(n=4) and 3 non-recurrent ACP were analysed using β-catenin, pERK1/2 immunostaining, DNA methylation array and RNA sequencing. Differential expression and methylation analyses confirmed differences between ACP and PCP, with over representation of WNT pathway genes in ACP and the MAPK pathway genes in PCP. All of the primary and all except for one of the relapsed ACP tumours showed a pERK1/2 expression. Differences in the immune environment were also identified between ACP and PCP, with higher levels of some inflammatory mediators and CD14+ cell signatures in PCP compared with ACP. Whilst differential methylation and expression analysis revealed relatively stable methylomes and transcriptomes between serial samples of cases, segmental chromosomal alterations were identified in recurrence samples from five ACP cases (5/11,45%). One relapsed case showed histological and molecular signs of malignant transformation, including high ki67 and deletion of *TP53*. Surprisingly, this malignant tumour showed nuclear beta-catenin in all neoplastic epithelial cells and absence of pERK1/2 staining, despite the primary tumour showing the typical beta-catenin and pERK1/2 expression patterns. These results suggest that the molecular landscape of craniopharyngioma remains stable between recurrences in most cases, but, there is evidence of molecular evolution in a subset of cases. Activation of the MAPK pathway in the vast majority of ACP tumours supports the clinical evaluation of MAPK pathway inhibitors in ACP patients.

RARE-09. TREATMENT OF CHILDHOOD-ONSET CRANIOPHARYNGIOMA PATIENTS USING PROTON BEAM THERAPY VERSUS PHOTON-BASED RADIATION THERAPY IN THE PROSPECTIVE KRANIOPHARYNGEOM 2007 TRIAL

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BACKGROUND: Proton beam therapy (PBT) compared to photon-based radiotherapy (XRT) offers the benefit to administer lower radiation doses to critical organs thereby possibly minimizing the risk of sequelae in patients with residual craniopharyngiomas (CP) after hypothalamus-sparing surgery. The validation in large CP patient cohorts is still pending. PATIENTS AND METHODS: Of 290 childhood-onset CP patients included 2007-2019 in the prospective multicenter trial KRANIOPHARYNGEOM 2007, 99 (34%) received external RT (65% PBT, 35% XRT). Outcome was compared between the different groups in terms of overall (OS) and event-free survival (EFS), quality of life (QoL using PEDQOL), functional capacity (FMH), and auxological data (BMI and height SDS) one, three and five years after irradiation/CP diagnosis. RESULTS: PBT became the predominant irradiation technique during the study period (used in 23% and 77% of all irradiated patients registered within the first and second half of the enrollment period, respectively). PBT as well as XRT were associated with high ($p<0.001$) EFS (PBT: 0.917 ± 0.040; XRT: 0.940 ± 0.041) compared to non-RT (EFS: 0.669 ± 0.044). OS was similar in all groups. No differences between PBT, XRT and non-RT CP patients concerning functional capacity and anthropometric parameters (height SDS, BMI SDS) have been obtained. Only in the PEDQOL domain "physical function", proxy-assessed QoL was lower one year after PBT when compared to XRT treated and non-irradiated CP patients. **CONCLUSION**: PBT is similar efficient in preventing relapses and recurrences in childhood-onset CP patients. During follow-up, no clinically relevant differences between PBT and XRT in terms of QoL, functional capacity and degree of obesity as a marker of hypothalamic syndrome were detectable. While PBT is increasingly applied, studies on larger CP cohorts with longer follow-up after RT are warranted to analyze, whether it can prevent sequelae such as hypothalamic syndrome and severe obesity compared to XRT.

RARE-10. NEUROCUTANEOUS MELANOCYTOSIS-ASSOCIATED HYDROCEPHALUS: THE MSK EXPERIENCE FROM 2001-2022

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OBJECTIVE: We hypothesize that patients with neurocutaneous melanocytosis-associated melanoma and ventriculoperitoneal shunts are at risk of developing intraperitoneal spread of melanoma. BACKGROUND: Neurocutaneous melanocytosis, a rare condition characterized by excessive proliferation and deposition of melanocytes in the leptomeninges and brain parenchyma, typically occurs in children with large congenital melanocytic nevi and multiple smaller congenital nevi. These patients are at heightened risk for developing NRAS+ melanomas in the central nervous system, which in turn may lead to symptomatic hydrocephalus requiring cerebrospinal fluid diversion for symptom relief. METHODS: Retrospective single-institution study of patients with histologically or radiographically confirmed NCM evaluated at Memorial Sloan Kettering Cancer Center (MSKCC) from 2001-2022. RESULTS: Of the 47 patients with a diagnosis of NCM, 44 patients had symptomatic neurological complications. Eleven patients developed hydrocephalus, 10 had CNS melanoma, and required ventriculoperitoneal shunt placement. Nine of the 10 patients ultimately died of their disease. Three patients were diagnosed with intraperitoneal melanoma, though data are unavailable for the remaining eight. CONCLUSIONS: All (n=11) patients with NCM-associated CNS melanoma required VP shunts for symptomatic relief. Ten of these patients died within 4.3 years of VP shunt placement, with a range of 1 month to 13.5 years prior to succumbing to their disease. While the intraperitoneal pathology remains unknown for 7 of the cases, 3 had confirmed intraperitoneal melanoma, suggesting that VP shunts provided the conduit to CNS melanoma seeding of the peritoneum. Obtaining baseline abdominal imaging studies prior to VP shunt placement may be helpful in the follow-up of these patients.

RARE-11. 60 YEARS SINGLE CENTRE EXPERIENCE OF CRANIOPHARYNGIOMA MANAGEMENT

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Adamantinomatous craniopharyngiomas are challenging intracranial tumours associated with significant morbidity. Management includes surgery and radiotherapy, with a shift towards more conservative surgery in recent years, aimed at preserving hypothalamic function. The West Midlands Regional Children's Tumour Registry collects detailed clinical, pathological and follow up information on patients treated within the region from 1957. 52 cases (26 male, 26 female) of craniopharyngioma treated at Birmingham Children's Hospital 1957-2018, were identified, with further clinical details obtained from patient records, where available. Visual symptoms were the commonest presenting feature (63%), followed by headache (48%), vomiting (31%), neurological symptoms (31%) and features of endocrine disorders (21%) with a median symptom duration of 6 months (range <1-24). Initial management was with gross total resection (GTR) in 14 patients, subtotal resection in 22 patients and subtotal resection with adjuvant radiotherapy in seven patients. Two patients received radiotherapy without resection, and five patients underwent cystic drainage procedures alone. Two patients initially underwent shunt insertion alone, but received radiotherapy at progression. 30 (58%) patients underwent relapse/progression, with a median time to progression of 1.2 years (range 0.2-6.3). 15 had further surgery. Radiotherapy was used in 14/15 patients who had not previously received radiotherapy, with the other undergoing a GTR. To date 10 patients have died, nine from tumour related reasons and one from pulmonary embolism. Where data was available at follow up, all patients had at least one endocrinopathy, with 38/45 patients having diabetes insipidus. Hypothalamic obesity was identified in 14/36 (39%) patients with sufficient records, with this more common in those undergoing GTR (7/9 (78%)) compared to other surgical procedures (7/27)(26%)($p<0.05$). Three patients have developed neurovascular complications and three fatty liver disease. This experience is consistent with the literature and supports the increasing usage of hypothalamic sparing surgical management.

RARE-12. PINEOBLASTOMA OF CHILDREN AND YOUNG ADULTS IN A NATIONAL POPULATION: AN ANALYSIS OF THE HIT-MED STUDY COHORT

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