 1 and 2). The differential diagnosis included lipoblastoma, ALT, and myxoid liposarcoma. Strong nuclear expression of MDM2 (Figure 3) and CDK4, together with FISH-confirmed MDM2 amplification, established the diagnosis of ALT. Subsequent targeted RNA sequencing identified an HMGA2::KERA gene fusion, providing additional molecular characterization of the tumour.

Conclusion: We report an unusual superficial presentation of ALT in an 11-year-old girl. The diagnosis was challenging because of its rarity in childhood and its clinical, radiologic, and morphologic overlap with lipoblastoma and myxoid liposarcoma. Strong MDM2 and CDK4 expression, together with FISH confirmation of MDM2 amplification, were critical in establishing the diagnosis. Targeted RNA sequencing additionally identified an HMGA2::KERA gene fusion. Recognition of this uncommon presentation and appropriate molecular workup are essential to avoid diagnostic pitfalls in pediatric adipocytic neoplasms. Importantly, lesions

arising in superficial and surgically amenable sites are associated with excellent local control and a low risk of recurrence.



Poster 28

2490929

Pediatric-Type Follicular Lymphoma in the Parotid Gland of a Two Year-Old Boy

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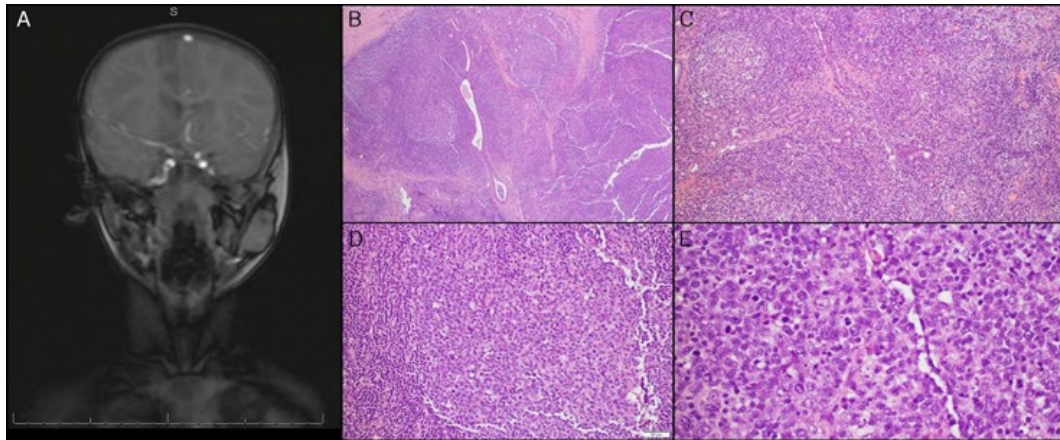
Background: Pediatric-type follicular lymphoma (PTFL) is a rare, indolent B-cell neoplasm of children and young adults. Per the World Health Organization classification (5th edition) and International Consensus Classification criteria, it is a strictly nodal disease. Lymphomas arising at extra nodal sites that are otherwise identical are excluded from the diagnosis.

Methods: Patient clinical, radiologic, histologic, immunophenotypic, and cytogenetic findings were reviewed. Targeted next-generation sequencing (NGS) using a 162-gene lymphoma panel was performed.

Results: A previously healthy two-year-old boy presented with a palpable mass in the left cheek. Ultrasound and MRI demonstrated a 4-cm multilobulated, infiltrative mass partially replacing the left parotid gland with no evidence of background nodal involvement. Parotidectomy showed an unencapsulated atypical follicular lymphoid proliferation effacing the salivary gland, with no lymph node capsule identified grossly or microscopically, to suggest a nodal origin. The lesion was composed predominantly of intermediate-to-large blastoid cells with frequent mitoses and apoptosis. The neoplastic cells were positive for PAX5, CD10, BCL6, and FOXP1 and negative for BCL2 and MUM1. Flow cytometry identified a lambda-restricted, CD10-positive B-cell population, and PCR confirmed a clonal B-cell rearrangement. No rearrangements in BCL2, BCL6, or IRF4 were detected by fluorescence in situ hybridization studies. Cytogenetics cultures unfortunately yielded no analyzable metaphases. NGS was pursued. Several missense variants of probable germline origin were identified: CIITA, FAT1 [×2], ITPKB, NFKBIE [×2], and PRDM1. A diagnosis of PTFL was rendered. The parotidectomy specimen was negative for lymphomatous involvement at the resection margins, and no additional treatment was prescribed. The patient remains on active surveillance without evidence of disease six years after diagnosis.

Conclusion: This case meets the morphologic, immunophenotypic, and molecular criteria for PTFL but lacks evidence for the nodal localization required by current classification systems. Other PTFL-like lymphomas have been reported at other extranodal sites, including the testis, conjunctiva, and dura. A subset have been shown to harbor the same alterations typically reported in PTFL, namely TNFRSF14/1p36, MAP2K1, and IRF8. All have followed an indolent course with excellent outcomes after resection. The presented case does not demonstrate the

recurrent genetic lesions reported in other PTFL cases but fits the low-genetic complexity characteristic profile seen in some PTFL cases and demonstrates the indolent clinical behavior expected of nodal PTFL. We believe cases like ours provide evidence that the definition of PTFL ought to be expanded to include extra nodal presentations.



Poster 29

2491109

Ductal Plate Malformation in an Infant with Biallelic CENPF Variants of Uncertain Significance: A Novel Presentation Expanding the Phenotype of Strømme Syndrome/Primary Ciliary Dyskinesia 31 (CILD31)

L Duzett¹, M Lovell²; ¹ Laura Duzett, ² Children's Hospital Colorado

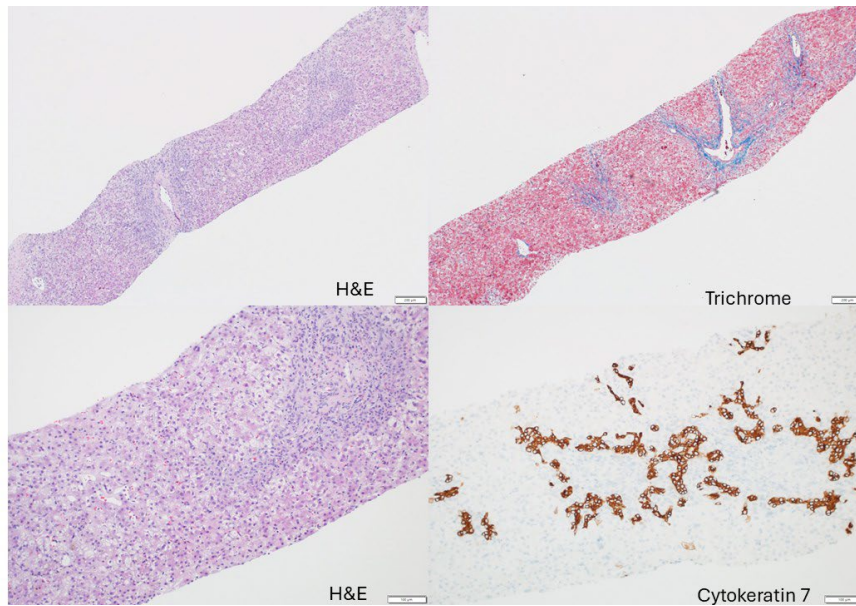
Background: A 2-month-old male was born at 31-weeks' gestation with septal defects, coarctation with aortic arch hypoplasia, and hypertrophic cardiomyopathy. Congestive heart failure developed, and the aortic arch and ventricular septal defect repaired at 60 days. Progressive cholestasis with elevated conjugated bilirubin and transaminases prompted hepatology consultation. Alpha-1 antitrypsin was normal and abdominal ultrasound was unremarkable. A liver biopsy was performed at 74 days and Ursodiol started. At 87 days of life, necrotizing enterocolitis necessitated small-bowel resection and subtotal colectomy. No intestinal atresia was identified. Intraoperatively, the liver was grossly enlarged and congested with hyperbilirubinemia; the cecum was abnormally mobile and located predominantly in the right upper quadrant with intact lateral peritoneal attachments consistent with intestinal malrotation. Terminally, renal failure developed within progressive multiorgan failure. The infant died at 88 days. Permission for autopsy was denied.

Methods: The biopsy was prepared using routine histologic processing with formalin fixation, paraffin embedment, sectioning at 4 microns and staining with H&E, trichrome and CK7 immunostain (Dako). DNA extracted from peripheral blood from the patient and his parents underwent Whole Genome Sequencing (WGS) on an Illumina NovaSeq X Plus platform then analyzed by an in-house bioinformatics pipeline, including read alignment to GRCh38/hg38 genome assembly, variant calling and annotation, and comprehensive variant filtering.

Results: The liver biopsy demonstrated ductal plate malformation (DPM), a histologic hallmark of hepatic ciliopathy, with prominent vessels, extensive fibrosis and hepatocytic and canalicular cholestasis (see Figure). WGS of the trio identified two CENPF missense mutations in trans: a paternally inherited c.1583C>T p.(Ala528Val) and a maternally inherited c.6580A>T p.(Met2194Leu).

Conclusion: Biallelic loss-of-function variants in CENPF cause Strømme syndrome/primary ciliary dyskinesia 31 (CILD31), an autosomal recessive ciliopathy classically characterized by a triad of apple-peel intestinal atresia, microcephaly, and ocular anomalies, with cardiac and other structural anomalies also reported. CENPF encodes centromere protein F, which is essential for both chromosome segregation and ciliogenesis. DPM reflects failed remodeling of the embryonic

ductal plate, a process that depends on functional primary cilia, and is the unifying lesion of the hepatic ciliopathies such as congenital hepatic fibrosis and Caroli disease. On literature review, DPM has not been reported previously in CENPF-related disease. The case expands the phenotypic spectrum of Strømme syndrome and highlights the value of histopathology in interpreting uncertain molecular findings.



Poster 30

2492305

Rapid-onset Obesity, Hypothalamic Dysregulation, Hypoventilation, Autonomic Dysregulation and Neuroendocrine Tumors, Oh My!: A Case Report

M Hyde ¹, R Sances ²; ¹ UTHSC College of Medicine- Knoxville, ² Dolly Parton Children's Hospital

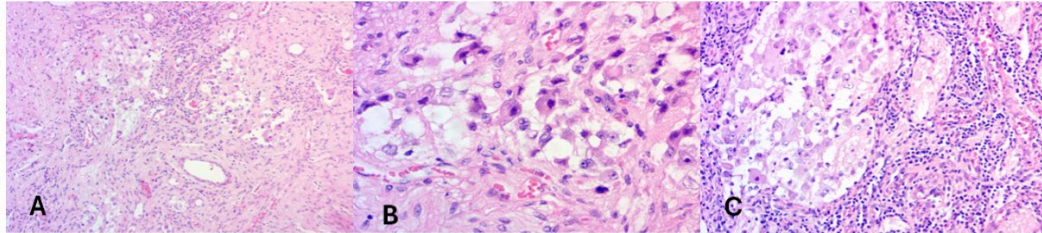
Background: Rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation (ROHHAD) is a rare and potentially fatal pediatric syndrome without a specific diagnostic biomarker. Approximately 40–50% of patients develop neural crest tumors, most commonly ganglioneuroma, ganglioneuroblastoma, or neuroblastoma. Identification of an associated tumor may provide an important diagnostic clue.

Methods: We present the clinical, radiologic, histopathologic, and genomic findings of a 3-year, 6-month-old female with clinical features concerning for ROHHAD and an associated retroperitoneal tumor. The resected tumor was evaluated morphologically and by immunohistochemistry with subsequent trio whole-genome sequencing and attempted tumor molecular profiling.

Results: The patient presented with severe hypoxemia and progressive respiratory acidosis requiring intubation. Her history included recurrent respiratory distress beginning in late infancy, approximately 60 pounds of rapid weight gain over the last year, hypothyroidism, hyperprolactinemia, hypernatremia, and elevated insulin. CT demonstrated a $3.8 \times 3.0 \times 3.9$ cm left periaortic retroperitoneal mass. Histologically, the tumor was composed predominantly of Schwannian stroma with intermixed mature ganglion cells and nests of differentiating neuroblasts. Tumor cells were positive for synaptophysin, with no mitotic figures, apoptotic bodies, macroscopic nodularity, or hemorrhage. Findings were diagnostic of ganglioneuroblastoma, intermixed subtype, favorable histology. Whole-genome sequencing identified a pathogenic 3.47-Mb deletion of 6p25.3-p25.2, consistent with 6p25 deletion syndrome. Although considered likely incidental, the deleted region contains FOXC1, a gene involved in neural crest development. Tumor molecular profiling was unsuccessful because of insufficient DNA and RNA due to low tumor purity.

Conclusion: This case highlights the strong association between ROHHAD and neural crest tumors and demonstrates how identification of a ganglioneuroblastoma may provide an important clue supporting the clinical diagnosis. On the other hand, recognition of the ROHHAD syndrome should prompt evaluation for an associated neural crest tumor. Histopathologic identification of a neural crest tumor can provide valuable diagnostic support in patients with

suspected ROHHAD. Although the significance of the 6p25 deletion remains uncertain, the involvement of FOXC1 raises the possibility of a relationship between altered neural crest development and ROHHAD-associated tumor formation. Increased awareness of this association may facilitate earlier diagnosis and appropriate tumor surveillance in affected children.



Poster 31

2493951

FGFR1::HCK Fused Pediatric Intramedullary Mesenchymal Neoplasm: A Potential Central Nervous System Counterpart for a Recently Described Evolving Soft Tissue Entity

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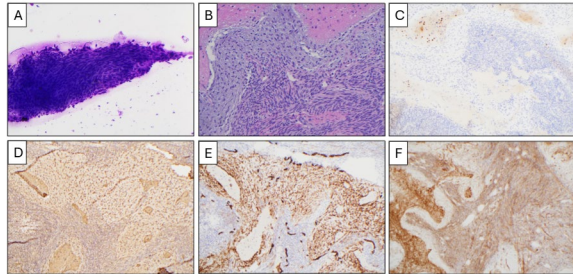
Background: Pediatric mesenchymal tumors with FGFR1 gene fusions share significant histologic overlap with infantile fibrosarcoma and NRTK-rearranged spindle cell neoplasms. Diagnosis of this emerging molecular class is essential, as these lesions may be locally aggressive and may benefit from targeted therapy. To the authors' knowledge, no reports exist of this entity arising in the spinal cord or harboring a FGFR1::HCK fusion. We present a novel case of a FGFR1 fused mesenchymal neoplasm arising in the central nervous system of an infant.

Methods: We report the clinical, histological, immunohistochemical (IHC), and molecular findings in an 11-month-old male with an intramedullary spinal cord neoplasm.

Results: An 11-month-old male presented with progressive bilateral lower extremity weakness, poor tone, and constipation. MRI spine showed a 6.2 cm heterogenous, intradural, intramedullary thoracolumbar mass. Intraoperative frozen sections demonstrated a spindle cell neoplasm. Histological analysis showed a biphasic neoplasm with mesenchymal differentiation; the first component was fascicular with hypercellular foci of spindle cells while the second component was hypocellular and contained oval cells in an amphophilic myxoid matrix. IHC stain for OLIG2 was negative, while GFAP was focally positive in the myxoid component. The fascicular component demonstrated focal patchy positivity for Pan-TRK, raising the possibility of a TRK fused neoplasm. FusionPlex next-generation sequencing identified a novel FGFR1::HCK in-frame fusion. DNA methylation profiling assays performed at several institutions (Northwestern, DKFZ, NCI) did not uniformly match a known tumor class. Given these findings, the lesion is most compatible with a pediatric mesenchymal tumor with a novel FGFR1 fusion arising in the spinal cord. Clinically, the lesion was grossly totally resected, and the patient is being followed closely with repeat MRIs.

Conclusion: This case highlights an intramedullary mesenchymal neoplasm with a previously undescribed FGFR1::HCK fusion driver. Known FGFR1 fusion partners result in the constitutive activation of the FGFR1 tyrosine kinase domain; HCK (hemopoietic cell kinase) is a non-receptor tyrosine kinase expressed mainly in hemopoietic lineages that has never been reported as a fusion partner with FGFR1. While a neuroepithelial tumor was initially considered due to

the location and focal positivity for GFAP, the morphology and molecular results are inconsistent with any established central nervous system entity. Pediatric mesenchymal tumors with FGFR1 gene fusions have been previously reported in the deep soft tissues, however, this lesion has never been reported in the spinal cord. Recognition and proper classification of similar entities is essential to guide proper treatment and further research.



Poster 32

2494463

Metastatic Grade 3 Well Differentiated Neuroendocrine Tumor in Fanconi Anemia with rare KMT2A::BCOR fusion: Evidence of Genomic Instability-Driven Tumorigenesis

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Background: Fanconi anemia (FA) is a cancer predisposition syndrome caused by defects in DNA interstrand crosslink repair and homologous recombination. Germline alterations in FANCA, a key tumor suppressor gene in the FA pathway, lead to genomic instability and increased susceptibility to hematologic and solid malignancies. Neuroendocrine neoplasms (NENs) are rarely reported in this population, and their molecular drivers remain poorly defined.

Methods: We report a 23-year-old woman with Fanconi anemia status post matched unrelated donor allogeneic bone marrow transplantation in 2007 (cyclophosphamide, fludarabine, antithymocyte globulin, and total body irradiation), who presented with acute abdominal pain. Imaging revealed numerous bilobar hepatic lesions with left portal vein thrombosis and intrahepatic biliary dilation, consistent with metastatic disease, as well as a gastric fundus mass.

Results: Biopsy of the gastric lesion demonstrated a well-differentiated neuroendocrine tumor with a Ki-67 proliferative index >20%, consistent with a WHO grade 3 well-differentiated neuroendocrine tumor despite low mitotic activity. The hepatic lesions were interpreted as metastatic disease. Molecular analysis identified a truncating FANCA pathogenic variant and partial copy number loss, consistent with the underlying FA diagnosis and defective DNA repair. Additional genomic alterations included low-level chromosome 7 copy number gain, supporting chromosomal instability, a feature associated with aggressive behavior in neuroendocrine tumors. Notably, next-generation sequencing revealed a rare KMT2A::BCOR fusion (KMT2A exon 6 to BCOR exon 7). BCOR encodes a chromatin regulatory protein with tumor suppressor function, while KMT2A (MLL1) encodes a histone methyltransferase involved in transcriptional activation. This fusion is predicted to result in loss of BCOR function and gain-of-function of KMT2A, leading to dysregulated epigenetic control. Although previously described in a pancreatic neuroendocrine tumor, this alteration is exceedingly rare and has not been reported in the context of FA.

Conclusion: This case describes a metastatic grade 3 well-differentiated neuroendocrine tumor arising in a patient with Fanconi anemia, characterized by coexisting FANCA deficiency, chromosomal copy number alteration, and a rare KMT2A::BCOR fusion. These findings suggest a cooperative model of tumorigenesis in which defective DNA repair in FA promotes genomic

instability, facilitating the emergence of uncommon structural variants and epigenetic driver alterations. This report expands the molecular spectrum of neuroendocrine tumors in FA and underscores the importance of comprehensive genomic profiling in this high-risk population.

Poster 33

2494937

Congenital Acinar Dysplasia: A Lethal Lung Developmental Disorder Diagnosed at Autopsy

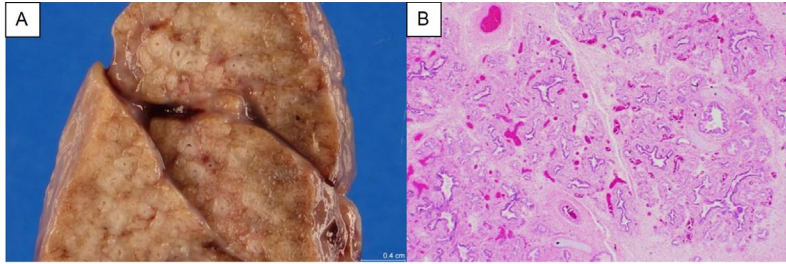
S Shah E Price, L Ernst; University of Chicago (NorthShore/Endeavor Health)

Background: Congenital acinar dysplasia (AcDys) is an exceptionally rare, lethal disorder of pulmonary development characterized by arrest of lung maturation at approximately the pseudoglandular stage. Affected infants may reach term without a definitive prenatal diagnosis but develop profound respiratory failure immediately after birth. We report a term infant with refractory hypoxemia in whom autopsy established the diagnosis of AcDys.

Methods: A complete autopsy was performed on a term male infant who died within 2 hours of birth despite intubation and aggressive resuscitation. Prenatal findings included polyhydramnios, ventricular wall thickening, and pericardial effusion. Postmortem radiography, gross examination, and histologic evaluation of the lungs and other organs were performed.

Results: Postmortem radiography confirmed bilateral pneumothoraces. The heart was structurally normal, with a small pericardial effusion, biventricular hypertrophy, and interventricular septal thickening. The lungs were markedly firm and hypoplastic, with a combined weight of 19 g (expected 42.6 ± 2.5 g), and lacked the normal spongy appearance (Figure 1A). Histologically, the lungs were diffusely immature, consisting of closely packed branching bronchiolar-type airways separated by abundant mesenchyme. The airways were lined by cuboidal-to-columnar epithelium without recognizable type I or type II pneumocyte differentiation. Saccules, mature alveoli, secondary septation, and distal acinar maturation were absent, recapitulating the pseudoglandular stage despite term gestation (Figure 1B). The differential diagnosis included congenital pulmonary airway malformation, primary pulmonary hypoplasia, congenital alveolar dysplasia, and alveolar capillary dysplasia with misalignment of pulmonary veins; however, the diffuse bilateral developmental arrest and absence of distal airspace maturation supported AcDys.

Conclusion: This case demonstrates a striking developmental paradox: a term infant with lungs arrested at an early stage of pulmonary morphogenesis. The absence of functional distal gas-exchanging units provided a direct morphologic explanation for otherwise refractory neonatal hypoxemia. Because prenatal findings are nonspecific, autopsy remains critical for definitive diagnosis of AcDys and may direct molecular evaluation with implications for recurrence-risk assessment and family counseling.



Poster 34

2495081

Intrapartum spontaneous fragmentation of a fetus with a COL1A1 variant – Is this the most severe overlap phenotype of osteogenesis imperfecta and Ehlers-Danlos syndrome?

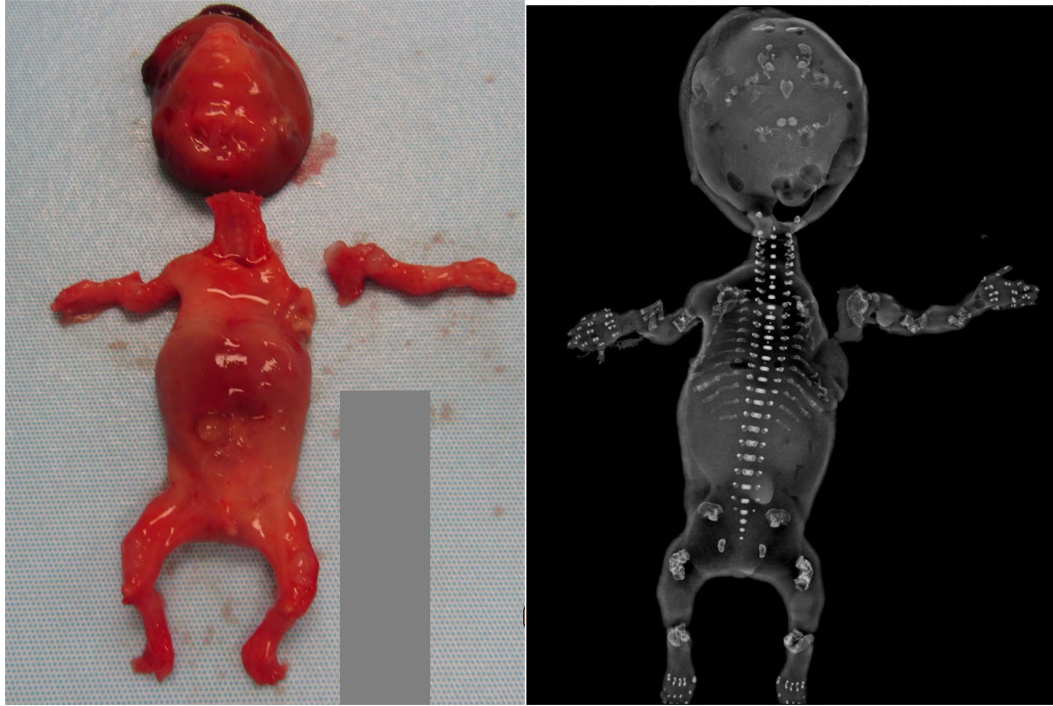
V Nguyen C Timmons; UT Southwestern Medical Center

Background: COL1A1/COL1A2-related osteogenesis imperfecta (OI) causes skeletal fragility, while some type I collagen variants produce overlapping OI/Ehlers-Danlos syndrome (EDS) phenotypes with prominent soft-tissue and joint fragility. Reported overlap phenotypes are predominantly nonlethal. We describe a fetus with lethal OI and intrapartum fragmentation, raising the possibility that profound extraskelatal connective-tissue fragility can accompany lethal COL1A1 disease.

Methods: A fetus at 18 6/7 weeks by last menstrual period and 16 2/7 weeks by ultrasound, with severe prenatal skeletal abnormalities, underwent gross, radiographic, histologic, and molecular evaluation. Next-generation sequencing of cultured fetal fibroblast DNA using a bone dysplasia panel was performed.

Results: The 55-g female fetus showed near-absent calvarial ossification, markedly shortened and bowed long bones and ribs with numerous fractures, and severely deficient bone matrix with sparse trabeculae, supporting lethal OI. During induced labor after rupture of membranes, the fetal head delivered detached from the body; the body and a detached left arm then delivered, followed by the placenta with umbilical cord avulsion. Additional disruptions included a scalp laceration with brain extrusion and left diaphragmatic and axillary chest wall defects with visceral extrusion. Sequencing identified a heterozygous pathogenic COL1A1 c.2848G>A (p.Gly950Arg) triple-helical glycine substitution.

Conclusion: The morphologic and molecular findings support a lethal COL1A1-related OI phenotype. The striking intrapartum fragmentation suggests failure of collagenous soft tissues in addition to bone. Although fetal fragmentation is not sufficient to diagnose EDS, this case suggests that EDS-like extraskelatal fragility may occur at the severe end of the COL1-related disease spectrum and may be clinically inapparent because of fetal or perinatal lethality.



Poster 35

2496073

DICER1-associated Sertoli-Leydig Cell Tumor Of The Adrenal Gland: Expanding The Spectrum Of DICER1-associated Tumors

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Background: Sex cord stromal tumors are common in the ovary but rarely described in the testis. Due to their similar embryology, sex cord stromal tumors may rarely be seen in the cortex of the adrenal gland. Herein, we describe a recently encountered case of Sertoli-Leydig cell tumor (SCLT) arising in the adrenal gland.

Methods: A 6-year-old male presented with a palpable abdominal mass and elevation of serum AFP level (3607 ng/ml; normal < 8.4 ng/ml). Imaging showed a 13.7cm cystic and solid heterogenous left abdominal mass with prominent mass effect, with difficulty in determining whether the mass was arising in the adrenal gland or the kidney. The clinical differential included neuroblastoma, sarcoma and less likely Wilms' tumor. No other sites of involvement were identified by imaging.

Results: The patient underwent left adrenal gland resection (430 g) and adjacent lymphadenectomy. Grossly, the tumor was encapsulated solid and cystic, with friable red-pink cut surface and foci of necrosis. Histologic sections demonstrated a primitive tumor with epithelial and mesenchymal differentiation, necrosis and cystic changes. Epithelial areas (positive for SF1, WT1, glypican-3, Hepar, inhibin, CD56, pankeratin and CK19) showed tubules/glands with papillary, glomeruloid, slit like and retiform histology, embedded in a loose edematous mesenchyme. The primitive, mesenchymal areas (positive for SF1, WT1, CD56, inhibin with focal calretinin and CD99) consisted of round to spindle cells with little cytoplasm, coarse chromatin, a mitotic rate of > 35/10 HPFs (> 35 mitoses per 2 mm²) and extensive skeletal muscle/rhabdomyosarcomatous differentiation highlighted by desmin and myogenin. FOXL2 was negative in both components. A morphologic diagnosis of poorly differentiated SLCT with heterologous elements prompted molecular testing that identified germline DICER1 (p.Gly1708Glu, likely pathogenic) and somatic DICER1 (p.Glu1705Val) and TERT (c.-124C>T) alterations, confirming the diagnosis.

Conclusion: As far as we are aware, primary SLCT of the adrenal gland has not been previously reported, but a Sertoli cell tumor has been reported at this site. In this case, this diagnosis was the index tumor for this patient with DICER1 germline alteration with the implications for the patient's course. While elevation of serum AFP along with positive (IHC) staining have been

described in SLCTs, it remains under recognized. These findings support the need to exclude a germ cell tumor, particularly when the elevation is as pronounced as in our patient, in whom the value exceeded 300 times the upper limit of normal.

Poster 36

2495093

When the Control Is Not in Control: A False-Negative β -Catenin Immunostain Obscuring the Diagnosis of Hepatoblastoma

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Background: Nuclear β -catenin immunoreactivity is an important diagnostic marker of Wnt/ β -catenin pathway activation in evaluating pediatric hepatocellular masses. A positive result would strongly argue against focal nodular hyperplasia (FNH), whereas a negative result would allow FNH to remain in the differential diagnosis. In studying a pediatric liver mass, we used a primary antibody against β -catenin. The product literature for this antibody recommends normal colon as a control, thus assuming that positive membranous staining is a surrogate for nuclear reactivity. A key point is that the recommended protocol specifies alkaline antigen retrieval (AR), a process known to be disproportionately harsh on nuclear antigens.

Methods: During a routine appendectomy, a liver mass was discovered. The mass was biopsied and studied with histochemical and immunohistochemical stains. Serum chemistry was also performed.

Results: Serum chemistry showed an alpha-fetoprotein level of 1,076.6 ng/mL, a value lower than expected for a hepatoblastoma the size of the current tumor but unusual for a benign lesion. A needle biopsy demonstrated hepatocellular nodules separated by dense fibrous septa with a preserved reticulin framework, suggesting FNH. In-house β -catenin immunohistochemistry (IHC) demonstrated preserved membranous staining and no nuclear staining. A glutamine synthetase stain was needed to confirm FNH; therefore, the case was sent out for the stain and a second opinion. At the referral institution, glutamine synthetase showed strong diffuse staining rather than the map-like pattern expected in FNH, and a repeat β -catenin stain (using citrate/acidic rather than alkaline AR) demonstrated strong diffuse nuclear staining. Additionally, glypican-3 was focally positive, and a final diagnosis of “fetal-type hepatocellular neoplasm, favor pure fetal hepatoblastoma” was made. As a follow-up study, the in-house β -catenin stain was repeated using acidic AR (citrate, pH 6.1), revealing weak nuclear positivity, likely reflecting the use of a dilute, prediluted primary antibody optimized by the manufacturer for the more sensitive alkaline AR method.

Conclusion: The typical FNH-like architecture, together with a modestly elevated AFP level and the absence of nuclear β -catenin staining, initially argued against a diagnosis of hepatoblastoma. Glutamine synthetase makes FNH unlikely, and the repeat β -catenin stain at the outside

institution, as well as the repeat in-house stain with citrate AR, confirmed that the initial β -catenin stain was a false negative caused by alkaline AR. This drives home the point that an immunostain for a nuclear antigen must have a control known to demonstrate nuclear positivity.

Poster 37

2496567

14-year-old with Renal Cell Carcinoma with Leiomyomatous Stroma: not to be confused with other pediatric renal cell carcinomas

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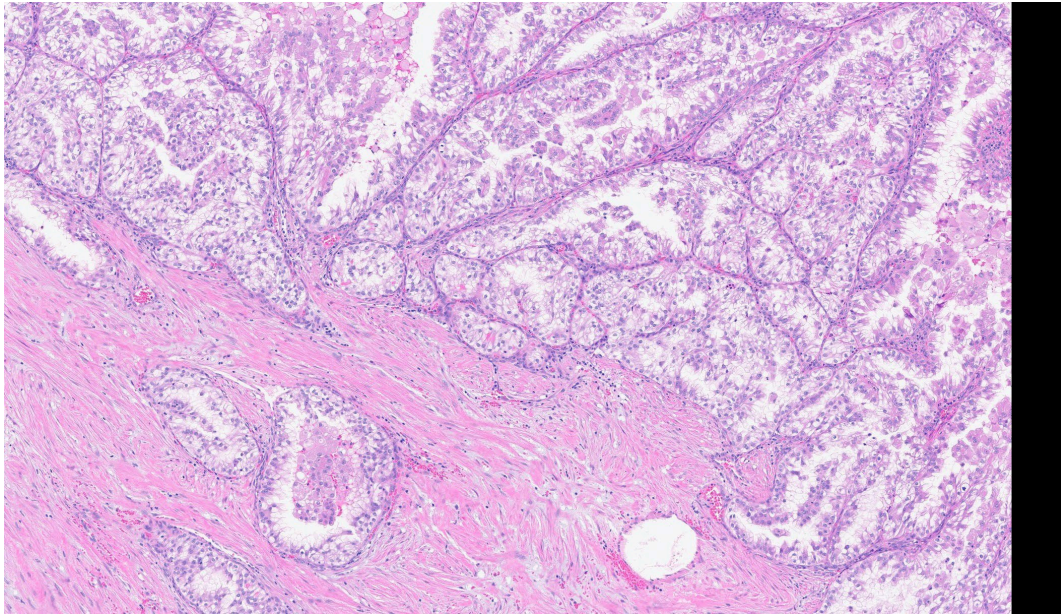
Background: Tuberous sclerosis complex (TSC) is an autosomal dominant disorder caused by pathogenic germline variants in TSC1 or TSC2 with tumorigenesis typically involving somatic inactivation of the remaining allele. Renal manifestations include cysts and angiomyolipomas (AML); renal cell carcinoma (RCC) is uncommon (< 5% of patients). RCC with leiomyomatous stroma (RCC-LS) is morphologically and molecularly heterogeneous. The 2022 WHO classification recognizes ELOC-mutated RCC as a distinct entity, while TSC/MTOR-altered RCCs with similar smooth-muscle stroma remain incompletely classified. Although most reported RCC-LS cases in adults appear indolent, rare cases have demonstrated lymph node metastasis. Pediatric cases are exceedingly rare, and the clinical, morphologic, immunophenotypic, and molecular features in children remain poorly characterized.

Methods: We describe a young patient with TSC and RCC with leiomyomatous stroma, integrating clinical, radiologic, morphologic, immunophenotypic, and available molecular findings.

Results: 11-year-old underwent evaluation for TSC after diagnosis in his half-sister, which identified a pathogenic TSC1 variant, c.561_562dup (p. Phe188Serfs*23), and consistent brain MRI. Abdominal MRI demonstrated bilateral subcentimeter renal cysts. 3 years later, surveillance MRI detected a new 9-mm left renal lesion. 11 months later, it measured 2.3 × 1.7 cm; a similar 1.5-cm right renal lesion was also present. Neither contained macroscopic fat, nor was imaging diagnostic of AML. Biopsy of the left lesion showed a low-grade epithelial neoplasm in nests, cords, and tubules intimately mixed with smooth-muscle stroma. Tumor cells had clear-to-eosinophilic cytoplasm and expressed PAX8, CK7 and CD10. CAIX showed membranous, box-like positivity. CK20 showed patchy apical staining rather than diffuse membranous or cytoplasmic staining. HMB45, Melan-A, and TFE3 were negative; stromal cells expressed SMA. SDHB and FH expressions were retained. Partial nephrectomy showed the same morphology as the biopsy with negative margins. LVI was present. Follow-up MRI at 3 months showed no recurrence with persistent right renal lesions.

Conclusion: This case documents RCC with leiomyomatous stroma in a young patient with germline TSC1 alteration and highlights unresolved classification of TSC-associated renal

epithelial tumors with smooth-muscle stroma. Recognition of biphasic morphology, appropriate immunohistochemistry, and clinicomolecular correlation can help avoid misclassification on histology from RCC mimickers, particularly as AML may be considered radiologically. Additional pediatric cases with genomic characterization and long-term follow-up are needed to define their relationship to adult TSC/MTOR-altered and ELOC-mutated RCCs, and their biologic behavior.



Poster 38

2495943

Six-year-old male with McCune-Albright Syndrome and Congenital Portal Systemic Shunt: Hepatic Neoplasms Co-incidence or Association

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Background: McCune-Albright syndrome (MAS) is a rare mosaic somatic disorder caused by postzygotic activating variants in the GNAS gene, resulting in constitutive Gs α -mediated cyclic AMP signaling. The clinical manifestations include café-au-lait macules, polyostotic fibrous dysplasia, gonadotropin-independent precocious puberty, hyperthyroidism, growth hormone excess, and neonatal hypercortisolism. There are rare reports of neonatal cholestasis and hepatic lesions. Congenital portosystemic shunts (CPSS) are rare developmental vascular anomalies in which portal venous blood partially or completely bypasses the hepatic circulation. Although CPSS is associated with multiple congenital and syndromic conditions, its association with MAS has not been established.

Methods: We describe a child with MAS and CPSS, integrating clinical, radiologic, morphologic, immunophenotypic, and available molecular findings.

Results: 6-year-old boy with a history of neonatal cholestasis, initially thought to be hypophosphatemic rickets was found to have MAS based on a pathologic diagnosis of fibrous dysplasia (FD) of the mandible, imaging findings of FD at other sites associated with fractures and deformities, endocrinopathies and a café-au-lait spot. Although blood was negative for GNAS alteration, tissue culture from bone was positive (GNAS, NM_000516.5; c.602G>A, p.R201H) consistent with mosaicism. MRI demonstrated two liver masses: 13.8 cm involving segments 4 and 8, and second 0.9 cm lesion in segment 6. There was an anomalous communication between the right portal venous and the inferior cava system consistent with CPSS/ Type 2. Biopsy demonstrated well differentiated hepatocellular carcinoma arising within an inflammatory adenoma with B-catenin activation (CRP diffuse positive, B-catenin nuclear positivity, and GS diffuse cytoplasmic positivity) resulting in transplant. The background liver demonstrated mild architectural disarray, anisocytosis, portal tracts with small to absent portal veins, patchy foci of increased arterial profiles and no fibrosis. Background liver showed diffuse immunoexpression for CRP secondary to flow abnormality, MAS, or both. Explant performed at an outside hospital identified 3 masses including a third satellite lesion (inflammatory adenoma) not appreciated on imaging. Next generation sequencing was performed on the lesion to reveal mutations in GNAS p.R201H and CTNNB1 p.T41A.

Conclusion: The coexistence of MAS and CPSS is extremely rare with only one other reported in literature and should be recognized as a clinically significant but non-classical association. Recognition of CPSS in patients with MAS is clinically important because altered hepatic blood flow may contribute to the increased risk and acceleration of the development of hepatic neoplastic lesions as seen in this case.

Poster 39

2495634

First Year Experience as a Remote Pediatric Pathologist

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Background: The increasing adoption of digital pathology, telepathology, and secure cloud-based platforms has created opportunities for pediatric pathologists to provide diagnostic and consultative services remotely. Successful remote practice requires appropriate infrastructure, regulatory compliance, and preservation of diagnostic quality and patient safety. We summarize key requirements and lessons learned during the first year of remote pediatric pathology practice.

Methods: A framework for remote pediatric pathology practice was developed based on the requirements of diagnostic pathology, digital pathology workflows, telemedicine regulations, lab accreditation standards, and pediatric subspecialty consultation needs. Key domains include medical licensure, lab credentials, digital infrastructure, information security, quality assurance, communication, and professional liability

Results: Remote practice requires an active medical license in the patient jurisdiction, appropriate hospital/laboratory privileges, compliance with applicable telemedicine, and accreditation regulations. For clinical diagnostic work, compliance with CLIA and CAP are essential. Essential infrastructure includes validated whole-slide imaging system, high-resolution diagnostic monitors, secure EMR and LIS access, reliable high-speed internet (at least 1G, ethernet port) and appropriate cybersecurity safeguards (institutional VPN). Remote pathologists must have access to relevant clinical history, imaging, laboratory data, prior pathology, and ancillary testing workflows. Effective communication with multidisciplinary pediatric teams and teaching can be maintained through virtual conferencing platforms. Clearly defined workflows are needed for specimen triage, ancillary testing, quality assurance, and cases requiring direct physical examination of the specimen. Key challenges encountered during implementation included delays related to digital slide acquisition and workflow dependencies, longer turn-around times compared to glass slide review (up to 30% more in one reviewer's experience), and occasional need for secondary review of microorganisms and small round blue cell metastases. Dedicated on-site support personnel in the laboratory, scanning and administrative roles were critical for maintaining efficiency and addressing urgent issues. Successful implementation also required patience and adaptation by both remote and on-site team members.

Conclusion: Remote pediatric pathology is feasible with modern digital pathology technology when implemented within a structured clinical and regulatory framework. Careful attention to workflow design, communication, quality assurance and institutional support is essential to maintain efficient and high-quality patient care.

Poster 40

2495211

Interstitial Pneumonitis with Autoimmune Features in a 12-Year-Old Female in the United States of America

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Background: Interstitial Pneumonitis with Autoimmune Features (IPAF) usually presents in the 5th and 6th decades and has only recently been reported (2020-2025) in children in China, Turkey, and France. A total of 23 cases have been reported, with a prevalence of 4.5-6.9% of the cases of interstitial lung disease studied in children in these series. Herein we report the first case in the United States of America.

Methods: A child with progressive systemic symptoms underwent chest imaging, bronchoscopy, pulmonary function tests (PFTs), laboratory testing, and lung biopsy with histopathologic, histochemical, immunohistochemical, and in situ hybridization studies.

Results: A 12-year-old female with β -thalassemia minor was evaluated by Pulmonology and Rheumatology for ~50-lb unintentional weight loss, fatigue, polyarticular inflammatory arthritis, malar/heliotrope rash, Gottron papules, nailfold capillary changes, fingertip ulcerations, and possible calcinosis cutis. Laboratory evaluation showed microcytic anemia, elevated ESR, elevated immunoglobulins (IgG, IgA and IgE), elevated AST and LDH, and proteinuria; peripheral blood flow cytometry was negative for abnormal hematolymphoid cells or blasts. Rheumatologic workup was unrevealing, including negative ANA, dsDNA, topoisomerase I (Scl-70), SSA/SSB, Smith, and RNP antibodies, with normal complement levels. Chest computed tomography (CT) demonstrated scattered ground-glass opacities and nodules, predominantly in the left lower lobe; CT of the abdomen and pelvis was normal. PFTs showed no obstruction or restriction, with mildly reduced diffusing capacity of the lung for carbon monoxide/alveolar volume (DLCO/VA) (72%). Bronchoscopy with bronchoalveolar lavage showed normal tracheobronchial anatomy, negative bacterial, fungal, acid-fast bacilli, cytomegalovirus and Epstein-Barr virus studies. Given the systemic inflammatory findings and pulmonary abnormalities, she underwent lung biopsy. Microscopic examination showed lymphoid interstitial pneumonia with infiltrates of lymphocytes and plasma cells and lymphoid follicles with germinal centers. Parenchymal lesions had associated Type II pneumocyte hyperplasia and clusters of foamy intra-alveolar macrophages that also contained a moderate amount of iron. Some alveoli were filled with dark pink fluid that was light-chain positive. The infiltrates were polyclonal by light chain in situ hybridization. The pleura showed fibrous thickening and numerous plasma cells. Appropriate findings in the clinical and morphologic domains warranted a diagnosis of IPAF.

Conclusion: We report the first case of IPAF in a child in North America, expanding the global range of the disorder. Series of childhood interstitial lung disease will have to be studied to determine the prevalence in our countries.

Poster 41

2495285

Lupus Nephritis With Strongly Positive MPO-ANCA and 100% Cellular Crescents in a 12-Year-Old Girl: Severe Lupus Nephritis or SLE/AAV Overlap?

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Background: Severe lupus nephritis (LN) may show crescent formation, but involvement of nearly all glomeruli is uncommon. Myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA) positivity occurs in approximately 15–25% of patients with LN, whereas necrotizing crescentic glomerulonephritis is characteristic of ANCA-associated vasculitis (AAV). Distinguishing severe ANCA-positive LN from systemic lupus erythematosus (SLE)/AAV overlap can therefore be challenging.

Methods: A previously healthy 12-year-old girl presented with left lower extremity deep venous thrombosis, fatigue, weight loss, and rapidly progressive acute kidney injury. Serologic evaluation supported SLE, with positive antinuclear antibody, anti-double-stranded DNA, anti-Smith antibody, and hypocomplementemia, while strongly positive MPO-ANCA and p-ANCA raised concern for SLE/AAV overlap. Despite intensive immunosuppressive therapy, she developed severe hypertension and dialysis-dependent renal failure, prompting a kidney biopsy.

Results: Light microscopy demonstrated severe active proliferative and crescentic glomerulonephritis, with cellular crescents involving 100% (15/15) of sampled glomeruli. The glomerular tufts showed diffuse endocapillary hypercellularity, segmental neutrophilic infiltration and karyorrhexis, and focal wire-loop lesions. Mild acute tubular injury and patchy interstitial inflammation were present, with minimal chronic tubulointerstitial injury. The NIH activity and chronicity indices were 12/24 and 3/12, respectively. Immunofluorescence demonstrated a classic full-house pattern with granular capillary wall and mesangial staining for immunoglobulins and complement. Electron microscopy revealed abundant subendothelial, subepithelial, mesangial, and paramesangial electron-dense deposits. The overall findings established active Class IV+V LN; however, the striking extent of crescent formation, together with strongly positive MPO-ANCA, supported concern for a superimposed ANCA-mediated component. Given the severity of renal injury and possible SLE/AAV overlap, immunosuppressive therapy was intensified. Renal function subsequently improved, allowing discontinuation of hemodialysis, with declining serum creatinine and proteinuria.

Conclusion: We present a 12-year-old girl with MPO-ANCA-positive LN and 100% cellular crescents who experienced renal recovery following treatment for possible SLE/AAV overlap. Although MPO-ANCA positivity should not be equated with AAV, SLE/AAV overlap should be

considered in patients with unusually severe crescentic LN, as its recognition may influence treatment intensity and improve renal outcomes.

Poster 42

2496359

Pediatric Primary Cardiac CIC::DUX4 Sarcoma: A Rare Molecularly Defined Round Cell Sarcoma

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Background: CIC::DUX4 sarcoma is a rare and aggressive undifferentiated round cell sarcoma that predominantly arises in the deep soft tissues of adolescents and young adults and is uncommon in children. Primary cardiac involvement is exceptionally rare and presents a significant diagnostic challenge given the broad differential diagnosis of pediatric cardiac tumors.

Methods: We report a 12-year-old male with a primary CIC::DUX4 sarcoma involving the right ventricle. Histologically, the tumor was composed of an undifferentiated round cell neoplasm with focally clear cytoplasm, irregular nuclear contours, coarse chromatin, and occasional intranuclear inclusions. Tumor cells expressed WT1 and BCOR, with focal CD99 staining. Rare tumor cells showed EMA and pancytokeratin expression. INI1 and BRG1 expression was retained. The tumor was negative for SATB2, NKX2.2, SSX, desmin, myogenin, pan-TRK, and MUC4. The morphologic and immunophenotypic findings raised consideration of Ewing sarcoma and other undifferentiated round cell sarcomas. RNA sequencing identified a CIC::DUX4 fusion, establishing the diagnosis of CIC::DUX4 sarcoma. The patient was treated with pazopanib but subsequently developed metastatic disease and died.

Results: CIC::DUX4 sarcoma may closely mimic Ewing sarcoma and other pediatric round cell malignancies, while its unusual cardiac location further broadens the differential diagnosis. A previously reported pediatric primary cardiac CIC-rearranged sarcoma demonstrated a CIC rearrangement without identification of a CIC::DUX4 fusion. Our case represents a molecularly confirmed CIC::DUX4 sarcoma arising primarily in the pediatric heart and highlights the importance of molecular characterization when morphologic and immunophenotypic findings are not definitive. The subsequent development of metastatic disease and death further illustrates the aggressive clinical behavior of this entity.

Conclusion: Primary cardiac CIC::DUX4 sarcoma is an exceptionally rare pediatric malignancy. Recognition of its characteristic morphologic and immunophenotypic features can prompt appropriate molecular testing. This case underscores the importance of integrating morphology, immunohistochemistry, and RNA-based fusion analysis for accurate classification of unusual

pediatric cardiac tumors.

Poster 43

2495331

A Decade in Disguise: Juvenile Xanthogranuloma Unrecognized in a Patient with Rosai-Dorfman Disease

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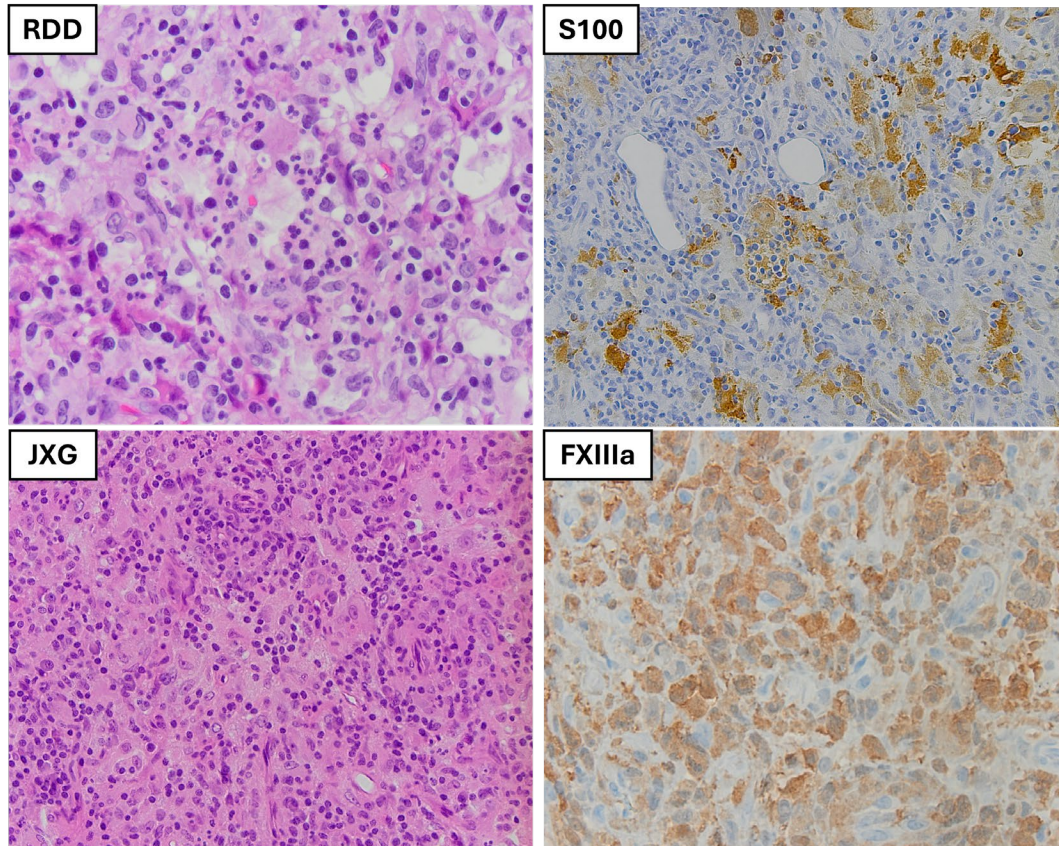
Background: Histiocytic disorders comprise a heterogeneous group of neoplasms with overlapping clinical, morphologic, and immunophenotypic features. Rosai-Dorfman disease (RDD) and juvenile xanthogranuloma (JXG) are non-Langerhans cell histiocytoses that share histiocytic markers but generally have distinct morphologic and immunophenotypic profiles. We present a 15-year-old girl with a 10-year history of multifocal osseous histiocytic lesions, in whom concurrent JXG remained unrecognized for a decade after an established diagnosis of RDD.

Methods: Available biopsies from multiple osseous lesions obtained between 2016 and 2026 were retrospectively reviewed. Histomorphologic and immunohistochemical findings were correlated with prior diagnoses, treatment history, and consultation results. Following recognition of JXG in a 2026 femoral biopsy, earlier specimens were retrospectively evaluated with S100 and Factor XIIIa to determine whether the femoral and humeral lesions represented the same or distinct histiocytic processes.

Results: In 2016, a right distal humeral lesion demonstrated numerous large histiocytes with abundant pale cytoplasm and prominent nucleoli within a mixed inflammatory infiltrate. Emperipolesis was readily identified. The histiocytes expressed S100 and CD68 and were negative for CD1a, establishing a diagnosis of RDD. The patient subsequently received chemotherapy. A separate femoral lesion was biopsied repeatedly over the following decade. Previous biopsies showed osseous involvement by a mixed lymphohistiocytic infiltrate and were interpreted on expert consultation as “histiocytosis, unclassifiable.” In 2026, another biopsy of the recurrent femoral lesion demonstrated foamy histiocytes and Touton-like giant cells within a mixed inflammatory background, with minimal emperipolesis. The lesional histiocytes expressed histiocytic markers and Factor XIIIa and were negative for S100. These findings confirmed a diagnosis of JXG. Retrospective S100 and Factor XIIIa immunohistochemistry performed on earlier femoral specimens supported a previously unrecognized diagnosis of JXG.

Conclusion: This case demonstrates that 1) failure to perform expanded immunophenotyping in the setting of nondiagnostic results may lead to a missed diagnosis that was otherwise readily obtainable; 2) failure to consider that a lesion at a second site may represent a different disease

process from that identified at the initial site can result in a delayed or missed diagnosis. Although emperipolesis is a characteristic feature of RDD, it has also been reported in JXG. Furthermore, JXG has been reported in a patient following an initial diagnosis of RDD, highlighting the potential coexistence of these two histiocytic disorders.



Poster 44

2495444

Olfactory Carcinoma: A Diagnostic Pitfall in the Pediatric Sinonasal Small Round Blue Cell Differential Diagnosis

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Background: Olfactory carcinoma is a recently described sinonasal malignancy with neuroectodermal and epithelial differentiation. It may closely mimic olfactory neuroblastoma, rhabdomyosarcoma, and other small round cell tumors, particularly on limited biopsies. We present a case highlighting these diagnostic challenges.

Methods: The patient underwent a thorough clinical exam and radiographic imaging. The tumor was evaluated histologically, supplemented with immunohistochemical stains, conventional cytogenetics, and whole-exome and targeted RNA sequencing.

Results: A 17-year-old male presented with a 1-year history of recurrent epistaxis. MRI showed a 3.4 cm enhancing left anterior superior nasal cavity mass extending into the anterior ethmoid air cells, which was debulked with suspicion for angiofibroma. The tumor histologically consisted of a high-grade round cell neoplasm arranged in nests with brisk mitotic activity, focal fibrillary background, and rare rosette formation. Tumor cells expressed synaptophysin, chromogranin, CD56, calretinin, and INSM1. EMA stained the majority of tumor cells and AE1/AE3 was focally positive. Although desmin was strongly positive in a subset, myogenin was negative and MyoD1 showed only rare weak staining. S100 highlighted only rare cells without a characteristic sustentacular pattern. Whole-exome sequencing revealed a truncating variant in ZNRF3 (a negative regulator of Wnt signaling), and beta-catenin showed diffuse nuclear positivity. Additional genetic alterations included a complex karyotype with gain of 1q and numerous copy number losses, including 17p (encompassing TP53). Targeted RNA sequencing was negative for pathogenic fusions.

Conclusion: The morphologic appearance, neuroendocrine and epithelial marker expression, and evidence of Wnt pathway alteration support a diagnosis of olfactory carcinoma. Olfactory carcinoma can be difficult to distinguish from olfactory neuroblastoma and rhabdomyosarcoma, especially in pediatric patients and on small biopsies, and this case demonstrates that desmin with minimal MyoD1 expression should not be interpreted as diagnostic of rhabdomyosarcoma in isolation. This patient underwent an initial intermediate rhabdomyosarcoma-directed treatment regimen (VAC with VI) and proton beam radiation therapy to the primary tumor site followed by

cisplatin/etoposide. He underwent resection of residual/recurrent primary tumor and was later confirmed to have pulmonary metastasis. After additional combinations of toripalimab, etoposide, and capecitabine, he currently remains stable on carboplatin/ifosfamide 17 months after his original biopsy.

Poster 45

2495601

A Rare Uterine MEIS1::NCOA2 Sarcoma With Rhabdomyoblastic Differentiation: Highlighting the Diagnostic Challenge and Aggressive Clinical Behavior

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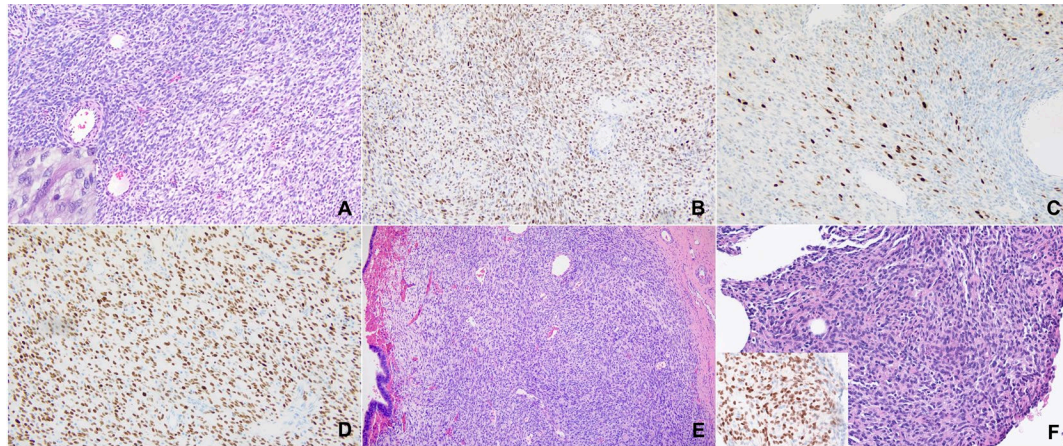
Background: Uterine sarcomas are exceedingly rare in pediatric, adolescent and young adult (AYA) population, with embryonal rhabdomyosarcoma (ERMS) being dominant. Recently, sarcomas with MEIS1::NCOA2/1 fusions have been recognized with a predilection for the gynecologic and genitourinary tracts. Initially thought to follow an indolent low-grade course, a subset with aggressive clinical behavior and distant metastasis has been emerging, frequently harboring additional genetic alterations.

Methods: We report a rare uterine MEIS1::NCOA2 sarcoma with rhabdomyoblastic differentiation mimicking ERMS in an 18-year-old, exhibiting an aggressive clinical course with multiple pulmonary metastases despite multimodal therapy.

Results: An 18-year-old female presenting with abdominal pain and an enlarging 10 cm uterine mass underwent myomectomy (piecemeal tumor removal) at an outside hospital, initially diagnosed as ERMS. Imaging showed round ligament involvement without distant metastasis. She presented for continuation of care. Pathology review demonstrated a malignant mesenchymal neoplasm with sheets and vague fascicles of monotonous primitive ovoid to short spindled tumor cells with scant cytoplasm in fibrous to multifocal myxoid stroma. Rare differentiating rhabdomyoblasts/strap cells are seen (Fig. 1). Scattered mitoses were present and no tumor necrosis was identified. Tumor cells were patchy to diffusely positive for Desmin and MyoD1, and patchy positive for Myogenin. Comprehensive next generation sequencing revealed a MEIS1::NCOA2 rearrangement; no other pathogenic genetic alterations identified. She was subsequently treated with chemotherapy (vincristine, dactinomycin, and cyclophosphamide), followed by total hysterectomy with bilateral salpingectomy that showed residual viable tumor and parametrium involvement, re-resection with bilateral oophorectomy (no viable tumor), and tumor-bed radiation. At 11 months follow up, PET scan demonstrated bilateral enlarging pulmonary nodules concerning for metastasis. Serial lung nodule wedge resections confirmed metastatic tumors with negative margins. Because of progression, systemic chemotherapy was restarted, during which she underwent an additional lung metastatic tumor resection followed by whole-lung radiation. Despite the multimodal approach, her imaging was still concerning for lung metastasis at 23 months follow up.

Conclusion: This rare case of uterine MEIS1::NCOA2 sarcoma with rhabdomyoblastic

differentiation highlights the diagnostic challenge in AYA population and underscores the value of molecular testing for accurate diagnosis. Contrary to the indolent behavior typically ascribed to this entity, this case expands the recently noted clinical spectrum to include distant metastasis in the absence of additional genetic alterations.



Poster 46

2495795

Lipofibromatosis-Like Neural Tumor With CCDC6::RET Fusion Presenting as a Subcutaneous Forearm Mass in a 5-Month-Old Infant

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Background: Lipofibromatosis-like neural tumor (LPF-NT) is a rare, locally aggressive soft tissue lesion that was first described in 2016. These lesions are composed of bland spindle cells with an infiltrative growth pattern which co-express S100 and CD34 by immunohistochemistry and are typically associated with NTRK1 gene fusions. Herein we report a case of LPF-NT with CCDC6::RET fusion in a 5-month old infant.

Methods: A 5-month-old female presented with a rapidly enlarging subcutaneous mass of the left forearm that was not associated with any trauma or tenderness to palpation. The lesion was noted to increase in size from 2-3 mm to 1.5 x 2.0 cm over the course of one month. Ultrasonography revealed a 1.5 x 0.8 x 1.4 cm solid, lobulated, ill-defined, echogenic mass which was subsequently excised.

Results: Gross examination of the excised specimen demonstrated a yellow-tan lobulated portion of tissue with yellow- to white-tan fibrofatty cut surface. Histologic sections revealed bland spindle cells arranged in fascicles and mature adipose tissue. No necrosis, brisk mitoses, or primitive mesenchymal nodules were identified. The spindle cells were positive for CD34 with patchy SMA and S100 expression and were negative for desmin, myogenin, and nuclear beta-catenin by immunohistochemistry. Somatic RNA sequencing identified a CCDC6::RET fusion.

Conclusion: LPF-NT is a rare pediatric soft tissue lesion that has limited supporting literature. Though these lesions are most often associated with NTRK alterations, RET alterations have been described. This entity should be considered in the differential for pediatric bland spindle cell tumors with adipose tissue along with lipofibromatosis and fibrous hamartoma of infancy. Furthermore, when considering diagnostic workup, RNA-based sequencing is necessary for definitive diagnosis, as the morphology and IHC may overlap with other pediatric spindle cell lesions and targeted NTRK testing may be misleading.

Poster 47

2495797

Uncommon pathology of vaping-associated lung injury at a pediatric autopsy

S Wilson C Bernard; McGill University

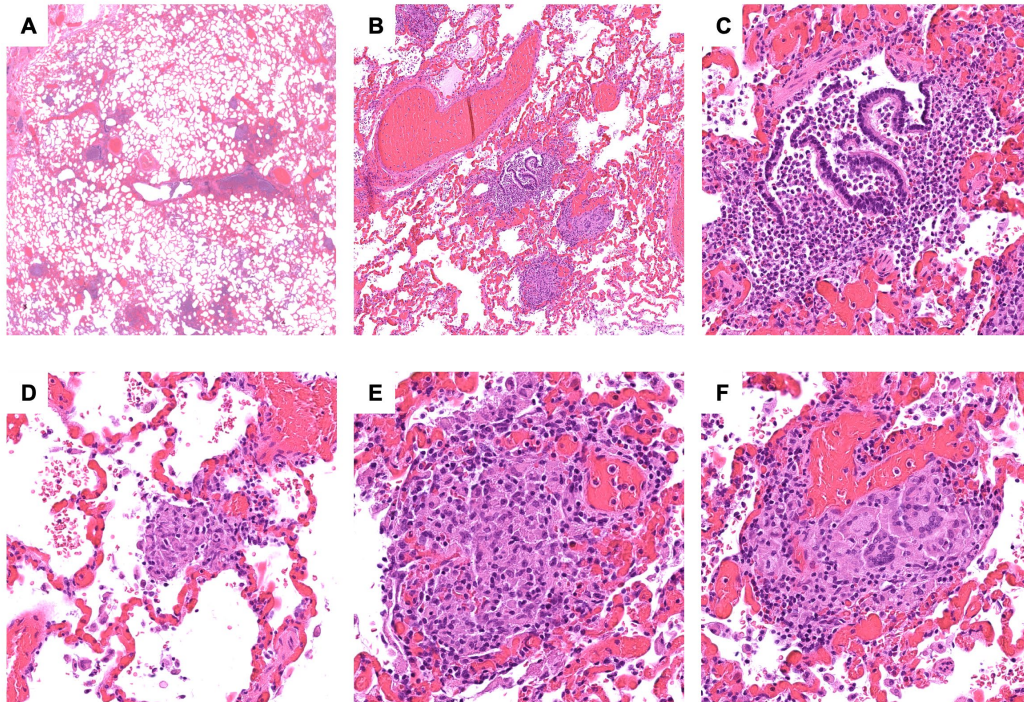
Background: E-cigarette or vaping product use-associated lung injury (EVALI) is a clinical diagnosis of exclusion. Histological correlates usually fall along a spectrum of acute lung injury with organizing pneumonia or diffuse alveolar damage, often bronchiolocentric and macrophage-rich. Airway-centered granulomatous patterns are uncommon and rarely documented.

Methods: Police investigation did not identify foul play, and an autopsy was requested by the coroner.

Results: A previously healthy 16-year-old boy was found dead in bed, in rigor, with froth at the mouth. Vaping devices, nicotine pouches, hash, mushrooms, and pills were recovered at the scene. The decedent had no documented medical history. External examination was unremarkable with no signs of trauma. Internally, the lungs were congested without consolidation or mass, and other organs were unremarkable. Postmortem toxicology demonstrated metonitazene, cocaine, THC, and oxycodone in serum and urine. Acute combined intoxication constituted the certified cause of death. The lung injury pattern is the focus of this report. Multiple sections from all lung lobes showed small, well-formed, non-necrotizing epithelioid granulomas centered on distal airways (Fig 1B,E,F), with associated acute bronchiolitis (Fig 1B,C). Polarization was negative for foreign material. Special stains for mycobacteria and other organisms were negative. Alveolar spaces contained rare clusters of foamy macrophages in loose aggregates (Fig 1D) but no hyaline membranes or organizing fibroblastic plugs (Fig 1A). Diffuse alveolar damage was not identified. Blood, spleen, and left lung cultures were negative; the right lung broth culture grew oral-type streptococci, interpreted as contaminants. Lung PCR for mycobacteria and a multiplex respiratory viral panel were negative. No granulomas were seen in any other organs, including lymph nodes. Neuropathology consultation of the brain was consistent with an antemortem hypoxic-ischemic interval of several hours.

Conclusion: The differential diagnosis for pulmonary granulomas is broad and includes infection, sarcoidosis, vasculitis, hypersensitivity pneumonitis, environmental exposures, foreign bodies, drug reactions, autoimmune conditions, and immunodeficiencies. In this adolescent vaper without clinical or pathological evidence indicating one of the aforementioned entities, granulomas point to EVALI even without diffuse alveolar damage. Correlation with toxicology and infectious studies helps distinguish airway granulomas from infection or systemic

granulomatous disease. Deaths at the intersection of substance use and inhalational lung injury illustrate the breadth of problems encountered in pediatric pathology practice and highlight the need to recognize EVALI patterns even when they are not the primary cause of death.



Poster 48

2495969

Novel Morphology in Pediatric Fibromyxoid Tumor with PLAG1 Fusion

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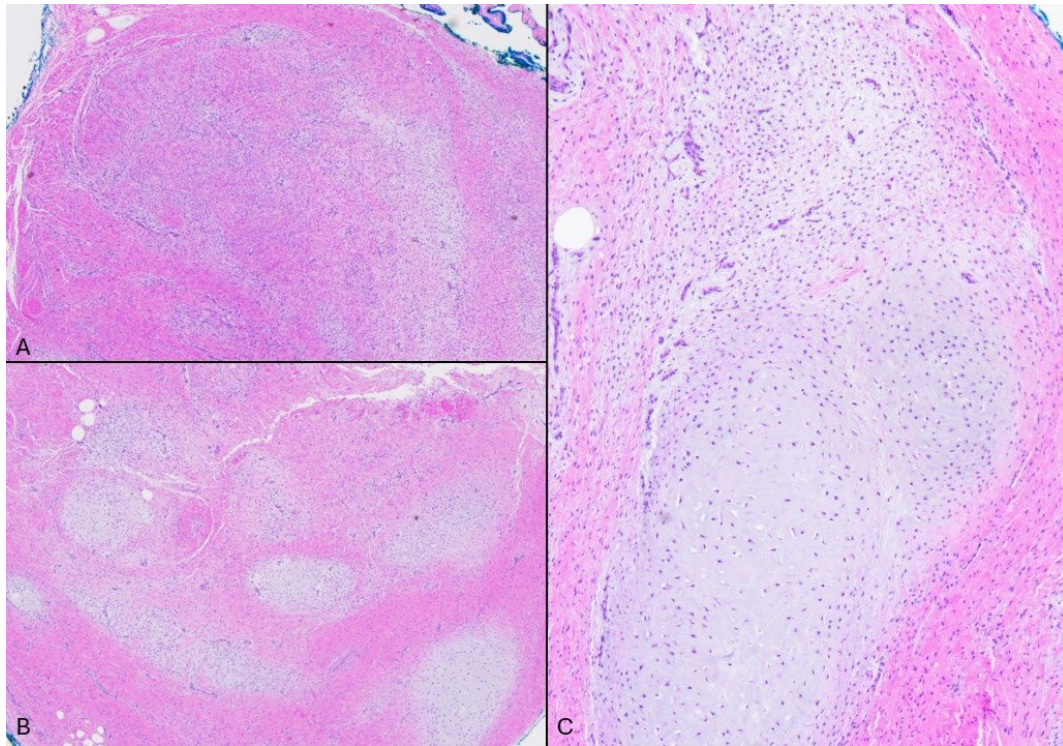
Background: PLAG1-rearranged pediatric fibromyxoid soft tissue tumors are rare and have only recently been identified as a separate entity. They are usually composed of bland spindled to ovoid cells set within a fibroblastic to myxoid background and often express CD34 and desmin. Fusion partners with PLAG1 are varied, including YWHAZ (4 cases), DLEU2 (4 cases), PCMTD1, COL3A1, EEF1A1, H3-3B, ZFHX41 and CHCHD7. Fourteen cases have been reported in the literature thus far. To date, no cases with chondroid histomorphology have been described.

Methods: A 20-month-old female presented with a 2-month history of a painless left upper arm mass. Ultrasound and magnetic resonance imaging showed an intramuscular, well-circumscribed, mobile lesion measuring 2.0 x 1.2 x 0.7 cm near the proximal humerus and brachial vasculature with a heterogeneously hyperintense T2 signal and central enhancement. Intraoperative evaluation on frozen section showed bland fibrous and cartilaginous components. No involvement of the adjacent neurovascular bundle was identified. On gross examination, the soft tissue mass was tan-white and firm.

Results: On microscopy, the neoplasm was biphasic and composed of dense fibrous tissue with multiple nodules of hyaline cartilage in varying degrees of differentiation. Swaths of bland, plump ovoid to stellate cells were set within a variably dense collagenous to loose fibromyxoid background, with regions of stellate cells within the myxoid background transitioning to small nodules of hyaline cartilage. Thin-walled blood vessels were present adjacent to and within the myxoid and cartilaginous areas. No significant ossification, cytologic atypia, necrosis, or increased mitotic activity was identified. Immunohistochemical (IHC) stains showed patchy weak cytoplasmic staining in a subset of cells with CD34. Desmin was strongly and diffusely positive within the neoplastic cells, with S100 positivity within the cartilage and in the adjacent neoplastic cells. SMA, SOX10, β -catenin, and MUC4 were negative. RNA next generation sequencing of the tumor was positive for a YWHA::PLAG1 fusion.

Conclusion: The histologic, immunohistochemical, and molecular findings were consistent with a PLAG1-rearranged fibromyxoid pediatric soft tissue tumor. Our findings expand on the morphologic spectrum of this tumor, as chondroid components have not been previously reported in this entity. This neoplasm should be considered when cartilaginous nodules are identified within a bland fibromyxoid or myxoid lesion. Performing CD34 and desmin IHC stains could be

helpful, and the diagnosis can be confirmed with molecular fusion testing.



Poster 49

2496467

Discordant Peripheral and Hepatic Disease Burden in Transient Abnormal Myelopoiesis: Clues to the Pathogenesis of Hepatic Fibrosis

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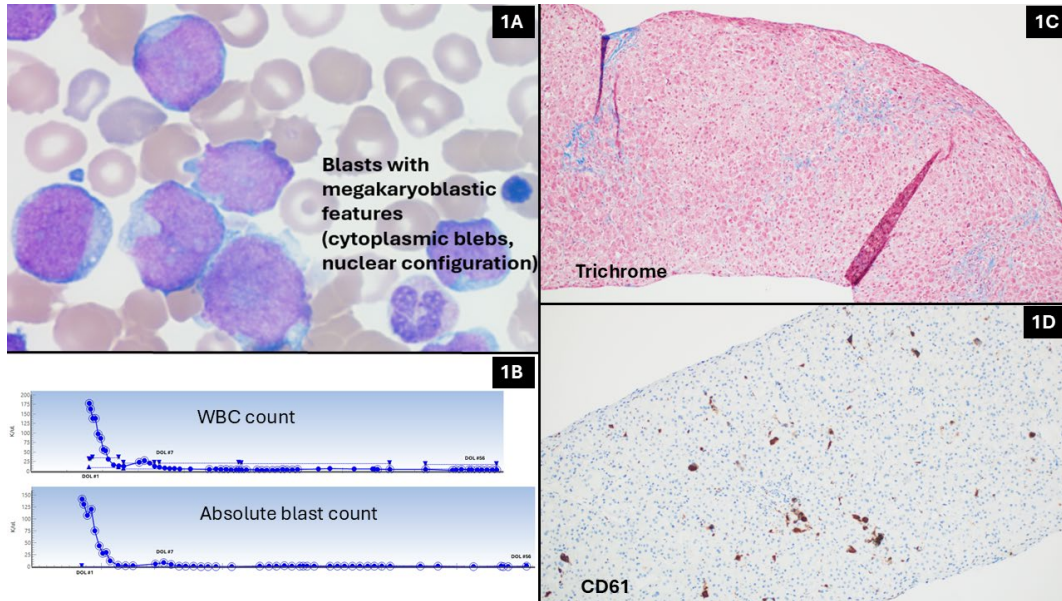
Background: Transient abnormal myelopoiesis (TAM) is a clonal myeloid proliferation in neonates with Down syndrome (DS) due to truncating GATA1 variants. The liver can harbor GATA1-mutated megakaryocytic cells & develop cholestasis & fibrosis. How peripheral disease, persistent hepatic TAM, & fibrosis relate remains incompletely understood.

Methods: .

Results: A 36-week male with DS presented on day of life (DOL) 1 with hepatosplenomegaly, leukocytosis (177.9 K/ μ L), & 80% megakaryocytic (CD41+) blasts. Bone marrow NGS identified truncating GATA1 variants c.85G>T (VAF 51.5%) and c.195del (VAF 34.2%). Two courses of low-dose cytarabine nearly eliminated blasts & normalized WBC by DOL 7; a 3rd was given at 7 wk. Despite a robust & sustained peripheral response, AST/ALT/direct bili remained elevated. DOL 56 liver biopsy showed cholestasis, mild interstitial & portal/periportal fibrosis with focal early bridging & frequent megakaryocytes in sinusoids & near portal tracts. Liver biopsy NGS detected GATA1 c.85G>T (VAF 11.55%), confirming persistent hepatic TAM. Hepatic dysfunction resolved about 1 mo later without further intervention & has not recurred at 11 mo.

Conclusion: TAM-associated liver disease may persist after circulating blasts disappear, & GATA1-abnormal megakaryocytes have previously been demonstrated in liver. This case adds clone-specific molecular confirmation of persistent hepatic TAM after marked peripheral response to cytarabine, with spatial characterization of megakaryocytes in sinusoids & near portal tracts. The fibrosis pattern & clinical course expand the reported spectrum. Prior cases commonly describe diffuse sinusoidal or pericellular fibrosis, often with severe or fatal liver disease. In contrast, this patient had frequent intrahepatic megakaryocytes but mild portal/periportal fibrosis followed by clinical resolution, suggesting that megakaryocyte burden alone does not determine fibrosis severity. This raises the hypothesis that systemic TAM burden may modify hepatic injury. TAM blasts can express profibrotic mediators, while circulating inflammatory cytokines/chemokines have been associated with leukocytosis, progressive liver disease, & adverse outcomes. Rapid reduction of peripheral disease might therefore lessen a systemic inflammatory or profibrotic contribution even when a hepatic clone persists. Although

not directly proven because cytokines were not measured in this patient, this may help explain limited fibrosis despite persistent hepatic TAM. The findings are also compatible with evidence that the fetal-liver microenvironment preferentially supports GATA1s-mutant cells. Overall, hepatic injury may reflect an interaction between persistent local disease, the hepatic microenvironment, & systemic inflammatory burden rather than pure hepatic involvement alone.



Poster 50

2480997

Autopsy Findings in a Child with Ischemic Stroke and Post-mortem Diagnosis of Vascular Ehlers-Danlos Syndrome with Heterozygous Protein C Deficiency

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Background: Childhood ischemic stroke is a rare occurrence that may be attributed to cervical artery dissection and/or hypercoagulable state. Vascular Ehlers-Danlos syndrome (vEDS) due to mutations in COL3A1 may lead to fatal arterial wall dissections or rupture. Congenital deficiency of protein C, a key regulator of coagulation, occurs due to mutations in PROC and may increase the risk of thromboembolism. We present a case of combined vEDS and congenital protein C deficiency in a child with acute ischemic stroke and arterial dissections, who passed unexpectedly due to massive hemorrhage.

Methods: The decedent was a 12-year-old otherwise healthy boy presenting with headache and eye pain for one month and acute-onset seizure. Diagnostic workup revealed acute ischemic stroke of the right M1 middle cerebral artery, right internal carotid artery dissection preventing mechanical thrombectomy, and decreased serum protein C activity (24%). After a short period of recovery, he developed tension hemothorax, profound anemia, and rapidly decompensated despite attempted resuscitative thoracotomy. Autopsy was conducted without limitations, including histological examination of arteries using elastin and collagen stains. Next generation sequencing studies resulted one month post-mortem and were reviewed alongside autopsy findings. A literature review of phenotypic manifestations of vEDS and protein C deficiency was performed.

Results: Findings include delicate facies and superficial hemorrhages, right cerebral hemispheric infarct with right internal carotid artery dissection/thrombus, and aortic dissection with massive hemorrhage in the mediastinum and retroperitoneum. The patient was heterozygous for pathogenic variants of COL3A1 and PROC, causing frameshift/premature termination and missense substitutions, respectively. Arteries affected by dissection microscopically exhibited varying degrees of medial degeneration, including mucoid extracellular matrix accumulation, elastic fiber loss, and smooth muscle necrosis/disorganization. Some uninvolved arteries also showed early medial degeneration and intrapulmonary arteries were irregular and thin-walled.

Conclusion: vEDS is a connective tissue disease that can remain undiagnosed until a serious complication such as stroke or arterial dissection occurs and may affect otherwise healthy-appearing children. Although typically associated with venous thromboembolism, congenital protein C deficiency may enhance the risk of arterial thrombosis in predisposing conditions.

Autopsy may be instrumental in elucidating collagen vascular disease in children with otherwise unexplained lethal hemorrhage or thrombosis, provide context for the interpretation of genetic studies resulting after death, and potentially help guide family members at risk for inherited disease.

Poster 51

2496598

Systemic Juvenile Xanthogranuloma in an Infant Girl with a Novel TPM3::ROS1 Fusion

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Background: Histiocytoses represent an uncommon group of hematopoietic tumors with macrophage or dendritic cell lineage harboring recurrent MAPK, PI3K/AKT, or RTK pathway abnormalities driving ERK overexpression. Juvenile xanthogranuloma (JXG) is the most common form of non-Langerhans cell histiocytosis (LCH) often manifesting as a solitary skin nodule. However, systemic involvement can occur in less than 5% of cases and a subset may present with a blueberry muffin rash. The JXG family of tumors can exhibit a variety of morphologies, and several mutations have been described involving the MAP2K1, KRAS/NRAS, CSF1R, ARAD, and BRAF genes. NTRK1 fusions have also been reported in JXG. Recently, a case of central nervous system non-LCH with JXG morphology was found to harbor an actionable ROS1::GIT2 fusion.

Methods: We present a case of systemic JXG with a novel ROS1::TPM3 fusion. The patient is a term infant girl admitted to the neonatal intensive care unit (NICU) with acute liver failure, thrombocytopenia, hyperferritinemia, and blueberry muffin rash. Initial workup for infectious causes and hemophagocytic lymphohistiocytosis was unrevealing, albeit her symptoms waned over a month with supportive care. At 8 months of life, she exhibited regression of developmental milestones and a possible seizure spell. Imaging studies showed disseminated disease involving the spinal cord, brain, lungs, and abdomen. She was initially treated with LCH-based chemotherapy regimens with progression, but subsequent treatment with a MEK inhibitor led to some improvement. After molecular-genetic testing, targeted therapy with lorlatinib was initiated, which resulted in sustained response. At 3 years old, the patient is alive with stable disease.

Results: During the NICU stay, liver biopsy showed neonatal giant cell hepatitis, plump histiocyte clusters in sinusoids, cholestasis, and mild fibrosis (periportal and portal). A skin biopsy revealed involvement by a non-LCH histiocytosis. At 8 months of life, the spinal cord biopsy showed a histiocytic proliferation with abundant Touton-type giant cells and admixed foamy xanthomatous cells compatible with a JXG phenotype. A panel of immunohistochemistry was positive for CD68, CD163, S100, Factor XIIIa, CD4, and CD31. ALK, BRAF VE1, and pan-TRK immunostains were negative. Next generation sequencing analysis confirmed the presence of ROS1::TPM3 fusion.

Conclusion: Histiocytoses can exhibit morphologic and genetic overlap. JXG can rarely present

with diffuse systemic involvement making clinical diagnosis and treatment challenging. Our case underscores the need for comprehensive genetic testing of histiocytosis, as well as highlights the clinical benefit and positive therapeutic response to targeted therapy in this patient.