lung cancer. All the patients received cranial radiation (range: 12–60 Gy). The median latency time between primary disease and RIG was 16 years (range: 9–30 years), which was not correlated with age at the time of primary disease. The median survival time of patients with RIG was 7 years (range: 0.3–18 years). Radiotherapy with or without chemotherapy was included in 45% of cases (67/147). Radiotherapy alone was correlated with improved survival (HR 0.65, 95% CI 0.47–0.90, p = 0.014). The median survival time of patients who received radiotherapy was 18 months (range: 0.3–48 months), while the median survival time of patients who did not receive radiotherapy was 6 months (range: 0.3–48 months).

INTRODUCTION: Malignant gliomas in children and adolescents are rare. They are difficult to treat and are associated with an extremely poor prognosis. SUBJECTS AND METHODS: The treatment and outcomes of WHO grade IV gliomas and diffuse intrinsic pontine gliomas (DIPGs) in children and adolescents (age 4–39, median 28) treated at our institute since 2001 were retrospectively reviewed. Thirty-five cases were included in this study. Nine cases were located in the brainstem and 2 of them were diagnosed as glioblastoma multiforme (GBM) clinically with DIPG. Three (3/35, 8.6%) of the cases were diagnosed histologically as glioblastoma. Expect for 2 cases, all were irradiated. Twenty-four cases were treated with temozolomide (TMZ).

HGG-40. EXCEPTIONAL SYNCHRONOUS OCCURRENCE OF A BRAF V600E MUTANT Glioblastoma and a H3 K27M MUTANT DIFFUSE INTRINSIC PONTINE GLIOMA: A CASE REPORT

Emile De Carli1, Blandine Boisselier2, Luc Le Fournier2, Stéphane Supot3, Coralie Mallebranche1, Stéphane Proust-Houdemont1, Mylene Duplan4, Isabelle Pellier2, and Audrey Rousseau1

1Pediatric Immuno-Hematology-Oncology Unit, University Hospital, Angers, France, 2Department of Cellular and Tissue Pathology, University Hospital, Angers, France, 3Center for Research in Cancers and Immunology Nantes, Angers, France, 4University of Poitiers, Angers, France, 5Department of Pediatric Neurosurgery, University Hospital, Angers, France, 6Department of Radiation Oncology, Institut de Cancérologie de l’Ouest, Nantes, St-Herblain, France, 7Center for Research in Cancers and Immunology Nantes, Angers, France, 8Center for Research in Cancers and Immunology Nantes/Angers, team 1, INSERM U1232, University of Angers, Angers, France

We report herein the case of a 17-year-old female who presented with intracranial hypertension and diplopia. Magnetic resonance imaging showed a large left cystic and solid temporoparietal lesion, associated with left temporal and occipital lobe edema. The patient presented with intracranial hypertension and diplopia. No predisposition syndrome was identified. Treatment with mTOR inhibitors was initiated. At 21-month follow-up, the patient remains with few symptoms. No predisposition syndrome was identified.

HGG-41. STRUCTURAL VARIANT DRIVERS IN PEDIATRIC HIGH-GRADe GLIOmA

Frank Dibua1,2, Ofir Shapira3,2, Noah Greenwald3,2, Travis Zdek1,2, Jessica W Tsai1,2, Ashot S. Harutyunyan2,3, Kiran Kumar2,3, Claire Smal1, Hayley Malkin1, Robert Jones1, Patricia Ho1, Ryan O’Rourke1, Kyung S Kang4, Nada Jabado1, Mark W Kieran1, Keith Ligon1,2, Pratim Bandopadhyay2,2, Dana-Farber Cancer Institute, Boston, MA, USA, 2Department of Neurology, Boston Children’s Hospital, Boston, MA, USA, 3INSERM U1232, CNRS ERL 6001, University of Nantes, Nantes, France, 4Center for Research in Cancers and Immunology Nantes/Angers, team 3, INSERM U1232, University of Angers, Angers, France

HGG-42. CLINICAL FEATURES AND TREATMENT OUTCOME OF MALIGNANT GILOMAs IN CHILDREN AND ADOLESCENTS

Hajime Yonezawa1, Hiroyuki Uchida, Naoyu Higa, Tatsuki Oyoshi, and Koji Yoshimoto2

1Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan

INTRODUCTION: Malignant gliomas in children and adolescents are rare. They are difficult to treat and are associated with an extremely poor prognosis. SUBJECTS AND METHODS: The treatment and outcomes of WHO grade IV gliomas and diffuse intrinsic pontine gliomas (DIPGs) in children and adolescents (Age 4–39, median 28) treated at our institute since 2001 were retrospectively reviewed. Thirty-five cases were included in this study. Nine cases were located in the brainstem and 2 of them were diagnosed as glioblastoma multiforme (GBM). Three (3/35, 8.6%) of the cases were diagnosed histologically as glioblastoma. Expect for 2 cases, all were irradiated. Twenty-four cases were treated with temozolomide (TMZ).

HGG-43. CONGENITAL Glioblastoma MULTIFORME: A CASE REPORT

Christina Amenu1, James Stables1, Shabbar Salama1, Erik Dedeken3, Angus grade IV) was administered as initial therapy in 1 case, radiotherapy after surgery or chemotherapy in 4 cases, and other treatments in 1 case. In total, 33/35 cases (94.3%) died within 1 year of diagnosis. Survival was not significantly correlated with age, gender, or histotype.

HGG-44. DEFECTS OF MISMATCH REPAIR PROTEINS IN PEDIATRIC HIGH GRADe GILOmAS

Christine Haberkkö,1 Philippe Muller2, Leonard Müllera, Andrea Perella3, Thomas Czeck1, Katharina Wimmer2, and Irene Slave2

1Division of Neuropathology and Neurochemistry, Department of Neurology, Medical University of Vienna, Vienna, Austria, 2Medical University of Vienna, Division of Neuropathology and Neurochemistry, Department of Neurology, Vienna, Austria, 3Clinical Institute of Pathology, University of Vienna, Vienna, Austria

CONCLUSION: As a whole, in our series, multidisciplinary treatment including surgery, radiation and chemotherapy including BEV improves outcomes.
Hetero- and homologous germline mutations of the mismatch repair genes, MLH1, MSH2 and MSH6 cause Lynch and constitutional mismatch repair (CMMRD) cancer predisposition syndrome, respectively. Affected CMMRD individuals are at risk to develop a variety of neoplasms including CNS tumors, particularly high grade gliomas (HGGs), during childhood due to an excess of CMMRD in children with pediatric HGG. We screened a consecutive series of 79 supratentorial HGGs. Tumor tissue was available in 42 patients, 5 were reclassified as non-HGGs. Immunohistochemistry with antibodies against MLH1, PMS2, MSH2 and MSH6 was performed in 37 tumors. Four patients (3 families) with known CMMRD were included. The evaluation of the slides was performed blinded to the CMMRD status. All four patients with known CMMRD (3 patients with PM2, one with MSH6 mutation) were identified, showing loss of FMS2 and MSH2/MSH6, respectively. Additionally, we identified 6 patients with loss of MSH2/MSH6 staining in tumor cells, but retained staining in preexisting cells, indicating a pattern like in Lynch syndrome. NGs sequencing of these tumor tissues revealed in 2 patients MSH2 mutations and in one patient a hypermutator phenotype with MSH2 and MSH6 mutations. In 3/6 patients no mutations in the MMR genes were detectable. In summary, we found a low prevalence of CMMRD among HGGs, but identified also 2 patients with probable Lynch syndrome. Immunohistochemistry is an effective tool to screen for patients with MMR defects and should be performed in HGGs to optimize treatment and offer affected families genetic counseling.

HGG-45. PROTEOMIC ANALYSIS OF PEDIATRIC DIFFUSE ASTROCYTOMAS YIELDS PATHWAYS ASSOCIATED WITH BOTH PROGRESSION-FREE AND OVERALL SURVIVAL

Blake Solle, Jessica Fleming, Richard Graham, Joseph McElroy, Justin Luke, Aline Moulton, Jonathan Clay, and Arnh Chakravariti; 1The Ohio State University, Columbus, OH, USA, 2St. Jude Children’s Research Hospital, Memphis, TN, USA, 3Nationwide Children’s Hospital, Columbus, OH, USA

Brain tumors are now responsible for more deaths each year than any other childhood cancer. Current studies aim to discover key molecular drivers that can explain prognosis and serve as targets for new therapeutic approaches, reducing morbidity. In this study, we performed LC-MS/MS proteomics on a cohort of 28 primary diffuse astrocytoma formalin-fixed paraffin embedded samples (WHO Grades II-IV) from patients at Nationwide Children’s Hospital with a median follow-up time of 2.3 (0.6–20.2) years. Ingenuity Pathway Analysis was used to analyze the proteomic data using age and grade as covariates and only including proteins with p-values less than 0.05. The upregulation of a well-known oncogenic pathway, the Protein Kinase A signaling pathway, was significantly associated with greater risk of progression and death (P = 3.3E-07 and P = 3.6E-07 for age and grade, respectively) in cancer, was similarly downregulated in those with greater risk of progression and death (P = 3.3E-07 and P = 3.6E-07 for age and grade, respectively). A global upstream analysis of the proteomic data also predicted activation of the oncogene MYCN in those who performed poorly, supporting previous studies. When comparing grade II (n=10) to grade III (n=8) and IV (n=10) primary tumors, the pathway most upregulated in higher histopathological grades was EIF2 Signaling (P = 4.9E-49). This pathway has previously been associated with resistance in adult glioblastoma. These pathways, and the proteins detected within, may provide novel means by which to better understand and treat pediatric diffuse gliomas. Ongoing studies are in progress to understand how these pathways drive aggressiveness and differ from adult astrocytomas.

HGG-47. DECREASED GROWTH VELOCITY WITH LONG TERM USE OF BRAFV600E AND MEK INHIBITION IN A PATIENT WITH ANAPLASTIC GANGLIOGLIOMA

Hung Tran, and Robert Cooper; Kaiser Permanente, Los Angeles, CA, USA

PURPOSE: To describe decreased growth velocity with long term use of RAFV600E and MEK inhibition in a patient with anaplastic ganglioglioma.

RESULTS: 4-year-old patient was found to have a 6 x 4.6 x 5 cm mass in the hypothalamus. Pathology consistent with anaplastic ganglioglioma. DNA from frozen and formalin fixed tissue was sequenced. Patient started on dabrafenib and trametinib and tumor decreased 85% after 3 months. She is stable without significant toxicities 39 months on therapy, and is now 8 years old. Patient had been growing at the 25% for weight and 12% for height but is now 65% for weight and 0.5% for height.

It is difficult to tease out the relationship between the tumor, the location of the tumor, and the BRAF and MEK inhibitors and their effect on growth. Discussions with the family and endocrinology are ongoing but being ≤1% for height will lead to decreased quality of life. COMBINATION BRAF-MEK inhibitor follow-up study is needed to determine if this is truly a long-term toxicity, or if this may just be a direct result of the location of the tumor. Would supplementation with growth hormone in this patient lead to losing control of a high grade tumor, or would it simply replace a hormone that is not produced?

HGG-48. ROS1 INHIBITOR ENTRECTINIB USE IN RELAPSE/REFRACTORY INFANTILE GANGLIOBLASTOMA WITH POSITIVE ROS1 FUSION - A CASE REPORT WITH PROMISING RESPONSE

Dennis Tak-Lou Kw, Matthew-Ming-Kong Shing, Godfrey Ch-Fung Chan, Eric Fu, Ping-Wa Yau, Chung-Wing Luk, King-Fai Cheng, Wilson Wai-Shing Ho, Ho-Keung Ng, Yin-Chung Po, and Alvin Su-Chieving Ling; 1Hong Kong Children’s Hospital, Hong Kong, Hong Kong, 2The University of Hong Kong, Hong Kong, Hong Kong, Chinese University of Hong Kong, Hong Kong, Hong Kong, 3Princess Margaret Hospital, Hong Kong, Hong Kong

INTRODUCTION: Infantile ganglioblastoma is rare with poor prognosis. Recent molecular study for infantile hemispheric high grade glioma found its association with ALK/ROS1/NTRK/MET pathway. This suggested the potential use of targeted therapy for refractory / relapse patients. CASE: A newborn presented with apnea, CT brain showed intracranial haemorrhage. MRI then showed a left parietal tumour with bleeding and mass effect. Surgery achieved subtotal resection. Chemotherapy alternating with CDDP/VP-16 was given for one year. Patient was stable with static residual tumour during chemotherapy. However patient developed status epilepticus two weeks after off treatment. MRI showed significant tumour progression which required 2nd & 3rd debulking surgery. Molecular assay by nanostring panel showed BRAF-KIAA1543 fusion. MEK inhibitor Trametinib was tried for 3 months and stopped as disease progression. Further molecular assay by RNAseq showed presence of ROS1 fusion (ZNCH8-RSOS1) while absent of BRAF fusion. Patient underwent 4th debulking surgery as impending herniation while waiting for the targeted therapy. It was complicated with right hemiplegia and facial nerve palsy postoperatively. Finally, ROS1 inhibitor Entrectinib was started 2 weeks later. It was well tolerated without significant adverse reaction. Patient made dramatic neurological recovery including improved facial nerve palsy, able to walk unaided and self feed. MRI brain 1 and 3 months after Entrectinib showed interval reduction in residual tumour. Patient is currently progression-free for 6 months. CONCLUSION: Early molecular study for infantile ganglioblastoma is useful to guide novel therapy. Molecular result may varies between different panels or change over time, to be interpreted with caution.

HGG-49. A PEDIATRIC THALAMIC HIGH-GRADE GLIOMA WITH H3F3A K27M AND BRAF V600E DOUBLE MUTATIONS

Kenta Terada,1 Masahiro Sugawa,1 Kenichi Sakamoto,2 Takakito Kyotani,1 Tomosuke Gorai,1 Takeru Nakamura,1 Takao Yano,1 Yoshikazu Kojima,1 Hiroshi Fujii,1 Noriyuki Nakano,1 Takako Yoshiba,1 Tetsuya Deguchi,1 Motohiko Kato,1 Daisuke Tomuzawa,1 Kenichi Usami,1 Hideki Ogawara,2 Yoshihiko Tsutsumi,1 Hiroshi Fujii,1 Noriyuki Nakano,1 Takako Yoshiba,1 Yosuko Nakano2, Koichi Ichimura,2 and Kimikazu Matsumoto2; 1Children’s Cancer Center, National Center for Child Health and Development, Tokyo, Japan, 2Department of Neurosurgery, National Center for Child Health and Development, Tokyo, Japan, 3Department of Diagnostic Radiology, National Center for Child Health and Development, Tokyo, Japan, 4Department of Radiation Oncology, National Center for Child Health and Development, Tokyo, Japan, 5Department of Pathology, National Center for Child Health and Development, Tokyo, Japan, 6Division of Brain Tumor Translational Research, National Cancer Center Research Institute, Tokyo, Japan

CASE: A 18-month-old boy presented with approximately 2 months history of progressive left hemiparesis and left exotropia. MRI study showed a 4-5 cm T1 iso, T2-hypointense tumor at right thalamus to midbrain with little contrast enhancement. The patient underwent endoscopic biopsy of the tumor, which showed relatively dense proliferation of small cells with round nuclei, mitosis of the tumor cell, but no necrosis. Immunohistochemical showed positive stain of GFAP and Olig2. Ki-67 was 34%. The histopathological diagnosis was compatible with high grade glioma. Chemotherapy with vincristine, cyclophosphamide, cisplatin and etoposide was initiated. Molecular testing of the tumor revealed H3F3A K27M and BRAF V600E double mutation (ZNCH8-RSOS1). The patient underwent 1st surgery where complete resection was achieved. Further molecular assay by RNASeq showed presence of ROS1 fusion (ZNCH8-RSOS1) while absent of BRAF fusion. Patient underwent 2nd surgery as impending herniation while waiting for the targeted therapy. Molecular assay by nanostring panel showed BRAF-KIAA1543 fusion. MEK inhibitor Trametinib was tried for 3 months and stopped as disease progression. Further molecular assay by RNAseq showed presence of ROS1 fusion (ZNCH8-RSOS1) while absent of BRAF fusion. Patient underwent 4th debulking surgery as impending herniation while waiting for the targeted therapy. It was complicated with right hemiplegia and facial nerve palsy postoperatively. Finally, ROS1 inhibitor Entrectinib was started 2 weeks later. It was well tolerated without significant adverse reaction. Patient made dramatic neurological recovery including improved facial nerve palsy, able to walk unaided and self feed. MRI brain 1 and 3 months after Entrectinib showed interval reduction in residual tumour. Patient is currently progression-free for 6 months. CONCLUSION: Early molecular study for infantile ganglioblastoma is useful to guide novel therapy. Molecular result may varies between different panels or change over time, to be interpreted with caution.