tumors. The presence of metastatic seeding is rare and has been reported as an adverse prognostic factor. We present 2 cases of young children with recurrent metastatic DIA/DIG to describe their presentation, therapeutic management and outcome and to highlight the importance of molecular characterization of these rare tumors to guide adjuvant therapy. CASES DESCRIPTION: The first patient developed metastatic recurrence after initial gross total resection (GTR) of a localized DIG. The disseminated relapse was treated with monthly carboplatin and vincristine (CB/VCR). Complete response was achieved after 15 cycles and the patient has remained in continuous complete remission for 5 years. Post hoc molecular analysis of the tumor revealed a BRAF-RDX fusion. The second patient presented with a disseminated intraventricular relapse following an incomplete resection of a DIA associated with a SPECC1L-NTRK2 fusion. The patient received 2 cycles of CB/VCR with minimal response and was then switched to Larotrectinib leading to a very good partial response (VGPR) 3 months into therapy and has remained on treatment since then with significant clinical improvement. DISCUSSION/ CONCLUSION: In our 2 cases, metastatic recurrence was responsive to adjuvant therapy leading to complete response with conventional chemotherapy in the first one and to VGPR with NTRK inhibitor in the second patient. Early molecular characterization of these benign tumors is critical in case of incomplete resection or metastatic seeding to widen therapeutic options and maximize chance of cure. Response with NTRK inhibitor appears rapid and significant but the total duration of treatment and sustainability of response after discontinuation remain unknown.

RARE-20. RETROSPECTIVE ANALYSIS OF 9 PINEOBLASTOMA

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BACKGROUND: Pineoblastomas (PBs) are rare, supratentorial, primitive neuroectodermal tumors. Little is known with the clinical features and outcomes of PBs. METHODS: We retrospectively analyzed consecutive patients with PBs who were treated in Guangdong Sanjiu Brain Hospital between December 2006 to May 2020. RESULTS: A total of 9 patients (7 males and 2 females) with PBs were treated in our hospital with a median age of 9 yrs (range: 1-36 yrs) at diagnosis. Total or near-total resection was achieved in 3 patients (33%), partially resection in 4 (44.4%),and biopsy in 2(22.2%). There were 4 patients have spinal cord metastasis at diagnosis. Five patients received craniospinal irradiation (CSI), with concurrent or adjuvant chemotherapy. The average total dose of CSI was 34.80±2.683Gy, and the average dose to local tumor bed was 56.08±6.41Gy. Two patients younger than 3 years old only received chemotherapy, while 1 patient did not receive any postoperative treatment, and 1 patients was unknown. The median followed up time is ? months(range:3-39 months). At the last follow up, 5 patients were died, 3 patients were survived, and 1 was lost to follow-up. The median OS was 31 months (95%CI 1.782-60.281). Disease progression occurred in 5 patients during the follow-up period, and the median PFS was 19 months. CONCLUSION: Pineoblastoma is a rare central nervous system malignancy with a tendency for disseminated disease. Comprehensive therapies such as surgical resection, radiation and chemo therapy are effective therapies for PBs.

RARE-21 *SOX2* PLAYS AN IMPORTANT ROLE IN CHOROID PLEXUS TUMOR DEVELOPMENT

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Choroid plexus (CP) tumors are rare primary brain neoplasms found most commonly in children and are thought to arise from CP epithelial cells. *Sox2* is a transcription factor that not only plays a role in development in the ventricular zone, CP, and roof plate, but also contributes to cancer stemness, tumorigenesis, and drug resistance. Gene expression studies demonstrate aberrant *Sox2* expression in human CP tumors, suggesting a role in tumor development. A subset of CP tumors exhibit abnormal NOTCH pathway activity. Using animal models, we previously show that sustained NOTCH activity leads to CP tumors. Immunofluorescence, RT-qPCR, and RNA scope assays have revealed increased *Sox2* levels in NOTCH-driven CP tumors compared to wild type CP in mice. To investigate the role of *Sox2* in CP tumors, we eliminated *Sox2* expression in NOTCH-driven CP tumors. Loss of *Sox2* almost completely blocked NOTCH-driven CP tumor growth in these mice, supporting a role for *Sox2* in these tumors. Ciliation regulation is one proposed functional pathway for tumorigenesis in CP tumors. Using immunofluorescence assays for cilia (ARL13b) and aquaporin transport protein 1 (AQP1) in combination with super resolution microscopy, we observe a stark contrast between wild type CP epithelial cells which are multiciliated and homogeneously express AQP1, indicative of normal epithelial differentiation, compared to NOTCH-driven CP tumors consisting of mono-ciliated cells with loss of AQP1 expression. In *Sox2*-deficient NOTCH-driven CP tumors, we observe tumor cells remain mono-ciliated and AQP1-negative, indicating that *Sox2* loss does not affect the ciliation machinery. Together this warrants further study into the mechanisms of *Sox2* functions in CP tumors. By unraveling the role of *Sox2* in CP tumors, we may better understand their origin and biology to ultimately design improved treatment options.

RARE-22 CHARACTERIZING THE LANDSCAPE OF STRUCTURAL VARIANTS IN ADAMANTINOMATOUS CRANIOPHARYNGIOMA

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INTRODUCTION: Adamantinomatous craniopharyngiomas (ACPs) are rare brain tumors that primarily occur in children and impact long-term morbidity and mortality. The canonical driver mutation for ACP growth occurs in *CTNNB1* and leads to constitutive activation of the Wnt/β-catenin signaling pathway. In this study, we outline the genomic, transcriptomic, and structural variant (SV) landscape in a cohort of 41 ACP samples. METHODS: We performed whole-genome sequencing (WGS) and RNA-sequencing of 41 ACP samples. Matched normal samples were also characterized by WGS. Mutect2 was used to detect single nucleotide variants (SNVs) and indels, and copy number data was generated using the GATK pipeline. SvABA was used to perform SV analysis and to identify significantly recurrent breakpoints and juxtapositions. DESeq2 was used to perform differential gene expression analysis based on clinical and molecular annotation data. RESULTS: 29/41 (70%) of the ACP samples harbored missense mutations in exon 3 of *CTNNB1*, all of which have previously been reported in ACP tumors. SV analysis identified a median of 11.5 events per tumor. Overall, 9.7% of events were interchromosomal. Of the remainder, the majority (78.6%) were deletions. No SVs occurred within *CTNNB1*. A positive correlation ($r = 0.533$) was observed between the frequency of SVs and SNVs within samples. Analysis of significantly recurring breakpoints (SRBs) did not identify recurrent breakpoint events. Differential gene expression analysis comparing samples with and without *CTNNB1* variants identified 2,143 differentially expressed genes with q-value < 0.05. CONCLUSION: This study identifies activating mutations in exon 3 of *CTNNB1* in a large cohort of ACP samples. We also integrate SV and transcriptomic data to comprehensively investigate ACP tumor genomes and identify putative novel tumorigenic mechanisms that advance our understanding of ACP biology.

RARE-23. PRESERVATION OF ENDOCRINE FUNCTION AFTER OMMAYA RESERVOIR INSERTION IN CHILDREN WITH CYSTIC CRANIOPHARYNGIOMA

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INTRODUCTION: Children with craniopharyngiomas (CP) can be subjected to significant morbidities caused by radical surgery and/or radiation with deleterious long-term consequences. Ommaya reservoir insertion (ORI) into cystic CP represents a minimally invasive procedure allowing immediate decompression and aims to avoid additional injuries. The purpose of this study was to determine the relevance of upfront ORI (+/- intracystic treatment) for preservation of endocrine function. METHODS: We performed a retrospective chart review of children with CP treated at the Hospital for Sick Children between 01/01/2000 and 15/01/2020 for review of endocrinological outcome after ORI. Endocrine function was reviewed at the time of initial surgery and throughout the course of follow-up. Event-free survival (EFS) was defined as the time to further surgical resection or irradiation. RESULTS: Seventy-nine patients were identified with a median age of 8.3 (range 2.1-18.0) years, 31 were males. Sixty-six patients underwent surgical treatment, including 41 ORI. ORI was performed as upfront treatment in 32 patients; 33 patients underwent gross total or partial resection and 1 patient radiotherapy as first treatment. Fifty-five of 79 patients had sufficient endocrine follow-up data. Endocrine function remained stable after ORI with a mean EFS of 27.64 (± 5.22) months. Surgical resection was associated with worsened endocrine function postoperatively with an EFS of 5.48 (± 1.74) months ($p < 0.001$). CONCLUSIONS: Upfront ORI (+/- intracystic treat-

ment) resulted in endocrine preservation of all patients and a significantly longer EFS when compared to upfront surgical resection in this single institutional retrospective review. Further analyses will elucidate the implications of ORI with respect to ophthalmological, vascular and neurocognitive outcome.

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 of these tumors, with 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 transfection and puromycin treatment for stable cell-line generation. Cell line validation included immunofluorescence with 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 and B-catenin in ACP-derived epithelial cells. Point mutation in exon 3 of the CTNNB1 gene was identified in ACP-derived epithelial cells. CONCLUSION: Initial limits 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 EWING 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 meningeal 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 56 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 patients 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 histology, 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), atypical choroid plexus papilloma (aCPP; n=5), 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, 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 aCPP 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 compared and reported. 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 3 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 (carboplatin, 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. CONCLUSIONS: Surgical resection remains the standard of care for patients with aCPP. However, chemotherapy based on the SIOP backbone may be useful to reduce the need for or to delay radiation therapy in select patients in the relapsed or metastatic setting.

RARE-28. THE USE OF SUBCUTANEOUS INTERFERON IN PATIENTS WITH CRANIOPHARYNGIOMA: AN INSTITUTIONAL RETROSPECTIVE REVIEW

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