pling. M0 diagnosed specimens containing >50% lytic cells and/or less than 10 nucleated cells showed a decreased 5y-PFS (61%). Further investigation of cytological parameters revealed a poor outcome for cases harboring > 3 tumor cell clusters and individual tumor cells (5y-PFS 33%) vs. cases with ≥ 2 individual tumor cells but no clusters (5y-PFS 61%). In bi-variable Cox-regression, ≥ 2 vs. 0 or 1 tumor cells were associated with a Hazard Ratio (HR) of 0.52 (95%-Confidence Interval (CI): 0.12, 2.30; p=0.39), whereas > 3 vs. no tumor cell clusters were associated with a HR of 8.94 (95%-CI: 1.66, 48.22; p=0.01). CONCLUSIONS: CSF staging in medulloblastoma should comprise lumbar specimens with <50% lytic cells and a minimum of 10 nucleated cells. The predictive value of CSF cytology in M1 cases may predominantly depend on tumor cell clusters. The latter finding needs to be confirmed in prospective trials.

PATH-08. THE IMPORTANCE OF RE-DIAGNOSIS OF TUMORS PREVIOUSLY CLASSIFIED AS CENTRAL NERVOUS SYSTEM PRIMITIVE NEUROECTODERMAL TUMORS

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BACKGROUND: The recent molecular analyses have revealed that central nervous system primitive neuroectodermal tumors (CNS PNETs) those having clusters of small round tumor cells are genetically different tumors. However, the concepts of CNS PNET are complicated, and it is difficult to diagnose them appropriately in clinical field. To overcome this difficulty, we reviewed previous studies associated with CNS PNETs, and carried out several approaches, those are relatively easy access to use in clinics, for our 8 samples of embryonal brain tumors diagnosed CNS PNETs in our institution, initially. METHODS: We used in combination with immunohistochemistry (IHC), Sanger sequence, Pyrosequence, polymerase chain reaction (PCR), real time PCR and copy number analysis referring recent reports. RESULTS: In terms of the diagnosis three out of 8 cases were changed based on the results in this study from previous diagnoses. CONCLUSION: In this review, it seemed that either the histopathological evaluation or molecular analyses would be not enough to make accurate diagnosis of CNS embryonal brain tumors, and it is essential to combine both of them including recent comprehensive analysis methods.

PATH-09. SJMB12 CLINICAL TRIAL: DISCREPANCY BETWEEN LOCAL AND CENTRAL PATHOLOGY IN ASSESSING ANAPLASTIC MEDULLOBLASTOMA – REPORT FROM A SINGLE SITE EXPERIENCE

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INTRODUCTION: SJMB12 is a phase 2 clinical trial led by the St. Jude Children's Research Hospital (St. Jude) that enrolls patients with medulloblastoma based on their biological subgroup. The large cell/anaplastic (LCA) histologic variant has been identified as an important independent risk factor associated with poor outcome. However, the histologic criteria for LCA is subjective, making the distinction between anaplastic and non-anaplastic medulloblastoma difficult in some cases. METHODS: Pathological central review was performed at St. Jude. For all patients enrolled in the study to date, concordance was assessed between the initial and central review diagnosis and histologic variant calls made at the Royal Children's Hospital Melbourne (RCH) and at St. Jude, respectively. RESULTS: Since the SJMB12 clinical trial opened locally in 2014, 34 patients were enrolled, and 31 were eligible for this retrospective study. A total of 12 (39%) cases with discordance were identified. The most frequent disagreement was between the designation of LCA (10 cases, 32%). In five cases the tumour was not designated as LCA variant locally. In five cases the initial designation of LCA was refuted centrally. Overall, this led to a change of treatment stratum for four patients (13%). CONCLUSION: A high discordance rate exists between neuropathologists in the designation of LCA variant. Differences in interpretation of the subjective histologic criteria and inconsistencies in the material submitted for central review contributed to the discordance. Incorporation of more objective histologic criteria and implementation of unbiased diagnostic tools may improve the generalisability of future risk stratification.

PATH-10. PROGNOSTIC RELEVANT IMMUNOPHENOTYPES OF PEDIATRIC HIGH-GRADE NON-BRAINSTEM GLIOMAS

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Pediatric diffuse astrocytomas comprise a wide range of malignancies with variable prognosis. The 4th grading system used now not always correctly characterizes the biological behavior of these tumors. We collected 24 pediatric supratentorial non-brainstem high grade glioma cases. Patient age ranged from 1 to 18 years old (median 11y). Main tumor locations were as follows: parietal lobe 8 cases; temporal lobe, 10 cases; frontal lobe, 3 cases; occipital lobe 3 cases. Eight of them were totally removed. All patients were treated with standard CT and RT. The main objective was to assess the prognostic impact of histopathological and molecular criteria on progression-free(PFS) and overall survival (OS) of high grade gliomas. The following criteria were analyzed: IDH1 R132H, BRAF V600E expression, ALT-phenotype, CDKN2A deletion, 1p/19q co-deletion, glial and neuronal markers expression. **RESULTS:** IDHR132H mutation was identified in 3 cases. 4 cases carried BRAFV600E mutation with CDKN2A deletion and displayed PXA phenotype. 5 cases showed undifferentiated glial morphology and ALT–phenotype. Also there was a group of tumors without any of the above mentioned genetic changes. Interestingly 3 of them were post radiation tumors. Statistical analysis showed that low OS correlated with ALT-phenotype(p-0.015), absence of neuronal markers expression and absence of molecular changes (p-0.03). Mutation of IDH1R132H was a favorable prognostic factor as in the adult population. PFS was affected only by the presence of neuronal expression (p-0.015). Employing immunohistochemical analysis with surrogate molecular markers in complex with FISH can provide additional prognostic information in case of pediatric high grade gliomas.

PATH-11. PROSPECTIVE (EPI-)GENETIC CLASSIFICATION OF > 1,000 PEDIATRIC CNS TUMORS—THE MNP 2.0 STUDY

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The large variety of CNS tumor entities affecting children and adolescents, some of which are exceedingly rare, results in very diverging patient outcomes and renders accurate diagnosis challenging. To assess the diagnostic utility of routine DNA methylation-based CNS tumor classification and gene panel sequencing, the *Molecular Neuropathology 2.0* study prospectively integrated these (epi-)genetic analyses with reference neuropathological diagnostics as an international trial for newly-diagnosed pediatric patients. In a four-year period, 1,215 patients with sufficient tissue were enrolled from 65 centers, receiving a reference neuropathological diagnosis according to the WHO classification in >97%. Using 10 FFPE sections as input, DNA methylation analysis was successfully performed in 95% of cases, of which 78% with sufficient tumor cell content were assigned to a distinct epigenetic tumor class. The remaining 22% did not match any of 82 represented classes, indicating novel rare tumor entities. Targeted gene panel sequencing of >130 genes performed for 96% of patients with matched blood samples detected diagnostically, prognostically, or therapeutically relevant somatic alterations in 48%. Germline DNA sequencing data indicated potential predisposition syndromes in ~10% of patients. Discrepant results by neuropathological and epigenetic classification (29%) were enriched in histological high-grade gliomas and implicated clinical relevance in 5% of all cases. Clinical follow-up suggests improved survival for some patients with high-grade glioma histology and lower-grade molecular profiles. Routine (epi-)genetic profiling at the time of primary diagnosis adds a valuable layer of information to neuropathological diagnostics and will improve clinical management of CNS tumors.

PATH-13. PLEOMORPHIC XANTHOASTROCYTOMA INTEGRATED GENOMIC CHARACTERIZATION - WHAT HAVE WE LEARNED?

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