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. The composition of human ACP tissues 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. Controls were carried out with non-A CP-derived immortalized cell lines from other tumors, with characteristics 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 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 data related to these cell lines is promising 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 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 frontal 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 in place. 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 demonstrated 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 studies 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 (CPT; 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=6) 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 is the mainstay of treatment, 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 cause 28 months from diagnosis. CONCLUSION: With CPT, local surgical resection remains the standard of care for patients with aCPP. However, chemotherapy based on the SIOP protocol 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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INTRODUCTION: Subcutaneous interferon (IFN) is a treatment modality for patients with craniopharyngioma (CP). Its mechanism of action is not completely understood and it is not approved by the U.S. Food and Drug Administration. It has been shown in previous studies that IFN significantly improves tumor control and decreases tumor recurrence for patients with recurrent or progressive CP. Patients with craniopharyngioma are often treated with surgery, radiation, and chemotherapy. The use of IFN in addition to these treatments has been shown to provide additional benefit in terms of tumor control and improved survival. However, the exact role of IFN in the management of CP is unclear. The purpose of this study is to evaluate the use of IFN in patients with craniopharyngioma at our institution. MATERIALS AND METHODS: We retrospectively reviewed the medical records of all patients diagnosed with craniopharyngioma at our institution from 2010 to 2019. The inclusion criteria for the study were as follows: patients who received IFN treatment for craniopharyngioma. RESULTS: A total of 25 patients were included in the study. The mean age at diagnosis was 39 years, and the mean follow-up duration was 24 months. Twelve patients received IFN treatment as first-line therapy, and 13 patients received IFN as salvage therapy. The most common type of CP was adamantinomatous craniopharyngioma (n=18), followed by papillary craniopharyngioma (n=7). IFN was administered as subcutaneous injections at a dose of 10 million units three times per week. The mean duration of IFN treatment was 24 months. Eight patients (32%) experienced complete tumor regression, nine patients (36%) experienced partial tumor regression, and eight patients (32%) had stable disease. CONCLUSION: Subcutaneous interferon is a promising treatment modality for patients with craniopharyngioma. Further studies are needed to evaluate the optimal dosing and duration of IFN treatment for patients with craniopharyngioma.
Abstracts

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Current strategies for managing craniopharyngioma result in significant morbidity. Successful treatment with interferon alfa (INF) after progression is reported in the literature. This retrospective review details our institutional experience with INF in craniopharyngioma patients. Method: Between 2001-2021, we treated 81 craniopharyngioma patients. Twenty-six patients received 26 treatment courses of subcutaneous INF. Twenty-three courses were evaluable for response. Results: Ten patients received upfront INF after cyst decompression (< 6 mmmaxs place). Progression free survival (PFS) ranged between 7-38mo. Three patients continued on treatment (10+, 12+, 14+mo); seven progressed (four on treatment (7, 9, 25, 38mo), three after treatment (13, 19, 32mo)). At progression, two underwent surgery alone, three underwent surgery and radiation, one resumed INF. Thirteen patients received INF after progression. Prior to INF, eight patients had surgery, eight had surgery and radiation. Two in each group had INF previously. PFS ranged between 5-82+mo. One patient remains on treatment (5+mo); four continue in follow-up without progression (23+, 40+, 64+, 82+mo) with two patients avoiding radiation to date; eight progressed (3 on treatment (6-85mo), 8 after treatment (16,24,26,67,170mo)). At progression, two underwent surgery alone, three underwent surgery and radiation, one received re-irradiation, two resumed INF. While receiving INF, two patients experienced serious adverse events (one intra-tracheal aspiration that required intubation; one superficial bacterial wound). One patient proceeded to radiotherapy. Both recovered. One tolerated retreatment with INF. Three additional patients stopped INF for intolerance, but two received INF at subsequent progression. No other unanticipated side effects were reported. Conclusions: While INF therapy in patients with both newly diagnosed and progressive craniopharyngioma delayed the need for aggressive surgical resection and/or radiotherapy in some cases. In some patients, INF resulted in prolonged stabilization of disease delaying or avoiding radiation. Overall, INF was well tolerated and manageable. These results are encouraging regarding INF therapy for patients with craniopharyngioma and warrant further evaluation with a clinical trial.

RARE-29. TRANSCRIPTOME CHARACTERIZATION OF PEDIATRIC ADAMANTINOMATOUS CRANIOPHYNGIOMA 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 an intracranial tumor with frequent epithelial components that are characteristic of 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 signaling is not well known. 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 activation and epithelial subpopulations. Paracrine signaling was inferred via CellChatDB. SASP Atlas was utilized to query marker gene lists. Pseudotemporal ordering was performed using monocyte3. 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. CONCLUSION: Based on gene expression, cell populations that correspond to the histologically identifiable epithelial whorls and paliADING epithelium can be identified. These subpopulations display unique functional signatures of inflammation and synergetic therapeutic targeting of these separate epithelial populations may lead to improved patient care.

RARE-30. NOVEL COLLISION TUMOR OF CRANIOPHYNGIOMA 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, Omnipaque, 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 a 0.5 cm ependymoma with classic histomorphology lacking anaplasia features. The ependymoma was positive for GFAP immunostain and EMA immunohistostaining 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 ependymoma was identified (including negative 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). Spine MRI was negative for metastatic disease. The role of interferon in the development of a collision tumor in this patient is 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.

RARE-31. RADIATION INDUCED MALIGNANCY ASSOCIATED WITH PEDIATRIC CRANIOPHYNGIOMA: A SINGLE INSTITUTION EXPERIENCE

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BACKGROUND: Therapy for pediatric craniopharyngioma, a rare suprasellar tumor, includes surgical resection with consideration for intraoperative radiation. Radiation has been associated with secondary malignancies. Between 2000 and 2021, 81 pediatric patients with craniopharyngioma were treated at our institution, 3 of 54 (5.6%) who received radiation therapy (RT) developed secondary malignancy within the treatment field. CASE DESCRIPTION: In all 3 cases, initial imaging demonstrated cystic/solid suprasellar mass and underwent resection; pathology revealed calcifications and wet keratin consistent with craniopharyngioma. None had known cancer predispositions. The first patient (male), presented at 4-years-old with headaches. He underwent subtotal resection (STR) with cyst fenestration/wCF) and received 53.8 Gy photon 3D-Conformal RT. Six-years later, the tumor progressed (edge of RT field). Patient underwent a second STR/wCF and fractionated RT(50.4 Gy). Both pathologies were consistent with papillary craniopharyngioma. Eight-years from first RT, progression occurred again within the RT field; pathology revealed an (adeno)squamous carcinoma. The second patient, a 5-year-old female, presented with vision loss, underwent partial resection and received 54 Gy focal proton therapy for an adenomatous craniopharyngioma. Almost 5-years later, an unrecteegable right basal ganglia/globus pallidus mass was noted in the 30-54 Gy field. Pathology was c/w anaplastic astrocytoma(AA). The third, a 9-year-old female was treated with 34 Gy photon radiation and 7 years later had evidence of increasing mass. Pathology revealed high-grade-diffuse-gloma(HGGD). Molecular analysis of AA/HGGD both revealed PDGFR A amplification and CDKN2A/B homoygous loss. DISCUSSION/CONCLUSION: Malignant CNS tumors are reported following radiotherapy for a variety of primary CNS neoplasms. Interferon alfa is a valuable therapy in achieving long-term disease control of pediatric craniopharyngiomas, it is important to understand the role of developing secondary malignant neoplasms. Our report adds to the body of literature describing secondary malignancies post radiation therapy for the treatment of pediatric craniopharyngiomas.