RARE-24. THE USE OF NOVEL IN VITRO MODELS TO STUDY ADAMANTINOMATOUS CRANIOPHARYNGIOMA DISEASE BIOLOGY AND DRUG RESPONSE
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BACKGROUND: Challenges around the design and investigation of cell culture models of adamantinomatous craniopharyngioma (ACP) have arisen from the cellular heterogeneity and spatial distribution of tumor populations that harbor disparate requirements in culture. Novel approaches to in vitro modeling of ACP are needed. METHODS: Intraoperatively collected tumor specimens were mechanically digested and plated under conditions tailored to the cell population of interest. ACP tumor-derived fibroblasts and epithelial cells were isolated using serum-containing and keratinocyte-specific media respectively. ACP-derived epithelial cells were immortalized via SV40 virus transduction and puromycin treatment for stable cell-line generation. Cell lines included immunofluorescence assays for markers appropriate for the cell population of interest. RNA sequencing of cell lines was compared to ACP transcriptome reference data. Cell typing was conducted using short tandem repeat sequencing. RESULTS: ACP fibroblasts and ACP epithelial cells maintained spindle-like and cobblestone morphologies respectively, even after 4 passages. Immunofluorescence staining confirmed high levels of Vimentin expression in ACP-derived fibroblasts, and panCK B-catenin in ACP-derived epithelial cells. Point mutation in exon 5 of the CTNNB1 gene was identified in ACP-derived epithelial cells. CONCLUSION: Initial data related to cell line development in ACP may be addressed through the isolation and culture-specific ACP cell populations. This experience demonstrates the maintenance of validated markers of the cell populations of interest ex vivo. While preliminary, such cell lines offer promise as tools for the identification and study of potential therapeutic vulnerabilities in ACP.

RARE-25. PRIMARY INTRACRANIAL EWSING SARCOMA IN A CHILD: CASE REPORT
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Ewing sarcoma is a rare childhood tumor which accounts for 3% of all pediatric malignancies. More so, primary intracranial involvement with meningeval attachment is even rarer, accounting for only 1% of all Ewing sarcoma. We report a case of a 5-year-old boy who presented with headache, vomiting, and left-sided weakness that rapidly progressed over a period of three months. Cranial MRI showed a 7.1 x 6.7 x 8.6 cm multilobulated, heterogeneously enhancing, mixed solid and cystic extra-axial tumor compressing the frontoparietal lobe and causing significant midline shift. It was attached to the falx and infiltrated the middle third of the superior sagittal sinus. We performed a large right frontoparietal craniotomy to excise the tumor. Because of massive bleeding from the tumor, only a subtotal resection was possible. The bone flap was left out. The patient was discharged fully awake but with right hemiplegia on the fourteenth post-op day. Histopathologic examination revealed a spindle cell neoplasm that exhibited diffuse membranous staining for CD99. Fluorescence in situ hybridization confirmed EWSR1 gene rearrangement, consistent with Ewing sarcoma. Three months after his surgery, the patient subsequently received 36 Gy of radiation therapy. At twelve months post-op, he remains fully awake and is back in school. He has residual left hemiparesis, but with antigravity movement. A multidisciplinary team involving Pediatric Oncology, Pediatric Neurology, Neurosurgery, Pathology, Radiation Oncology, and Rehabilitation Medicine is essential for patients with rare central nervous system tumors, to maximize effective treatment strategies despite limited resources.

RARE-26. EVALUATING THE CLINICAL UTILITY OF DNA METHYLATION PROFILING FOR CHOROID PLEXUS TUMORS
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INTRODUCTION: Choroid plexus tumors (CPT) are rare, potentially aggressive CNS tumors with defined histologic criteria for grading. In recent years, several CPTs within our practice have demonstrated discordance between histological diagnosis and clinical behavior. DNA methylation profiling has emerged as a potential diagnostic adjunct for aiding clinical planning and treatment approach. In this study, we sought to retrospectively evaluate the clinical utility of DNA methylation profiling within our cohort of patients with CPT. METHODS: We performed a retrospective chart review of all patients with choroid plexus tumors treated at Dana-Farber / Boston’s Children’s Cancer and Blood Disorder Center between 1990-2021, evaluating the histologic, treatment approach, and clinical outcome. Available tissue samples were sent to the National Institute of Health for DNA methylation profiling. RESULTS: Seventeen patients with CPT were identified. Median age at diagnosis was 1.8 years (range: 0.4-27.7). Histologic diagnosis included choroid plexus papilloma (CPP, n=4), and choroid plexus carcinoma (CPC, n=8). DNA methylation in an initial subset placed these tumors with the pediatric type A (n=5), pediatric type B (n=6), and adult (n=1) subgroups. For one patient with CPC, methylation profiling returned as unclassifiable (possibly representing an alternative diagnosis). Discrepancies with the histologic grade were noted in several cases: one patient diagnosed with CPP grouped with pediatric type B CPT on methylation analysis, had rapid recurrence, and a diagnosis of CPC was made on a re-resection specimen; another patient with a CPP with concerning features was classified as pediatric type A by methylation, and is without evidence of disease after initial complete resection. Survival outcomes based on histologic diagnosis and molecular subgroups are comparable. CONCLUSION: DNA methylation profiling is a useful tool for the diagnosis of CPT and may have the potential to guide clinical planning and management.

RARE-27. TREATMENT AND OUTCOMES IN ATYPICAL CHOROID PLEXUS PAPILLOMA: A SINGLE INSTITUTION EXPERIENCE
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BACKGROUND: Atypical choroid plexus papillomas (aCPP) are rare central nervous system (CNS) tumors often occurring in very young children. While surgical resection has been a mainstay of therapy, there is no consensus and limited data on the treatment of relapsed or metastatic tumors. METHODS: Retrospective review of the treatment and outcome of patients diagnosed with aCPP since 2011 was performed. RESULTS: Of the seven patients, 4 were male and 3 were female with a median age of 2 years at diagnosis (range: antenatal to 18 years old). All non-metastatic patients (six) were treated with surgery and all achieved gross total resection. Two patients had diffuse leptomeningeal contrast enhancement on diagnosis MRI that resolved after resection of primary tumor alone. One patient developed local relapse underwent re-resection with a GTR then was treated with 4 cycles of chemotherapy based on CPT-SIOP-2000 protocol (caspoflutro, etoposide) and has not had further relapse in 24 months. One patient had metastatic disease at the time of diagnosis. They were treated with adjuvant chemotherapy which stabilized disease for 36 months until they had progression. Additional four cycles were given and has again stabilized disease now 8 months from completion of that therapy. One non-metastatic patient died of unknown causes 28 months from diagnosis. CONCLUSION: ACP and CPC with concerning features was classified as pediatric type A by methylation, and is without evidence of disease after initial complete resection. Survival outcomes based on histologic diagnosis and molecular subgroups are comparable. CONCLUSION: DNA methylation profiling is a useful tool for the diagnosis of CPT and may have the potential to guide clinical planning and management.

RARE-28. THE USE OF SUBCUTANEOUS INTERFERON IN PATIENTS WITH CRANIOPHARYNGIOMA: AN INSTITUTIONAL RETROSPECTIVE REVIEW
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RARE-29. TRANSCRIPTOME CHARACTERIZATION OF PEDIATRIC ADAMANTINOMATOUS CRANIOPHARYNGIOMA AT THE CELLULAR LEVEL

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BACKGROUND: Adamantinomatous Craniopharyngioma (ACP) is a neurologically devastating brain tumor that affects children and adults. It is characterized by the nuclear accumulation of mutated β-catenin, and activated Wnt signaling. Current models suggest that ACP growth is driven through paracrine mechanisms characterized by the senescence-associated secretory phenotype (SASP). However, detailed paracrine-mediated SASP mechanisms are unknown. Improved definition of the various cellular phenotypes that comprise ACP will inform and advance our understanding of this disease.

METHODS: Single cell RNA-sequencing (scRNA-seq) and multiplex ELISA were performed on pediatric ACP tissue and cyst fluid, respectively. Reference scRNA-seq data was obtained from PanglaoDB. Preprocessing and standard analyses were conducted using Seurat software. Cellular phenotypes were annotated using the Human Primary Cell Atlas. Differential expression and functional enrichment analyses were utilized to identify Wnt signaling and Wnt signaling activation and epithelial subpopulations. Paracrine signaling was inferred via CellChatDB. SASP Atlas was utilized to query marker gene lists. Pseudotemporal ordering was performed using monocle3.

RESULTS: ACP tissue is heterogeneous and contains multiple distinct immune signatures. ACP tissue contains 2 unique epithelial subpopulations, which demonstrate canonical Wnt-signaling and SASP, respectively. Pseudotemporal ordering suggests the initial oncogenic event to be of epithelial character, with subsequent aggressive behavior from a separate epithelial cell population. CONCLUSIONS: Based on gene expression, cell populations that correspond to the histologically identifiable epithelial whorls and palisading epithelium can be identified. These subpopulations display unique functional signatures, senescence and synergistic therapeutic targeting of these separate epithelial populations may lead to improved patient care.

RARE-30. NOVEL COLLISION TUMOR OF CRANIOPHARYNGIOMA AND EPENDYMOMA IN A PEDIATRIC PATIENT: A CASE STUDY

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Collision tumors are rare tumors comprised of two distinct histologies. In this case report, we discuss a suprasellar collision tumor consisting of adamantinomatous craniopharyngioma and supratentorial ependymoma in a pediatric patient. Case Presentation: Our patient was a two-year-old female with progressive craniopharyngioma status post cyst decompression with Ommaya reservoir placement, subcutaneous peginterferon, Omaya taps, and subtotal resection. An MRI three months post-resection showed progression and treatment was started with subcutaneous interferon alfa. After eight weeks, she presented with new onset headaches and vomiting. MRI revealed had had tumor progression with associated obstructive hydrocephalus. She underwent a subtotal resection. Pathology revealed recurrent adamantinomatous craniopharyngioma and a 0.5cm ependymoma with classic histomorphology lacking anaplasia features. The ependymoma was positive for GFAP immunostain and EMA immunohistochemistry highlighted a ‘dot-like’ reaction. The Ki-67 proliferation index was very low (<1%). The limited diagnostic material precluded further genomic characterization of the ependymoma. The previous pathology was reviewed and no evidence of recurrence was identified. Spine MRI was negative for metastatic disease. The role of interferon in the development of a collision tumor in this patient in unknown, but we suspect it to be unrelated. Conclusion: To our knowledge, this is the first documented case of a suprasellar collision tumor comprised of craniopharyngioma and ependymoma. Discovery of the collision tumor impacted the patient’s treatment plan.