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In the recent 5th edition of the WHO classification of CNS tumors, 'Astroblastoma, *MN1* altered' is recognized a distinct brain tumor type, occurring in children and young adults. Due to its rarity and novelty, little is known about clinical and molecular traits. Therefore, we initiated an international effort and collected tissue samples, clinical and molecular data from 176 patients with Astroblastoma, *MN1* altered, identified by their distinct DNA methylation profiles. DNA methylation-based *t*-SNE clustering analyses revealed that Astroblastoma, *MN1* altered tumors form one distinct main cluster (n=158) showing *MN1:BEND2* and single cases with *EWSR1:BEND2* fusions and a further adjacent, but distinct smaller cluster (n=18) mostly defined by *MN1:CXXC5* fusions. Both fusion partner-defined groups show a median age of 12 years but distinct copy-number aberrations, characteristically a gain of chromosome 5 in one third of the *CXXC5*-fused group and a loss of chromosome 16q in one third of *BEND2*-fused cases. As previously reported, a vast majority of Astroblastoma, *MN1* altered patients are female, which we confirm for the *BEND2*-fused group (85%). The *CXXC5*-fused group, however, shows 75% male patients. Interestingly, 9/10 tumors of the few male patients observed in the *BEND2*-fused group were all located infratentorially or in the spinal cord, whereas almost all female cases show a supratentorial location (85/87). Histologically, the *BEND2*-fused group was primarily reported as Astroblastoma (39%), whereas in the *CXXC5*-fused cases, 31% CNS-PNET and only 8% Astroblastoma histologies were originally assigned. Preliminary clinical analyses showed that the *BEND2*-fused group has a relatively good 5/10-year OS of 97%/89%, but a less favorable 5/10-year PFS of 48%/35%, in line with previous studies. Patients showing CXXC5-fused tumors (n=8) indicated 5/10-year OS and PFS rates of 83%/83% and 60%/60%, respectively. Additional survival and molecular analyses are being conducted to further characterize Astroblastoma, *MN1* altered tumors and its molecular subgroups.

RARE-16. DIFFERENTIAL EXPRESSION OF MIRNAS IN ADAMANTINOMATOUS CRANIOPHARYNNGIOMA REVEALS DYSREGULATION OF PATHOGENIC PATHWAYS

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MicroRNAs (miRNAs) are small non-coding RNAs that regulate the expression of target mRNAs and can control whole gene networks. ACPs are benign pituitary tumours that can result in significant morbidity and premature mortality. ACPs harbour mutations in CTNNB1 and are driven by the activation of the WNT/beta-catenin pathway. We sought to explore the expression of miRNAS in adamantinomatous craniopharyngioma (ACP) in a cohort of samples previously subjected to RNA-Seq analysis (Apps et al, Acta Neuropathologica, 2018, May;135(5):757-777). Total RNA ACP samples (n=18), non-functioning pituitary adenomas (n=3) and normal foetal pituitaries (n=3) underwent miRNA sequencing using the Qiagen miRNA library prep kit on a NextSeq 500 to a depth of 16 million reads. Differential expression was performed using DESeq2 and functional analysis with mirPath v.3. Expression of miRNAs was correlated with previously published mRNA expression We found that 210 miRNA were upregulated and 275 down regulated in ACP compared with controls (adjusted p-value <0.1). MIR-205-5p was the most upregulated miRNA (619 fold) and its expression correlated with genes expressed within the tumour epithelium (e.g. TP63). miR-375 an inhibitor of the WNT pathway was the most down regulated miRNA (361 fold). KEGG Pathway analysis identified Glycosphingolipid synthesis as the most enriched pathway targeted by upregulated miRNAs. Pathways that were enriched by down regulated miRNAs included: ECM-receptor interaction, fatty acid biosynthesis, Hippo, TGF-beta, WNT, and ErbB pathways. Down regulation of miR-132 has previously been suggested as a marker of aggressiveness in ACP, and was 16 fold down regulated (adjusted p-value<0.001) in this cohort and expression was inversely correlated with genes relating to epithelial development. This data confirms previous studies indicating that miRNA expression is altered in ACP. In silico analysis suggest that the dysregulation of miRNA affects the expression of genes involved in pathogenic pathways in ACP.

RARE-17. MULTI-INSTITUTIONAL CRANIOPHARYNGIOMA COHORT HIGHLIGHTS NEED FOR MORE COMPREHENSIVE DATA COLLECTION ON COMORBIDITIES AND QUALITY OF LIFE

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BACKGROUND: Pediatric craniopharyngioma is associated with long-term survival, but tumor- and therapy-related complications often negatively impact quality of life (QoL). Standard treatments include resection and radiation, but institutional practices vary and recurrence rates remain high. In this review, we utilized a cohort from the Children's Brain Tumor Network (CBTN) to evaluate outcomes for craniopharyngioma. METHODS: CBTN provides clinical and genomic data for pediatric patients diagnosed with primary central nervous system tumors across 25+ institutions. We collected data for 124 patients, ages 0-21, diagnosed with craniopharyngioma between 2012-2020. Variables collected included treatment, recurrence/progression, and comorbidities. RESULTS: Excluding patients without confirmed pathologic diagnosis (n=10) or follow-up data (n=39), 75 patients remained. For initial treatment, most (n=46, 61%) received surgery alone (9 partial, 33 near-total resection). Twenty-six (35%) underwent both surgery and radiation, with 9 receiving both therapies upfront and 17 receiving radiation at progression/recurrence. Four (5%) patients received chemotherapy. Over half of the cohort (n=39, 52%) had at least one progression/recurrence, and four died (5%). Significantly higher rates of progression/recurrence (84% vs. 32%, p=4.0e-5) were identified in patients that had surgery and radiation, compared to surgery alone. Time to recurrence, progression, or death was shorter for the surgery and radiation group (HR=4.1, p<1.0e-4), and for those that underwent partial versus near-total resection (HR=2.7, p=0.1.2e-2). Comorbidities were likely underreported, based on low rates of visual (32%), neuroendocrine (27%), and neurologic (28%) deficits at diagnosis, and 29 patients (39%) with unspecified medical history. CONCLUSIONS: CBTN provides a robust repository of information on treatment and survival of craniopharyngioma patients. However, we found a paucity of data on associated comorbidities and QoL outcomes. We advocate that future datasets and clinical trials routinely collect functional outcomes alongside therapy and survival data, particularly in craniopharyngioma where long-term survival is balanced with future QoL.

RARE-18. PEDIATRIC CRANIOPHARYNGIOMA; SINGLE CENTER EXPERIENCE IN 246 CASES WITH DIFFERENT MANAGEMENT MODALITIES

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PURPOSE: To report our experience with different craniopharyngioma management strategies done for 246 patients in a single institution during a period of 14 years. METHODS: The medical records of all children with the diagnosis of craniopharyngioma treated at Children's Cancer Hospital Egypt (CCHE-57357) during the period from July 2007 to December 2021 were retrospectively reviewed. RESULTS : our registry included 246 pediatric craniopharyngiomawith median age of 7.4 years old. The main strategies of management after initial surgery were follow up, radiotherapy or administration of intracystic interferone post ommaya insertion. The number of cases in each group were 92, 147,and three respectively. Three patients were not operated upon because of heavily calcified lesions, two of them received radiotherapy while the third was kept under follow up. Overall gross or near total total excision was achieved in 31.2 % , subtotal resection was the case in 42.1% while Ommaya insertion and biopsy was done in 21.1 % of cases. Total number of patients received radiotherapy initially or on progression was 195 patients(78.9%). The five-year overall survival was 88% (95% CI 82.9 – 93.1) while 5- year progression free survival (PFS) was 49.2% (95% CI 41.2—57.2). The five-year PFS rates for patients in the follow up group versus radiotherapy group were 25.2% and 68.7% respectively (P< 0.0001). Beta catenin was positive in 76.4% of cases that were available for testing (123/161). CONCLUSION: management of craniopharyngioma should be individualized with the main objective is the quality of life. Conservative surgery which entails gross total safe resection whenever possible or lesser extent of resection followed by radiotherapy is the main strategy followed in our institution.

RARE-19. MOLECULAR CHARACTERIZATION AND TREATMENT RESPONSE OF METASTATIC DIA/DIG

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INTRODUCTION: Desmoplastic infantile astrocytoma (DIA) and desmoplastic infantile ganglioglioma (DIG) are glioneuronal tumors of early childhood. Surgical resection is usually sufficient to cure these benign