An 18 month-old female presented with 4-months of weight loss, bilateral galactorrhea and constipation. Her weight decreased from the 15th to below the 1st percentile. CBC, celiac and thyroid studies were normal. Prolactin was at the upper limit of normal (25.8;ref 3.3–26.3). Breast ultrasound demonstrated symmetric breast tissue development. She was referred to pediatric gastroenterology for constipation and failure to thrive. Caloric supplementation, bowel regimen and barium enema were recommended. One week later, she was admitted with dehydration, painful constipation and further weight loss in the setting of an acute febrile illness. MRI revealed a normal pituitary and an intraventricular mass without hydrocephalus. She underwent gross total resection of the mass, later determined to be a choroid plexus papilloma. The patient's galactorrhea resolved abruptly following resection. Because of her galactorrhea, our patient underwent neuroimaging revealing an incidental mass without associated hydrocephalus. To our knowledge, precocious puberty and hyperprolactinemia have not been described in neoplasms distant from the pituitary. Thus, these lesions should be recognized as a potential etiology of precocious puberty and hyperprolactinemia.

RARE-50. TREATMENT RESPONSE OF CNS HIGH-GRADE NEUROEPITHELIAL TUMORS WITH MN1 ALTERATION

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BACKGROUND: CNS high-grade neuroepithelial tumor with MN1 alteration (CNS HGNET-MN1) are a rare entity recently described as a high-grade tumor containing a mixture of solid and pseudopapillary patterns with MN1 rearrangement. METHODS: CNS HGNET-MN1 patients were identified using genome wide methylation arrays across 5 institutions (the Hospital JP Garrahan, Hospital for Sick Children, the University Hospital Motol, Royal Children`s Hospital and Christchurch Hospital) and was correlated with treatment and outcome. Central imaging review with radiological features analysis was performed. RESULTS: We identified 9 patients harboring CNS HGNET-MN1 tumors through application of the Heidelberg brain tumor classifier. Seven tumors were T supratentorial and two in the spinal cord. Median age was 5 (range 3.6–14.6). All patients had surgery (6 GTR and 3 STR) as initial management followed by radiotherapy (focal 5/CSI 1) and systemic chemotherapy in 2 patients. Four of the 9 patients relapsed by 3 years post diagnosis, with 2 local and 2 metastatic failures despite complete surgical resections and radiotherapy. Three patients died due to tumor relapse after 24 months despite upfront radiotherapy. Seven of 9 patients had an initial diagnosis of ependymoma. CONCLUSION: Treatment of CNS HGNET-MN1 remains a major challenge with multiple failures, despite aggressive surgical resections and upfront involved field radiotherapy. Further multicenter, international prospective studies are required to determine the optimal treatment strategy for this group of tumors.

RARE-51. MOLECULAR INSIGHTS INTO MALIGNANT PROGRESSION OF CHOROID PLEXUS PAPILLOMA (CPP)

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Malignant transformation of CPP is rare and the mechanisms remain elusive. We report a case of progression of papilloma into carcinoma where we performed molecular sequencing of both samples. A boy was found to have a brain mass soon after birth. The gross total resection (GTR) was diagnostic of CPP. Six years later he developed a recurrent mass that demonstrated progression to a choroid plexus carcinoma (CPC). The patient received chemotherapy according to a "HeadStartII" protocol. He is 2.5 years off therapy and disease-free. A sequencing study consisting of 1700 genes and tumor transcriptome was done. The analysis of both samples revealed a germline variant of TP53(R248W) with LOH and an allele frequency of 39% in the germline sample, suggesting a mosaicism. Analysis of both samples identified extensive aneuploidy and similar pattern of gains in chromosomes 7/8/12/20/21/X. Copy number aberrations newly acquired in the carcinoma included copy gain of chromosomes 5q/12/15q/20, and copy loss of chromosomes 5q/13/22. The papilloma was found to harbor 3 somatic mutations with 4% to 21% allelic fractions, all lost in the carcinoma. These mutations were of unknown significance and with too low allelic fractions to be responsible for the transformation. More pertinently, chromosomal aneuploidy was significant with additional losses in the carcinoma. This resulted in the losses of two critical tumor suppressor genes, RB and BRCA2, playing a possible role in the observed transformation. The "HeadStart" experience suggested that the prognosis of TP53 mutant CPC may be improved in the absence of radiation therapy.

RARE-52. *RB1* GENE DELETIONS ARE THE NOVEL MECHANISM OF CHOROID PLEXUS TUMORS (CPT) ONCOGENESIS

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BACKGROUND: CPTs are known to be rare *TP53*-dependent neoplasms, while major molecular alterations underlying tumor progression, especially in *TP53*-wild type cases, are still unclear. METHODS: 18 primary CPT, including 16 choroid plexus carcinomas (CPC) and two atypical choroid plexus papillomas (CPP), were evaluated for copy number status of 87 major oncogenes and tumor suppressor genes by nCounter Cancer CNV assay by Nanostring and *TP53* and *RB1* by MLPA. Germline *TP53* nucleotide substitutions were analyzed by Sanger sequencing. RESULTS: Pathogenic germline *TP53* variants were present in 4 cases confirming Li-Fraumeni syndrome (LFS). Two patients have somatic *TP53* substitutions. Only one patient with LFS harbored somatic *TP53* deletion. In 7 patients, heterozygous deletions of *RB1* involving from 3 exons to the whole coding sequence detected by MLPA were discovered. All these findings were validated by nCounter CNV assay. Additionally, four patients have *WT1* deletions, two patients – *BRCA2*, and in 1 case - *NF1*, concomitant with *RB1* deletions in 3 cases. Interestingly, in one patient who faced a progression of CPP to CPC germline, *RB1* deletion was detected, and in both subsequent tumors, the length of the deleted region progressively increased. Notably, that *RB1* deletions are mostly mutually exclusive to *TP53* substitutions. 3 of 4 patients with *RB1* deletions having follow-up period >1 year faced with tumor-related adverse events. CONCLUSIONS: Somatic or uncommon germline *RB1* heterozygous deletions have been unraveled as a novel mechanism of aggressive CPT and could be implemented in prognosis definition schemes.

RARE-53. PINEAL PARENCHYMAL TUMOR OF INTERMEDIATE DIFFERENTIATION (PPTID) AND DICER1 SYNDROME: A CASE REPORT

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BACKGROUND: DICER1 syndrome is a rare inherited tumor predisposition syndrome linked to an increased risk of several malignancies. Affected individuals most commonly develop pleuropulmonary blastoma (PPB) and ovarian sex cord-stromal tumors. Brain tumors in these patients are rare, however; the increased frequency of pineoblastoma in this population has been established. Traditionally, pineal parenchymal tumors of intermediate differentiation (PPTIDs) have not been associated with DICER1 syndrome, with research suggesting alternative mutations driving tumorigenesis. These tumors are pathologically and clinically diverse, with long-term surveillance based on therapeutic interventions. Here we describe a case of a germline DICER1 mutation in a patient with a PPTID, suggesting that this mutation is not limited to pineoblastoma as previously reported. CASE: We describe a 19 year-old female with a WHO grade III PPTID treated with multimodal therapy including surgery, craniospinal irradiation (CSI) and chemotherapy. She was noted to have a thyroid mass at diagnosis and was subsequently diagnosed with a benign thyroid nodule, followed most recently by a cataract with pathology concerning for medulloepithelioma of the ciliary body. Due to the known association between medulloepithelioma and DICER1 syndrome, targeted germline sequencing was obtained and confirmed a pathogenic heterozygous mutation. CONCLUSION: To our knowledge this