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Pleomorphic xanthoastrocytoma (PXA) is a rare astrocytoma occurring predominantly in children and young adults. It is characterized histologically by large pleomorphic, spindled and lipidized cells with frequent eosinophilic granular bodies and pericellular reticulin deposition. *BRAF* p.V600E mutation and *CKDN2A/B* deletion are the most common genetic alterations. We report the integrated genomic characterization of a cohort of 67 patients (37 F, 30 M; median age 20.3 years (interquartile 13.4–32.9) with histologically defined PXA (52, 78%) or anaplastic PXA (A-PXA) (15, 22%), using genome-wide cytogenetic (ThermoFisher Oncoscan, n=67), methylation profiling (Illumina EPIC array, n=43), and targeted next generation sequencing (n=32). *BRAF* p.V600E mutation (n=51, 76.1%) and *CDKN2A/B* deletion (n=63; 94%) were the most frequent alterations. Of 16 *BRAF* p.V600E negative cases, 7 showed an alternative *BRAF* activating mutation (n=2), *NF1* (n=3) mutation or *ATG7-RAF1* fusion (n=2). Targeted *TERT* analysis found promoter mutations in 3 (of 58) cases, but TERT amplification was absent. Supervised and unsupervised methylation profiling against a comprehensive reference cohort demonstrated consensus grouping with the PXA class in 36 of 43 cases; while the minority grouped with a ganglioglioma class (n=3), with reactive brain or had no resolvable subgroup (n=4). Follow-up was available in 61 patients (91.0%) (median 63 months). Overall survival was significantly different between PXA and A-PXA (5-year:80.4% vs. 55.1%; p=0.001), but not progression-free survival (5-year:61.7% vs. 39.8%; p=0.128). Our data confirm the high frequency of MAP-K abnormalities and *CDKN2A/B* deletion in PXA. WHO grade remains a strong predictor of patient overall survival.

PATH-14. GENETIC SUSCEPTIBILITY AND OUTCOMES OF PEDIATRIC, ADOLESCENT AND YOUNG ADULT IDH-MUTANT ASTROCYTOMAS

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INTRODUCTION: Previously thought to be rare, recent case series have shown that *IDH* mutations in young patients are more common than previously described. In this study, we analyzed *IDH*-mutant tumors to determine clinical significance of these mutations in children, adolescents and young adults. METHODS: Through this multi-institution study (10 institutions), we collected 64 IDH1/2-mutant infiltrating astrocytoma specimens from 58 patients aged 4–26 (M:F, 0.4:0.6). Specimens included 46 low-grade (LGG) and 18 high-grade (HGG) astrocytomas. Tumor sequencing data (n=45), germline sequencing data (n=37) and outcome data (n=40) was analyzed. RESULTS: Similar to adults, most sequenced tumors had a co-mutation in the *TP53* gene, while *ATRX* mutations were less common and primarily seen in HGGs. Approximately 60% (n=21) of patients with germline data available had a mutation in a cancer predisposition gene. Mismatch repair (MMR) mutations were most common (n=12; MSH6 n=9), followed by *TP53*mutations (n=7). All patients with MMR gene mutations had HGGs and poor progression free (PFS=10% at 2 years, mean TTP=9 months) and overall (OS <30% at 2 years) survival. Despite an OS of 90% at 5 years, many LGG patients had tumor progression/recurrence requiring additional treatment (PFS= 80% at 2 yrs, 40% at 5 yrs, mean TTP=3.5 years). Four LGG tumors (2 with *TP53+ATRX*loss, 2 with *TP53* loss+1p19q co-deletion) underwent malignant transformation. CONCLUSION: *IDH*-mutant tumors in pediatric patients are strongly associated with cancer predisposition and increased risk for progression/recurrence or malignant transformation. Routine screening for *IDH1/2* mutations in children with grade 2–4 astrocytomas could greatly impact patient management.

PATH-15. PROTEOMIC SIGNATURES PREDICT GRADE IN PEDIATRIC AND YOUNG ADULT INFILTRATIVE ASTROCYTOMAS

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BACKGROUND: Infiltrative astrocytomas in children and young adults pose a treatment challenge due to the difficulty of achieving gross total resection and tumor resistance to irradiation and chemotherapy. Histopathologic grade is an essential part of determining prognosis and treatment, but it is subjective and provides limited understanding of the molecular mechanisms underlying tumor development and progression. METHODS: We performed liquid chromatography/mass spectrometry (LC/MS-MS) on 28 FFPE samples of primary infiltrative astrocytomas (10 grade II, 8 grade III and 10 grade IV – WHO classification) from Nationwide Children's Hospital (NCH). Initial unsupervised clustering was performed. Lasso regression yielded a protein signature separating low- and high-grade tumors which was validated using a similar cohort of pediatric and young adult infiltrative astrocytomas from the Proteomic Data Commons (PDC) (n=28) of the National Cancer Institute. RESULTS: Unsupervised clustering of NCH samples essentially recapitulated grade and lasso regression yielded a 10-protein signature that distinguished grade II from grade III/IV tumors. This 10-protein signature when applied to the PDC validation dataset, accurately predicted grade for 89.3% of the tumors (p=0.00014). CONCLUSIONS: We identified a quantitative protein signature that can reliably distinguish between low- and high-grade infiltrative astrocytomas from FFPE tissue. Further validation will enable the development an objective prognostic proteomic clinical test that complements and may outperform current histopathological strategies. Additionally, proteomic profiling of tumors will clarify the molecular mechanisms contributing to treatment resistance and tumor progression and help identify novel treatment targets. Independent functional validation and characterization of proteins is ongoing.

PATH-16. CORRELATION OF PATHOLOGICAL AND RADIOGRAPHICAL DIAGNOSES FOR CHILDREN WITH BRAIN TUMORS AT TWO MAJOR HOSPITAL IN KENYA

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BACKGROUND: Central nervous system (CNS) tumors are the leading solid tumors in the childhood population but vastly underreported in the African population. There's limited data on childhood brain tumors as well as the histopathological distribution in Kenya. Our study aimed at assessing the spectrum as well as the level of correlation with imaging in diagnosis of brain tumors within two major hospital settings. DESIGN: This was a cross-sectional retrospective descriptive study conducted at the two major hospitals in Kenya: Kenyatta National Hospital (KNH) and Moi Teaching and Referral Hospital (MTRH). Children who underwent treatment for brain tumors between 2015 and 2017 and whose tissue biopsies were available at the laboratory archives were included. RESULTS: 87 cases were available for review, and the majority of the affected population were of ages 5–9 years. The most affected site was infratentorial compartment (48.3%) with gliomas and medulloblastoma being equally distributed. Majority of the gliomas were low grade (69%) with pilocytic astrocytoma being the most common subtype (42.9%). The overall sensitivity for the diagnosis of brain tumors through radiology was 69.4%. The level of correlation of histopathological to radiological diagnosis was statistically insignificant with P and kappa values of 0.814 and -0.024 respectively. CONCLUSION: Gliomas and medulloblastomas were the commonest tumors at both centers. Histopathological diagnoses have a high concordance of agreement among various morphologists. The level of correlation between histopathological and radiological diagnosis was high. Next steps include standardizing clinical, radiological and pathological details within Kenya.

PATH-17. INTRAGENIC COPY NUMBER BREAKPOINT ANALYSIS OF METHYLATION DATA FROM CNS TUMOURS IDENTIFIES NOVEL SUBGROUP-SPECIFIC CANDIDATE FUSION GENE ENRICHMENTS

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Methylation array-based molecular profiling has redefined the classification of brain tumours and now forms an important part of their integrated