The most common deficits for all patients were neuro-endocrine followed by vision and neurocognitive problems. Neuro-endocrine complications were self-reported as the biggest impact on QOL. Families reported that they would prefer treatment options with the possibility of improved QOL. German QOL also carried an increased risk of recurrence. Craniohypophyseal surgery continues to be predominantly treated with surgery and radiation initially and with recurrence. Survivors have multiple comorbidities, with an interest in targeted therapies that preserve QOL. Novel therapies to prevent co-morbidities and provide long term benefits are necessary and upcoming.

RARE-14. NEWBORN WITH HYPOTHALAMIC HAMARTOMA AND PALLISTER-HALL SYNDROME

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A female full-term newborn of 41 + 2 weeks gestational age with a respiratory adaptation disorder and hypercapnia was transferred from an external maternity clinic to our pediatric intensive care unit. The child is the second child of healthy, non-consanguineous parents. Multiple dysmorphias were noticed at arrival. We assumed an underlying genetic cause of the congenital malformations. Whole exome sequencing revealed a compound heterozygous mutation of the chromosome. It is inherited in an autosomal dominant manner and its prevalence is 1/2,000,000.

On arrival. We identified a choanal atresia/stenosis on both sides in the respiratory tract, a high palate, a submucous cleft palate, a bifid uvula, a laryngeal cleft and a bronchus s. The child required intubation and ventilation. In addition, we recognized brachydactyly of the hands and feet. The phalanges were not usually separate short. A large nail hypoplasia and rocker bottom feet on both sides. Furthermore, we saw an anal atresia. In routine laboratory work-up, a hypoglycemia and not measurable low TSH serum concentration was noticed. Extended endocrinological laboratory diagnostics revealed a complete pituitary insufficiency. On cranial computed tomography, a large, iso to hypodense, non-enhancing, occupying mass (3.8x3.7x2.5 cm), originating from the hypothalamus was observed. The brainstem was displaced posteriorly by the mass. The imaging is consistent with a hypothalamic hamartoma. With regard to the present findings, we assumed an underlying genetic cause of the congenital malformations. As a clinical diagnosis, a Pallister-Hall syndrome was suspected. As described in our case, we saw the characteristic features: dysmorphism of the hands and feet, upper respiratory tract, anal atresia, and hypothalamic hamartomas. The Pallister-Hall syndrome is caused by mutations in the GLI3 gene on the 7p13 chromosome. It is inherited in an autosomal dominant manner and its prevalence is unknown. In our patient, a heterozygous, probably pathogenic variant in the GLI3-Gene was proven by Next Generation Sequencing (NGS).

RARE-15. ASTROBLASTOMA, MIN ALTERED COMPRISES TWO MOLECULARLY AND CLINICALLY DISTINCT SUBGROUPS DEFINED BY THE FUSION PARTNERS BENDZ AND CXX5

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In rare childhood astroblastomas, the most common genetic alteration is the restoration of the chromosome. It is inherited in an autosomal dominant manner and its prevalence is 1/2,000,000. On cranial computed tomography, a large, iso to hypodense, non-enhancing, occupying mass (3.8x3.7x2.5 cm), originating from the hypothalamus was observed. The brainstem was displaced posteriorly by the mass. The imaging is consistent with a hypothalamic hamartoma. With regard to the present findings, we assumed an underlying genetic cause of the congenital malformations. As a clinical diagnosis, a Pallister-Hall syndrome was suspected. As described in our case, we saw the characteristic features: dysmorphism of the hands and feet, upper respiratory tract, anal atresia, and hypothalamic hamartomas. The Pallister-Hall syndrome is caused by mutations in the GLI3 gene on the 7p13 chromosome. It is inherited in an autosomal dominant manner and its prevalence is unknown. In our patient, a heterozygous, probably pathogenic variant in the GLI3-Gene was proven by Next Generation Sequencing (NGS).
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 3′-SNE clustering analyses revealed that Astroblastoma, MN1 altered tumors form one distinct main cluster (n=138) 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 chromosomes 8 or 16 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, 910 tumors of the few male patients originated in the BEND2-fused group with wild-type chromosome 8 or the spinal cord, whereas almost all female cases show a supratentorial location (85%). Histologically, the BEND2-fused group was primarily reported as Astroblastoma (39%), whereas in the CXXC5-fused cases, 31% CNS-PNET and 29% Pilocytic astrocytoma. Of the astrocytoma histologies, 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) included 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 their molecular subgroups.

**RARE-16. DIFFERENTIAL EXPRESSION OF MiRNAs IN ADAMANTINOMATOUS CRANIOPHARYNGIOMA 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 tumors that can result in significant morbidity and premature mortality. ACPs harbor 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 sequenced by NextSeq analysis (Appens, 2018, May;131(5):757-777). Total RNA ACC samples (n=18), non-functioning pituitary adenomas (n=3) and normal fetal 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 clinical and functional analysis with mirPath v3. Expression of miRNAs was correlated with previously published mRNA expression We found that 210 miRNA were upregulated and 273 down regulated in ACC compared with controls (adjusted p-value <0.1), MLR-205-5p was the most upregulated mRNA (619 fold) and its expression correlated with genes expressed within the tumor epithelium (e.g. TPE3). miR-375 an inhibitor of the WNT pathway was the most down regulated mRNA (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 agressiveness 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 ACC. In silico analysis suggest that the dysregulation of miRNA affects the expression of genes involved in pathogenic pathways in ACC.

**RARE-17. MULTI-INSTITUTIONAL CRANIOPHARYNGIOMA CENTER OUTLOOK: NEED FOR A 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 radiation 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 recurrence, progression, or death (5%). Significantly higher rates of progression/recurrence (84% vs. 32%, p=0.0e-5) were seen in surgery and radiation group (HR=4.1, p=0.1e-4), and for those that underwent partial versus near-total resection (HR=2.7, p=0.1e-2). Comorbidities were likely underreported, based on low rate of self-assigned comorbidities (32%), low rate of self-assigned developmental (27%), and low rate of self-assigned 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.