when allowed to drink to thirst, mitigating the need for desmopressin. Temozolomide was not restarted and the symptoms of polyuria and polydipsia resolved and did not recur. Upon review, the tumor did not involve the pituitary or hypothalamus. Additionally, these areas were not involved in the irradiation field. CDI is a rare but clinically significant side effect of temozolomide, reported in adults. Given this is the first report of CDI secondary to temozolomide in a pediatric patient, we speculate that this is likely under-recognized in children. Prompt recognition and treatment is necessary to prevent severe sequelae of hypernatremia.

OTHR-12. ANEURYSMAL BONE CYST RESEMBLING A POSTERIOR FOSSA TUMOR

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We presented the case of a 6-year-old boy who was seen in the emergency room because of signs of intracranial hypertension and left cerebellar syndrome. The CT scan revealed a heterogeneous lesion within the left hemisphere displacing the fourth ventricle and eroding the occipital bone. The MRI showed the same heterogeneous lesion majorly cystic, involving the bone and displacing the left cerebellar hemisphere. A minor hydrocephalus was evident in both studies. A suboccipital craniectomy was done and a cystic epidural tumor remodeling and eroding the bone was noted. The histopathological diagnosis corresponded to an aneurysmal bone cyst. Aneurysmal bone cyst is a rare benign tumor accounting for 3–6 % of tumors of the cranial base. We discuss the unusual location of the lesion.

OTHR-14. DIENCEPHALIC SYNDROME SECONDARY TO PITUITARY STALK THICKENING

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BACKGROUND: Diencephalic syndrome (DS) is a rare condition associated with neoplastic lesions of the sellar-suprasellar region, whose pathophysiological mechanisms are still unclear. DS occurs in <10% of hypothalamic gliomas and has also been described in suprasellar germinomas, craniopharyngiomas, epidermoid cysts, rarely with non-suprasellar lesions such as brainstem gliomas. DS has not been associated with isolated pituitary stalk thickening. Isolated pituitary stalk thickening (IPST) presents a diagnostic challenge, ranging from benign (craniopharyngioma) to malignant lesions (germinoma, metastasis, histiocytoses of the Langerhans group). The coexistence of diabetes insipidus (DI) with anterior pituitary dysfunction and IPST implies more risk to harbor neoplasia. CASE REPORT: A 6-year old girl presented with DI and inadequate weight gain (despite regular caloric intake) and preservation of linear growth. Neurological examination showed no abnormalities. However, physical examination revealed a malnourished patient (both weight-for-age value and body-mass-index below the third percentile). Blood tests and negative IgA anti-endomysial antibodies excluded malabsorption as a cause of her malnutrition; endocrine work-up excluded thyroid dysfunction, growth hormone deficiency, and adrenal insufficiency. Magnetic resonance imaging (MRI) showed thickening of the pituitary stalk with a transverse diameter of 7 mm. The patient underwent a biopsy through a supraorbital eyebrow approach. Histopathological examination revealed lymphocytic hypophysitis, with tissue markers all negative for germinoma. The girl is currently under follow up with serial MRI every three months. CONCLUSION: DS should be considered as a differential diagnosis in any child with failure to thrive, and imaging studies should be performed even if there are no additional neurological symptoms.

OTHR-16. CONCURRENT USE OF APREPITANT AND IFOSFAMIDE IN PEDIATRIC CANCER PATIENTS

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BACKGROUND: Aprepitant, a selective neurokinin-1 receptor antagonist, is commonly used for prevention of chemotherapy-induced nausea and vomiting. Its use with ifosfamide is controversial due to the putative risk of potentiating neurotoxicity via inhibition of cytochrome P450 3A4 (CYP3A4). The current literature examining this interaction is inconclusive, and little data exists in pediatrics. We seek to describe a single-institution experience with concurrent aprepitant and ifosfamide administration. METHODS: A retrospective review of patients treated with ifosfamide and aprepitant from 2009–2018 was conducted. Data collected included demographics, tumor type, number of days of concurrent therapy, dosing, and documented of neurotoxicity. RESULTS: Twenty patients aged 7–21 years (median 17 years) were identified. Diagnoses included thirteen sarcomas and seven CNS tumors (6 germ cell tumors; 1 intracranial sarcoma). Five patients received high dose ifosfamide (>2,000mg/m^2/day). The number of concurrent ifosfamide and aprepitant doses ranged from 2–18 (median, 8.5). Only one patient (5%) developed ifosfamide-induced neurotoxicity: a 7-year-old female with a nongerminomatous germ cell tumor who presented with seizures and somnolence. She received methylene blue and returned to her neurologic baseline. She completed her ifosfamide course without incident. She was the only patient to require weight-based aprepitant dosing and to receive the liquid formulation. CONCLUSIONS: Aprepitant should be used with caution when administered concurrently with ifosfamide due to the risk of neurotoxicity. However, the incidence of neurotoxicity in this retrospective pediatric cohort was low. This interaction may be more significant in younger patients due to age-related differences in hepatic metabolism, but further study is required.

PATHOLOGY AND MOLECULAR DIAGNOSIS

PATH-01. MOLECULAR PROFILING OF PAEDIATRIC CENTRAL NERVOUS SYSTEM TUMOURS IN AUSTRALASIA – AN UPDATE ON THE AIM BRAIN AND MNP2.0 PROJECTS

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The Access to Innovative Molecular Profiling for Paediatric Brain Cancers (AIM BRAIN) project is a trial testing the feasibility of clinical implementation of diagnostic methylation and molecular profiling for central nervous system (CNS) tumours in Australia and New Zealand. AIM BRAIN builds on an existing study, MNP2.0, and allows cross-validation of results derived from identical samples in separate laboratories in Melbourne, Australia, and DKFZ, Heidelberg, Germany. Parallel methylation profiling (Illumina 850K EPIC array) from co-enrolled cases has revealed excellent concordance between laboratories with 50/51 cases (98%) yielding identical classification using the DKFZ Molecular Neuropathology 2.0 Classifier v11b4. 77/91 (85%) of AIM BRAIN cases classified concordantly by methylation array when compared to their diagnostic histopathology. Of these 77 cases, 16 had classifications below a threshold of 0.90, however still classified correctly. In 14 discordant cases either the histopathology was not well defined, not represented on the classifier, or a very low classification score was obtained. Molecular profiling through MNP2.0 identified 49/167 (29.3%) tumours with gene fusions including BRAF-KIAA1549 (n=29), *RELA-C1lorf95* (n=5) and 15 rare or novel fusions. BRAF-KIAA1549 was almost exclusively associated with pilocytic astrocytoma (28/29) and RELA-*C1lorf95* with ependymoma. Six pathogenic germline mutations were identified in *TP53* (n=2), *BRCA1*, *NF1*, *LZTR1* and *ATM*. The incidence of germline predisposition was low (4%) and sex biased towards females (5F:1M), (p<0.08). Our findings confirm methylation profiling as a robust platform for classifying CNS tumours with potential to reveal new CNS tumour entities when combined with molecular profiling.

PATH-03. HIGH-GRADE NEUROEPITHELIAL TUMOR SHOWING BCOR IMMUNOPOSITIVITY WITHOUT EXON 15 INTERNAL TANDEM DUPLICATIONS IN A FIVE-YEAR-OLD BOY: A CASE REPORT

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Recent DNA methylation profiling clarified several rare entities of pediatric CNS tumors from institutionally-diagnosed primitive neuroectodermal tumors (PNETs). One of which is CNS high-grade neuroepithelial tumor with *BCOR* alteration (CNS HGNET-*BCOR*), and it carries in-frame internal tandem duplications (ITD) of the *BCL6 corepressor (BCOR)* in exon 15. In the report, we describe a case of immunohistologically-diagnosed CNS HGNET-*BCOR*, which lacks exon 15 ITD of *BCOR*. A five-year-old boy visited a local hospital complaining uncontrolled vomiting for two months,

and magnetic resonance imaging (MRI) showed a large well-circumscribed mass in his left cerebellum with ventricular dilatation. He referred to our hospital, and an additional MRI revealed diffuse and weak enhancement of gadolinium and low ADC values in mass. Immediately, he underwent total removal of the tumor and ventricular drainage, and his consciousness recovered soon after surgery. The tumor presented high BCOR expression by IHC, but target PCR did not identify exon 15 ITD of *BCOR*. As the previously-reported clinical and imaging features of CNS HGNET-*BCOR* resembled our case, we clinically diagnosed it as a similar phenotype of CNS HGNET-*BCOR* without exon 15 ITD. He received 60 Gy of extended-local irradiation with concomitant temozolomide and discharged without any neurological deficits. Since *BCOR* alterations, including ITD, gene fusions, and mutations, play an oncogenic role in several cancers, the present case might harbor another gene aberration of *BCOR*.

PATH-04. AN ENHANCED AI-DRIVEN PLATFORM FOR PRECISION MOLECULAR BRAIN TUMOR DIANOSTICS

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Tumors of the CNS represent one of the most complex groups of human cancer, with a vast number of different entities occurring across a spectrum of ages and anatomic locations. This heterogeneity makes accurate diagnosis challenging, with the current gold standard relying on multiple subjective elements. We recently proposed a classification algorithm based on tumor DNA methylation profiling as an objective way to assign samples to over 80 distinct molecular classes. Here we present a substantial update to our machine learning-based algorithm, with more than 170 molecular classes now being represented amongst the 5,915 samples in our reference cohort. These new classes include further subclassification of known groups such as medulloblastoma and ependymoma, as well as multiple new molecular entities described here for the first time. A further improvement is the introduction of a more rationally layered output, making use of 'families' of closely-related molecular classes to improve the compatibility with the current WHO classification of CNS tumors. This approach is designed to increase the clinical relevance of the primary output, while also retaining the full information content from the random forest-driven classification. Benchmarking our new algorithm by cross-validation and on an independent validation cohort indicates a retention of the excellent accuracy of diagnosis (error-rate < 4%), with a significant improvement in the proportion of confidently classifiable tumors compared with our previous tool. We believe that this approach, freely accessible through an online web portal, has the potential to enhance diagnostic precision and thereby support clinical care for brain tumor patients.

PATH-05. A CASE OF PILOCYTIC ASTROCYTOMA HARBORING THE FGFR1 GENE MUTATION WITH A PREDOMINANT OLIGODENDROGLIOMA-LIKE COMPONENT

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Pilocytic astrocytomas rarely present with oligodendroglioma-like morphological features, which gives rise to a diagnostic challenge. In this report we present a case of pilocytic astrocytoma harboring the FGFR1 mutation, accompanied with a predominant oligodendroglioma-like component, thus initially diagnosed as oligodendroglioma. A 14-year-old female presented with syncope and simple partial seizure involving her right upper limb. Contrast-enhanced MRI revealed an enhancing lesion with substantial cystic portion and perifocal edema in the left parietal lobe. Open surgery was performed and a gross total resection of the tumor was achieved. On initial histopathological diagnosis, tumor cells with monotonous round nuclei and perinuclear halo predominated with branching capillaries, which were strongly suggestive for oligodendroglioma. Immunohistochemically, IDH1 R132H was negative, and Ki-67 index was around 5%. The patient was thus initially diagnosed as oligodendroglioma, WHO grade II, based on the 2007 WHO classification criteria. However, histopathological re-review revealed a minor astrocytic component with Rosenthal fibers and rare eosinophilic granular bodies, thus the diagnosis was changed as pilocytic astrocytoma. FGFR1 K654E mutation was confirmed by Sanger sequencing. Although she postoperatively developed mild sensory disturbance in her right hands, finger agnosia, and left-right disorientation, her symptoms had gradually improved, and she was discharged on day 17 with a Karnofsky performance status (KPS) of 90 and no cognitive decline. Without any adjuvant therapies, she has remained recurrence-free for 85 months. While the diagnosis of pilocytic astrocytoma with predominant oligodendroglioma-like component can be challenging, analysis of IDH1 and FGFR1 mutations can be beneficial in certain cases.

PATH-06. IMAGE-BASED MACHINE LEARNING CLASSIFIER FOR PEDIATRIC POSTERIOR FOSSA TUMOR HISTOPATHOLOGY

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BACKGROUND: Pediatric posterior fossa (PF) tumors can include astrocytomas, ependymomas, and medulloblastomas, all of which demonstrate unique histopathology. Whole slide image analyses can be time consuming and difficult. Therefore, we used machine learning to create a screenshot-based histopathology image classifier that can distinguish between types of pediatric PF tumors. METHODS: We took 179 histopathology slides from Stanford University, dated from 2008–2019: 87 astrocytomas, 42 ependymomas, and 50 medulloblastomas, per pathology report. Each slide was viewed under a microscope at 20x. Then, a screenshot was taken of the region of interest representative of principal slide pathology, confirmed by a trained neuropathologist. These screenshots were used to train Resnet-18 models pre-trained on the ImageNet dataset and modified to predict three classes. Various models with different hyperparameters were trained using a random hyperparameter search method. Trained models were evaluated using 5-fold cross-validation, assigning 20% of the dataset for validation with each evaluation. Qualitative analysis of model performance was assessed by creating Class Activation Map (CAM) representations of image predictions. RESULTS: The top performing Resnet-18 model achieved a cross-validation F1 of 0.967 on categorizing screenshots of tumor pathology into three types. Qualitative analysis using CAMs indicated the model was able to identify salient distinguishing features of each tumor type. CONCLUSIONS: We present a PF lesion classifier capable of distinguishing between astrocytomas, ependymomas, and medulloblastomas based on a histopathology screenshot. Given its ease of use, this tool has potential as an educational tool in an academic setting.

PATH-07. QUALITY ASSURANCE IN CEREBROSPINAL FLUID CYTOLOGY ASSESSMENT FOR MEDULLOBLASTOMA STAGING LEADS TO POTENTIAL IMPROVED RISK-GROUP ASSESSMENT IN THE PROSPECTIVE MULTICENTER HIT-2000 TRIAL

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BACKGROUND: Cerebrospinal fluid (CSF) dissemination of medulloblastoma (M1 stage) is a high-risk prognostic factor. However, because diagnostic criteria for M1 staging are missing we specified process-related and cytomorphological parameters influencing the predictive value of the CSF status. PATIENTS AND METHODS: CSF samples and cytology reports from 405 medulloblastoma patients of the prospective multicenter trial HIT-2000 were reviewed and related to 5-year progression free survival (5y-PFS). RESULTS: Tumor cells were detected in 237/1073 CSF cytospins. M1-patients and M2/3 patients with radiologically detected metastases showed a worse 5y-PFS than M0 patients (54% and 52% vs. 76%; p=0.01 and p<0.001). Lumbar sampling was more sensitive than ventricular sam-