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The 2021WHO CNS tumor classification includes CNS tumors with internal tandem duplications in the BCL6 corepressor (BCOR) gene as a new entity of CNS embryonal tumors labelled high-grade neuroepithelial tumors with BCOR alterations (HGNET-BCOR) are characterized by genetic aberrations in the BCOR gene located at Xp11.4, leading to increased expression of BCOR mRNA and distinct DNA methylation profiles. currently no agreement on the optimal strategy to manage these rare tumors, which mostly occur in young children These tumors are usually treated as high grade glioma HGG with upfront radiation therapy with poor outcome. We report 2.5 years old boy presenting with headache and vomiting. MRI showed a well-defined left cerebellar mass, hyperintense in T2 and hypointense in T1, with restricted diffusion and no spinal CSF seeding metastases. He underwent gross surgical resection of the tumor initial pathological diagnosis was epithelioid high grade malignant neoplasm. Brain tumor methylation classifier analysis of resected tumor tissue confirmed a CNS tumor with BCOR internal tandem duplication (WHO grade 4). The patient was treated per COG ACNS0334 (3 induction cycles of vincristine, cyclophosphamide, cisplatin, etoposide, HDMTX, followed by consolidation with 3 cycles of carboplatin and thiotepa with autologous hematopoietic stem cell rescue). MRI brain before the start of chemotherapy showed a small recurrent mass within the surgical cavity. post-induction MRI detected stable-sized residual lesion in the surgical cavity; however, post-consolidation MRI showed complete resolution of the residual mass. The patient subsequently received craniospinal irradiation (36 Gy [CSI]) with a boost to the tumor bed up to 54 GY. By the time of writing this report our patient is still in complete remission. Our case showed that this aggressive brain tumor may respond well to intensive multimodalities therapy Further case studies and international prospective trials are needed to optimize the clinical management of these rare tumors.

ETMR-02. OVEREXPRESSION OF LIN28A IN NEURAL PROGENITOR CELLS IN VIVO DOES NOT LEAD TO BRAIN TUMOR FORMATION BUT RESULTS IN REDUCED SPINE DENSITY

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The RNA binding protein LIN28A is a stem- and progenitor marker and one of the factors necessary to induce pluripotent stem cells. An overexpression of LIN28A has been identified in malignant brain tumors called embryonal tumors with multilayered rosettes (ETMR) but its specific role during brain development remains largely unknown. Radial glia cells of the ventricular zone (VZ) are proposed as a cell of origin for ETMR. We asked whether an overexpression of LIN28A in such cells might affect brain development or result in the formation of brain tumors. Constitutive overexpression of LIN28A in *hGFAP-cre::lsl-Lin28A* (GL) mice led to a transient increase of proliferation in the cortical VZ at embryonic stages but no postnatal brain tumor formation. Postnatally, GL mice displayed a pyramidal cell layer dispersion of the hippocampus and altered spine and dendrite morphology, including reduced dendritic spine densities in the hippocampus and cortex. GL mice displayed hyperkinetic activity and differential quantitative MS-based proteomics revealed altered time dependent molecular functions regarding mRNA processing and spine morphogenesis. Phosphoproteomic analyses indicated a downregulation of mTOR pathway modulated proteins such as Map1b being involved in microtubule dynamics within a crosstalk of Gsk3b/Rho-Rac/Map1b signaling. In conclusion, we show that Lin28A overexpression transiently increases proliferation of neural precursor cells but it is not sufficient to drive brain tumors *in vivo*. In contrast, Lin28A impacts on protein abundancy patterns related to spine morphogenesis and phosphorylation levels of proteins involved in microtubule dynamics, resulting in decreased spine densities of neurons in the hippocampus and cortex as well as in altered behavior. Our work provides new insights into the role of LIN28A for neuronal morphogenesis and development and may reveal future targets for treatment of ETMR patients.

ETMR-03. INTRA- AND EXTRA-CRANIAL BCOR-ITD TUMOURS ARE SEPARATE ENTITIES WITHIN THE BCOR-REARRANGED FAMILY

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BCOR-ITD tumours form an emerging family of aggressive entities with an internal tandem duplication (ITD) in the last exon of the *BCOR* gene. The family includes cerebral tumours, termed central nervous system *BCOR*-ITD (CNS *BCOR*-ITD), and sarcomatous types described in the kidney as clear cell sarcoma of the kidney (CCSK), in the endometrium as high-grade endometrial stromal sarcoma (HG-ESS), in bone, and in soft tissue as undifferentiated round cell sarcoma (URCS) or primitive myxoid mesenchymal tumour of infancy (PMMTI). Based on a series of 33 retrospective cases, including 10 CNS *BCOR*-ITD and 23 *BCOR*-ITD sarcomas, we interrogated the homogeneity of the entity regarding clinical, radiological and histopathological findings, and molecular signatures. Whole transcriptomic sequencing and DNA methylation profiling were used for unsupervised clustering. Histopathological review revealed marked differences between CNS *BCOR*-ITD and *BCOR*-ITD sarcomas. These two groups were consistently segregated by unsupervised clustering of expression (n=22) and DNA methylation (n=21) data. Proximity between the two groups may result from common somatic changes within key pathways directly related to the novel activity of the ITD itself. Conversely, comparison of gene signatures with single-cell RNAseq atlases suggests that the distinction between *BCOR*-ITD sarcomas and CNS *BCOR*-ITD may result from differences in cells of origin.

ETMR-04. EMBRYONAL TUMOR WITH MULTI-LAYERED ROSETTES (ETMR) LOCATED IN THE BRAINSTEM: A CASE REPORT ON CLINICAL DECISION-MAKING AND A MULTIMODAL, INTERDISCIPLINARY TREATMENT APPROACH INCLUDING INTERSTITIAL BRACHYTHERAPY

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OBJECTIVE: Embryonal tumors with multi-layered rosettes (ETMR) (CNS WHO grade 4) comprise a rare and malignant tumor type affecting predominantly infants below 3 years of age. The treatment consists of maximal safe surgical resection, irradiation, and intensive medulloblastoma type chemotherapy. Despite aggressive treatment, the prognosis of these patients remains poor, especially for brainstem tumors. We present the case of a male infant diagnosed with a brainstem ETMR, successfully treated with an interdisciplinary multimodal approach, including stereotactic interstitial brachytherapy. RESULTS: A 19 month old boy first presented with hemiparesis, intermittent bradycardia and reduced consciousness. Initial imaging showed a brainstem lesion with characteristic features of a diffuse intrinsic pontine glioma (DIPG). We performed stereotactic biopsy to confirm the diagnosis and initiated temozolomide treatment. While the pathology result was still pending, the boy's clinical condition deteriorated to a soporic state with stretch synergisms. By emergency open surgery, partial resection was achieved. Eventually, the patient recovered rapidly. After the diagnosis of ETMR was established, medulloblastoma type chemotherapy (systemic carboplatin/etoposide; intrathecal methotrexate) was administered. After two cycles, the patient showed only residual right-sided hemiparesis. However, imaging demonstrated only a minimal reduction of the tumor size. Therefore, stereotactic interstitial brachytherapy using 125iodine seeds and subsequent high-dose chemotherapy (HDCT) with autologous stem cell transplantation (ASCT) was performed and overall tolerated well. After two months of brachytherapy and two