

(OS) were 9.7% (95% CI:2.6–36.0%) and 13% (95% CI:4.5–37.5%), respectively. Three patients survived beyond five years. Nineteen patients relapsed in the following sites: local site (n=4), distal site (n=6), local and distal sites (n=9). Favorable OS prognostic factors were CSI (hazard ratio (HR)=0.30 (0.11–0.86), p=0.025), and HDCx/AuHCR (HR=0.40 (0.16–0.99), p=0.047). CONCLUSION: CSI and HDCx/AuHCR were statistically associated with improved survival. The overall poor outcomes and high PD rate during later induction cycles and following consolidation chemotherapy warrants consideration of fewer induction cycles before consolidation and the intensification of consolidation with multiple cycles of marrow-ablative chemotherapy.

RARE-36. DYSEMBRYOPLASTIC NEUROEPITHELIAL TUMORS: A REVIEW OF CLINICAL AND MOLECULAR CHARACTERISTICS, AND OUTCOME IN A PEDIATRIC POPULATION AT A SINGLE CENTER

Valerie Cruz Flores, Thomas Geller, Ignacio Gonzalez Gomez, Luis Rodriguez, Javier Quintana, and Stacie Stapleton; Johns Hopkins All Children's Hospital, St. Petersburg, FL, USA

BACKGROUND: Neuronal and mixed neuro-glial tumors of the central nervous system (CNS) are relatively rare. Dysembryoplastic neuroepithelial tumor (DNET) is a benign, rare, slow-growing tumor, but in many cases is associated with intractable epilepsy. **OBJECTIVE:** To report the experience with DNET at a single free-standing children's institution. **METHODS:** A retrospective chart review of 24 patients with confirmed DNET between 2001 and 2019 was performed. Data was collected on clinical characteristics, tumor location, surgical management, histopathological and molecular findings, and outcomes. **RESULTS:** Mean age at diagnosis was 10 years (range 2 to 19 years), with female predominance (54.2%). Most common presenting symptoms were seizures (79.2%) and headaches (12.5%). Location of the tumor was temporal (29.2%), frontal (25.0%), parietal (16.7%), cerebellar (12.5%) and occipital (4.2%). A gross total resection was achieved in half the cases. Recurrence occurred in 4 patients (16.7%), all of whom had subtotal resections. The average follow up since diagnosis was 4.6 years (range 0.3 to 14 years). Nineteen patients presented with seizures, of which 63.2% were seizure free after surgery. The samples with molecular genetic testing (microarrays or FISH), were all normal except one patient positive for BRAF V600E mutation. **CONCLUSIONS:** This is the first and largest review of pediatric DNETs in the last 10 years. Despite majority of patients having a favorable outcome after surgery, a subset of patients remains symptomatic. As molecular mechanisms in DNET remain unknown, future aim is to describe the molecular characteristics of our DNET population, and correlate with outcomes.

RARE-37. NOONAN SYNDROME AND GLIONEURONAL TUMORS: A CENTRAL NERVOUS SYSTEM CANCER PREDISPOSITION ASSOCIATION?

Margaret Shatara¹, Elizabeth A. Varga¹, Daniel R. Boué², Lisa Martin³, Jerome A. Rusin³, Diana P. Rodriguez³, Jeremy Jones³, Aaron McAllister³, Jeffrey R. Leonard⁴, Jonathan Pindrik⁴, Kathleen M. Schieffer⁵, Kristen M. Leraas⁵, Tara M. Lichtenberg⁵, Elaine R. Mardis⁵, Catherine E. Cottrell⁵, Diana S. Osorio¹, Mohamed S. AbdelBaki¹, and Jonathan L. Finlay¹; ¹The Division of Hematology, Oncology, Blood and Marrow Transplant, Nationwide Children's Hospital and The Ohio State University, Columbus, OH, USA, ²Department of Pathology and Laboratory Medicine, Nationwide Children's Hospital, Columbus, OH, USA, ³The Department of Radiology, Nationwide Children's Hospital, Columbus, OH, USA, ⁴The Division of Pediatric Neurosurgery, Nationwide Children's Hospital and The Ohio State University, Columbus, OH, USA, ⁵The Steve and Cindy Rasmussen Institute for Genomic Medicine, Nationwide Children's Hospital, Columbus, OH, USA

BACKGROUND: Noonan syndrome (NS) is associated with germline Ras signaling pathway mutations, RAS overactivation and increased tumorigenesis risk. Rosette-forming glioneuronal tumors (RFGT) are rare indolent tumors. We report the molecular profiling of two patients with NS and RFGT. **PATIENT 1:** A 22-year-old male with NS was diagnosed with RFGT after partial tumor resection followed by focal irradiation. He was enrolled on a comprehensive genomic profiling study involving paired tumor-normal whole exome sequencing and RNA sequencing of the disease-involved tissue, revealing a germline *PTPN11* alteration (p.Gly60Ala) consistent with NS, and a somatic deletion (p.Ile442_Thr454del) in *PIK3R1* and a somatic variant (p.Lys656Glu) in *FGFR1* with concomitant increased expression of *PIK3R1* and *FGFR1* by RNA-sequencing. The patient remains without tumor progression now nine months since irradiation. **PATIENT 2:** A 19-year-old male with persistent headaches, underwent a brain MRI demonstrating multiple abnormal signals in the pineal region and midbrain. He had a stereotactic biopsy revealing RFGT. He was enrolled on the genomic study revealing a germline *PTPN11* alteration (p.Asn308Asp) resulting in a new diagnosis of NS. Several family members were subsequently identified

with clinical features of NS, including his mother and two siblings, enabling appropriate counseling. Two somatic variants were found in *trans* in *PIK3R1* (p.Thr454_Phe456del and p.Glu451_Asn453delinsAsp), and a somatic variant (p.Val695Met) in *FGFR1*, with resultant overexpression of *PIK3R1*. The patient is monitored with surveillance imaging. **CONCLUSION:** We report the molecular profiling of two patients with NS and RFGT; strongly suggesting their connection to RASopathies through the overactivation of the MAPK and PI3K/AKT/mTOR signaling pathways.

RARE-38. CLINICAL PRESENTATION OF MGA-NUTM1 FUSION TRANSCRIPT SARCOMA

Pongpak Pongphittha¹, Nongnuch Sirachainan¹, Artit Jinawat², Atthaporn Boonkird³, Putipun Puataweepong⁴, Chaiyos Khongkhatithum¹, Samart Pakakasama¹, Usanarat Anurathapan¹, Duantida Songdej¹, Eric Bouffert⁵, and Suradej Hongeng¹; ¹Department of Pediatrics, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, ²Department of Pathology, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, ³Department of Surgery, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, ⁴Department of Radiology, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, ⁵Division of Hematology/Oncology, Pediatric Brain Tumor Program, The Hospital for Sick Children, Toronto, ON, Canada

BACKGROUND: MGA-NUTM1 fusion gene tumor are recently described as new subtype of NUTM1-rearranged tumors. Regarding its rarity, standard treatment has not been reported. Here we described clinical presentation, radiologic finding, immunohistological profile, and treatment of a boy with MGA-NUTM1 fusion gene tumor. **CASE REPORT:** A 13-year-old boy with 2-month history of progressive right hemiparesis and headache. Magnetic resonance imaging (MRI) revealed 7.8 x 10.6 x 8.0 cm well defined heterogeneous enhancing mass at left fronto-parietal lobe. CT chest and abdomen, bone scan, MRI spine, and CSF studies were unremarkable. He underwent craniotomy with total tumor removal. Pathology demonstrated high grade spindle cell sarcoma. The immunohistological profile was positive for BCOR, NUT1, and TEL1, but negative for CD34, STAT6, desmin, SMA, actin sarcomeric, EMA, PR, S100, SOX10, BCL 6, and SABL2. The INI-1 showed nuclear expression and Ki-67 was positive in 50% of tumor nuclei. Molecular test for MGA-NUTM1 fusion transcript was positive, while SYT-SSX1, SYT-SSX2, and SYT-SSX4 fusion transcripts were negative. Four months after operation, MRI showed newly-seen two small enhancing foci at lateral and inferior aspects of the surgical cavity. He underwent re-surgery. Then focal radiation (54Gy and boost up to 60Gy at recurrent area) to the resection cavity was decided. Post-radiation chemotherapy including ifosfamide 3 g/m² and etoposide 150 mg/m² on Day 1–2, and carboplatin 500 mg/m² on Day 3, every 21–28 days was started. He has completed the first course of chemotherapy without any complication. **CONCLUSION:** MGA-NUTM1 fusion CNS sarcoma is rare. Treatment may require surgery, radiation and chemotherapy.

RARE-39. MOLECULARLY CONFIRMED ATYPICAL CHOROID PLEXUS PAPILLOMA WITH INTRACRANIAL DISSEMINATION

Masato Yanagi¹, Kohei Fukuoka¹, Yuko Matsushita², Yuko Hibiya², Satoko Honda³, Makiko Mori¹, Yuki Arakawa¹, Koichi Ichimura², Yutaka Tanami⁴, Atsuko Nakazawa⁵, Jun Kurihara⁵, and Katsuyoshi Ko¹; ¹Department of Hematology/Oncology, Saitama Children's Medical Center, Saitama, Saitama, Japan, ²Division of Brain Tumor Translational Research, National Cancer Center Research Institute, Chuo-ku, Tokyo, Japan, ³Department of Clinical Research, Saitama Children's Medical Center, Saitama, Saitama, Japan, ⁴Department of Radiology, Saitama Children's Medical Center, Saitama, Saitama, Japan, ⁵Department of Neurosurgery, Saitama Children's Medical Center, Saitama, Saitama, Japan

INTRODUCTION: Among choroid plexus tumors (CPTs), metastasis occurs more frequently as pathological grading increases. There could be an underestimation of pathological diagnosis if disseminated CPTs are diagnosed with lower grade tumors such as choroid plexus papilloma (CPP) or atypical choroid plexus papilloma (aCPP). Thus, molecular diagnosis using genome-wide DNA methylation profiling may be useful to clarify malignant potential among the tumor entity. Here, we report about a case of aCPP with intracranial dissemination that was molecularly diagnosed by methylation profiling. **CASE DESCRIPTION:** A 2-year-old girl presented with a history of vomiting. Brain magnetic resonance imaging showed a large tumor mass in the right lateral ventricle and diffuse enhancement surrounding her brainstem, which suggested dissemination. Gross total resection of the mass was performed. Intraoperative findings revealed multiple spot metastatic lesions on the inner wall of lateral ventricle. The pathological diagnosis was aCPP owing to the presence of a glandular structure with a papillary pattern suggesting a neoplasm of epithelial origin, increased cellularity, several necrotic areas, and an intermediate number of mitoses. The CPT-SIOP-2000 treatment protocol was followed without radiation therapy, and the disseminated lesion was disappeared during the chemotherapy. Methylation data of the current case was entered into a recently

published classifier, and the tumor was classified as methylation class “plexus tumor, subclass pediatric A” with high confidence (calibrated score 0.96), which includes cases diagnosed as CPP and aCPPs. **CONCLUSION:** Our case indicates the clinical significance of molecular confirmation of diagnosis among CPTs, particularly lower grade tumors with dissemination.

RARE-40. CASE REPORT: LONG-TERM SURVIVOR OF A RARE, PEDIATRIC PRIMARY HISTIOCYTIC SARCOMA (HS) OF THE CENTRAL NERVOUS SYSTEM (CNS) FOLLOWING COMPLETE RESECTION, CHEMOTHERAPY AND ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (ALLO-HCT)

Diana S Osorio¹, Rolla Abu-Arja¹, Mohamed S. Abdel-Baki¹, Jeffrey R. Leonard², Eric A. Sribnick², Jonathan L. Finlay¹, David W. Ellison³, Jennifer Picarsic⁴, Samir Kahwash⁵, and Daniel R. Boue^{3,5}; ¹The Division of Hematology, Oncology, Blood and Marrow Transplant, Nationwide Children’s Hospital and The Ohio State University, Columbus, OH, USA, ²Department of Pediatric Neurosurgery, Nationwide Children’s Hospital and The Ohio State University, Columbus, OH, USA, ³Department of Pathology, St. Jude Children’s Research Hospital, Memphis, TN, USA, ⁴Department of Pathology, Cincinnati Children’s Hospital, Cincinnati, OH, USA, ⁵Department of Pathology and Laboratory Medicine, Nationwide Children’s Hospital and The Ohio State University, Columbus, OH, USA

We report an unusual case of a patient with primary CNS-HS a very rare neoplasm of histiocytic lineage with usually poor prognosis. An 8 year old boy presented with a one month history of headaches, nausea and vomiting. Physical examination revealed nystagmus and dysmetria. Brain MRI revealed a localized 2.4 cm posterior fossa (cerebellar) mass with restricted diffusion. The patient underwent a gross total resection of the mass. Initial post-operative lumbar puncture was positive for rare malignant cells. Pathology showed a focally necrotic neoplasm, composed of nests and cords of large relatively uniform cells with abundant eosinophilic cytoplasm, moderately pleomorphic nuclei and numerous mitotic figures, consistent with CNS-HS with juvenile xanthogranuloma phenotype, as supported by positive IHC expression of CD163, CD68, CD14, fascin, and Factor XIIIa, while negative for CD1a, Lymphoid and Myeloid markers, and BRAFv600e mutation. He was treated with two cycles of clofarabine and cytarabine and triple intrathecal (IT) chemotherapy. He developed generalized seizures and MRI showed demyelination consistent with IT methotrexate toxicity; MTX was then discontinued. He was then given two additional cycles of cladribine and weekly intrathecal therapy prior to consolidation with an Allo-HCT using a 10/10 HLA allelic-matched unrelated donor. His conditioning regimen included total body irradiation and cyclophosphamide. He did well post-transplant with peripheral blood chimerism at 1 year showing > 95% donor cells. He remains disease-free with an excellent quality of life since August 2016. We report one of the few known survivors of this unusual and highly malignant entity.

RARE-41. SECOND MALIGNANCIES FOLLOWING TREATMENT FOR PRIMARY CENTRAL NERVOUS SYSTEM TUMORS IN PEDIATRIC PATIENTS: A SINGLE-INSTITUTIONAL RETROSPECTIVE REVIEW

Nicholas Pytel, Erik Dedekam, M. Shahriar Salamat, and Diane Puccetti; University of Wisconsin, Madison, WI, USA

Second malignant neoplasms following treatment for primary central nervous system (CNS) tumors in children are rare occurrences but may often have dire consequences, particularly, if thought to be induced by prior therapies. The authors retrospectively reviewed pediatric patients with primary CNS malignancies from the University of Wisconsin over the last 25 years (1994 – 2019) with any secondary malignant neoplasm and determined seven patients met criteria. Treatment modalities were reviewed with all patients receiving surgery, chemotherapy, and radiotherapy for treatment of their first malignancy. The second neoplasms found included 4 high-grade gliomas, 1 meningioma, 1 thyroid carcinoma, and 1 myelodysplastic syndrome. The median latency time between diagnoses was 9 years (range 4 -17 years). The outcomes varied according to histopathology of the second neoplasm with the high-grade glioma patients all deceased from progressive disease. The high-grade gliomas were thought to have been induced by prior radiation in most cases. The remaining patients are still alive, at the time of this writing, and in follow up after treatment for their second neoplasm. Thus, long-term follow up is essential for children treated for a primary CNS tumor given the variety of second neoplasms that could arise with differential consequences. In addition to our single institutional outcomes, we will also present an updated review of the literature of pediatric patients with primary CNS tumors and second malignancies.

RARE-42. PRIMARY INTRACRANIAL SARCOMA WITH DICER1-MUTATION - TREATMENT RESULTS OF A NEW MOLECULAR ENTITY

Rosdali Diaz^{1,2}, Martin Mynarek³, Sandro Casavilca⁴, Antonio Wachtel Aptomizer⁵, Pamela Mora⁶, Christian Koelsche^{7,8},

Andreas Von Deimling^{9,8}, Ulrich Schüller^{10,11}, Raymundo Sernaque¹², Gustavo Sarria^{13,14}, Tatiana Negreiros¹³, Luis Ojeda¹⁵, Pamela Garcia-Corrochano¹⁵, Danny Campos¹⁶, Jimena Ponce¹⁷, Stefan Rutkowski³, and Juan Garcia^{1,17}; ¹Instituto Nacional de Enfermedades Neoplásicas, Pediatric Oncology Department, LIMA, Peru, ²Global Alliance for Pediatric Neuro Oncology GAP-NO, International, Peru, ³University Medical Center Hamburg-Eppendorf, Department of Pediatric Hematology and Oncology, Hamburg, Germany, Hamburg, Germany, ⁴Instituto Nacional de Enfermedades Neoplásicas, Pathology Department, LIMA, Peru, ⁵Clinica Angloamericana, Lima, Peru, ⁶Instituto Nacional de Enfermedades Neoplásicas, Genetics Department, Lima, Peru, ⁷Institute of Pathology, Heidelberg University Hospital, Department of Neuropathology, Heidelberg, Germany, ⁸Clinical Cooperation Unit Neuropathology, German Cancer Research Center (DKFZ), Heidelberg, Germany, ⁹Institute of Pathology, Heidelberg University Hospital, Department of Neuropathology, Heidelberg, Germany, ¹⁰University Medical Center Hamburg-Eppendorf, Department of Pediatric Hematology and Oncology, Hamburg, Germany, ¹¹Institute of Neuropathology, University Medical Center Hamburg Eppendorf, Hamburg, Germany, ¹²Instituto Nacional de Enfermedades Neoplásicas, Radiology Department, Lima, Peru, ¹³Instituto Nacional de Enfermedades Neoplásicas, Radiotherapy Department, Lima, Peru, ¹⁴Clinica Delgado, Oncosalud, Lima, Peru, ¹⁵Instituto Nacional de Enfermedades Neoplásicas, Neurosurgery Department, Lima, Peru, ¹⁶Clinica Angloamericana, Neurosurgery Department, Lima, Peru, ¹⁷Clinica Angloamericana, Pediatric Oncology Department, Lima, Peru

OBJECTIVE: An unexpectedly high incidence of sarcomas of the Central Nervous System (SCNS) was recently observed in Peru. We describe clinical and biological characteristics of the disease. **METHODS:** Seventy pediatric patients with primary SCNS diagnosed between January 2005 and June 2018 were analyzed. DNA methylation profiling and gene panel sequencing was available from 28 and 27 tumors, respectively. **RESULTS:** Median age was 6 years (range 2–17.5), 66/70 patients had supratentorial tumors, 56 patients intratumoral hemorrhage at diagnosis. Three patients fulfilled clinical criteria of NF1; 35 had café-au-lait spots and/or freckling. DNA-methylation profiling classified 28/28 as “intracranial spindle cell sarcoma with rhabdomyosarcoma-like features and DICER1 mutations”. *DICER1* mutations were found in 26/27, *TP53* mutations in 22/27, and *RAS*-pathway gene mutations (*NF1*, *KRAS*, *NRAS*) in 19/27 tumors, all of which were somatic (germline control available in n=19 cases). Survival was analyzed in 57 patients with non-metastatic disease who received adjuvant therapy. Two patients had metastatic disease, eleven did not receive or abandoned treatment. Two-year OS was 66.3% (95%-CI: 54–81%), 2-year PFS 51% (38–67%). PFS was highest in patients treated with postoperative ICE chemotherapy followed by radiotherapy and ICE (2y-EFS 79% [59–100%], n=18) and worse after upfront radiotherapy followed by ICE (40% [19–85%]; n=10) or VAC (50% [28–88%], n=12) and radiotherapy only (21% [6–71%], n=11; p=0.008). **CONCLUSION:** Primary SCNS with *DICER1* mutation have an aggressive clinical course. A combination of chemotherapy and radiotherapy seems beneficial. A link to a cancer predisposition syndrome could not be established so far.

RARE-43. FAVORABLE OUTCOME OF A YOUNG GIRL WITH RECURRENT METASTATIC PINEOBLASTOMA ASSOCIATED WITH A DICER1 MUTATION

Adam Rossi¹, Gregory Verona², Ann Ritter³, Hope Richard⁴, India Sisler¹, and Zhihong Wang¹; ¹Pediatric Hematology Oncology, CHoR at VCU, Richmond, VA, USA, ²Department of Pediatric Radiology, CHoR at VCU, Richmond, VA, USA, ³Department of Neurosurgery, VCU, Richmond, VA, USA, ⁴Department of Pathology, VCU, Richmond, VA, USA

Pineoblastomas have been thought to portend a poor prognosis, especially in younger children or those with metastases. Long term survivors after relapse, especially for those with metastatic disease are rare. We report a young girl with a *DICER1* mutation who survived recurrent metastatic pineoblastoma. She was initially diagnosed at the age of 3 with a localized pineoblastoma, underwent gross total surgical resection, and received high dose chemotherapy with autologous stem cell transplant per COG ACNS0334 without radiation therapy. 16 months after completion of treatment, she relapsed at primary site with widespread spinal metastasis. She then received cranial spinal radiation of 3600Gy with proton beam, with boost to primary to 5580Gy, followed by chemotherapy with Temozolomide, Irinotecan and Avastin per COG ACNS0821. She is now 3 years and 3 months from completion of treatment, is doing well clinically with stable imaging findings. No particular alteration was identified from the tumor molecular testing of her initial pineoblastoma. Of note, she was diagnosed with pleuropulmonary blastoma soon after her initial diagnosis of pineoblastoma, and was found to have a *DICER1* mutation (c.2062C>T; pR688*) thought to be a nonsense mutation. While radiation therapy following recurrence is known to improve the outcome, more recent studies suggest that tumors lacking the molecular features of high grade glioma also has a positive impact on prognosis. In addition, we speculate that *DICER1*