geted agents are increasingly being utilized to treat LGG, but the effect of these agents on accompanying neurologic complications are poorly understood. CASE: An 8-years old male with Neurofibromatosis Type 1 (NF1), medically refractory epilepsy and deep extensive glioma (extending from the optic pathway and involving the basal ganglia and corpus collosum) began selumetinib therapy due to radiographic and symptomatic tumor progression. Radiographic response (resolution of enhancement) was observed at 12 weeks of therapy, accompanied by improvement in seizure frequency, hemiparesis, and academic performance. Due to cardiotoxicity observed at that time (asymptomatic decreased ejection fraction and shortening fraction on echocardiogram), selumetinib was reduced to 50% dosing. On this reduced dose of selumetinib, seizures increased in frequency with subsequent worsening hemiparesis and recurrence of learning difficulties. One month later, dosing was escalated back to 100% due to interval resolution of cardiotoxicity, resulting in resolution of seizures and improvement in focal neurologic deficits and cognition. DISCUSSION: Dose-dependent response to MEK inhibition was observed without concurrent changes in anti-epileptic medications. The tumor was stable in size despite improved enhancement with treatment, suggesting that objective response by RANO criteria is not necessary for improved seizure control in LGG. Recent work has implicated the RAS/MEK/ERK pathway in neuronal precursor cells as a cause for epilepsy, suggesting that MEK inhibition of NF1-heterozygous neurons could be contributing to treatment response in this patient. Improvements in weakness and academic performance may have been due to improved seizure control or a direct effect of MEK inhibition on NF1-heterozygous neurons. CONCLUSION: MEK inhibition may have a clinically relevant anti-seizure effect for patients with pediatric LGG or NF1.

LGG-39. ASCITES IN A MEDULLARY AND LEPTOMENINGEAL GANGLIOGLIOMA PATIENT FOLLOWING CISPLATIN TREATMENT NECESSITATING CESSATION OF THERAPY AND CONVERSION TO VA SHUNT

Evan Cantor, Andrea Ogle, Ashley Meyer, Margaret Shatara, Nicole M. Brossier, Mohamed S. Abdelbaki, Jennifer Strahle, Andrew Cluster; Saint Louis Children's Hospital, St. Louis, MO, USA

INTRODUCTION: Ganglioglioma is a low grade neoplasm consisting of dysplastic neuronal and neoplastic glial cells and accounts for 5% of pediatric CNS tumors. Management often includes CNS diversion. There have been case reports in which platinum containing chemotherapy has been thought to contribute to CSF malabsorption leading to ascites. CASE: A 13 month old male developed progressive macrocephaly, developmental delay, chronic emesis, and intermittent bilateral cranial nerve VI palsy over the 5 months prior to presentation. MRI brain/spine was significant for an enhancing nodule in the left posterior lateral medulla, nodular thickening and enhancement along the brainstem down to the conus medullaris and in the tentorium, with associated hydrocephalus. Biopsy of the medullary nodule and of the enhancement were consistent with ganglioglioma with BRAF-KIAA1549 fusion, equivocal MYCN amplification, and no BRAF V600E mutation. A ventriculo-peritoneal shunt was placed at the time of biopsy. Therapy was initiated with vincristine (1.5 mg/m2) and carboplatin (175 mg/m2.) Following the 12 week induction phase of therapy, he developed increasing diarrhea, emesis, and abdominal ascites. Peritoneal fluid analysis had no malignant cells and low protein compared to CSF. Ascites was responsive to drainage but would rapidly re-accumulate. Ultimately the patient's chemotherapy was discontinued after 2 maintenance cycles due to continued symptoms. Acetazolamide was trialed but discontinued due to side effects, so its efficacy could not be determined. He underwent shunt externalization followed by venticulo-atrial (VA) shunt re-internalization. He has not had ascites since that time, at 4 months from surgery. His CNS disease burden has been stable at 6 months off therapy. DISCUSSION: Ascites was most likely due to CSF malabsorption in the abdomen with a possible contribution from platinum containing chemotherapy and less likely secondary to malignant peritoneal cells. Resolution since VA shunt internalization makes alternate explanations less likely.

LGG-40. GROWTH HORMONE REPLACEMENT IN CHILDREN ON THERAPY WITH VEMURAFENIB FOR LOW GRADE GLIOMA

Antonio Verrico[1], Marco Crocco[1], Emilio Casalini[2], Antonia Ramaglia[3], Andrea Rossi[3], Valentina Iurilli[4], Gianluca Piccolo[1], Claudia Milanaccio[1], Maria Luisa Garrè[1], Natascia Di Iorgi[2]; [1]Neuro-Oncology Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy. [2]Endocrinology Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy. [3]Neuroradiology Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy. [4]Pharmacy, IRCCS Istituto Giannina Gaslini, Genoa, Italy

BRAF inhibitors (iBRAF) are a therapeutical option for pediatric Low-Grade-Gliomas (pLGG), but their chronic use may be needed to prevent tumor regrowth. Growth hormone (GH) replacement in children with GH deficiency (GHD) and on oncological treatment is under debate. We report on our experience of recombinant human GH (rhGH) replacement in two children (1 Female, 1 Male) which started Vemurafenib therapy, at 5 (F) and 9,25 (M) years of age, for recurrent/progressive chiasmatic-hypothalamic pLGG, with partial response (RANO criteria) and subsequent stable disease. A diagnosis of GHD was established at 9,2 (F) and 11,2 (M) years of age (GH peaks to stimulation tests <3mcg/L), 4,2 (F) and 1,9 (M) years after Vemurafenib start. Both patients were treated with GnRH analogues for precocious puberty. rhGH dose was titrated to 0.020 mg/kg/day during follow-up based on IGF-1 levels < +2 SDS. Height remained stable in both (F: -3,4SDS; M: 0SDS), with a mean growth velocity after 2 years around 6 cm/yr. BMI increased in the F (1,59 to 1,78 SDS) and decreased in the M (2,66 to 2,56 SDS); Dual-X-ray absorbiometry confirmed high fat mass at T0 (F:54,6%; M:48%) and at T24 (F:49,2%; M:48,1%). Lipid profile improved in both patients (F: Triglycerides 175 to 152 mg/dl, LDL 195 to 155 mg/dl; M: Triglycerides 138 to 118 mg/dl, LDL 147 to 147 mg/dl, at T0 and T24, respectively), while baseline blood glucose increased (F: 83 to 96 mg/dl; M 82 to 91 mg/dl). Residual tumor was stable in both patients. CONCLUSIONS: In 2 GHD patients due to pLGG and treated with Vemurafenib, two-years of low-dose rhGH showed beneficial effects on height stabilization and on lipid profile, and a different impact on body composition parameters; rhGH was safe and not associated with residual tumor growth.

LGG-41. THE CLINICAL AND MOLECULAR LANDSCAPE OF GLIOMAS IN ADOLESCENTS AND YOUNG ADULTS

Julie Bennett[1], Liana Nobre[1], Javal Sheth[1], Scott Ryall[1], Karen Fang[1], Monique Johnson[1], Logine Negm[1], Jiil Chung[1], Martin Komosa[1], Nuno M. Nunes[1], Mary Jane Lim Fat[2], James Perry[2], Arjun Sahgal[2], Jay Detsky[2], Eric Bouffet[1], Lili Naz-Hazrati[1], Peter Dirks[1], Birgit Ertl-Wagner[1], Paul Kongkham[3], Gelareh Zadeh[3], Warren Mason[3], Seth Climans[4], Michael Cusimano[5], Sunit Das[5], Andrew Gao[3], Derek Tsang[3], Lananh Nguyen[5], Normand Laperriere[3], Julia Keith[2], David Munoz[5], Uri Tabori[1], Cynthia Hawkins[1]; [1]The Hospital for Sick Children, Toronto, Ontario, Canada. [2]Sunnybrook Health Sciences Center, Toronto, Ontario, Canada. [3]University Health Network, Toronto, Ontario, Canada. [4]London Health Sciences Center, London, Ontario, Canada. [5]Unity Health, Toronto, Ontario, Canada

OBJECTIVE: Gliomas in adolescents and young adults (AYA) are commonly treated with a standard chemo-radiation approach based on data from adults. The clinical impact of paediatric-type alterations in these tumours is unknown. METHODS: We compiled a multi-institutional cohort of patients diagnosed with glioma between 15-39.9 years over 20 years. Complete molecular analysis, therapeutic data and outcome was collected. For specific alterations, analysis included patients aged 0-39.9 years. RESULTS: A total of 1900 patients with 876 AYA gliomas were included. Ongoing analysis reveals genetic alterations in 95% of available tumours. IDH-mutant tumours account for only 53%, while paediatric-type mutations were found in 35% of AYA tumours with IDH-WT GBM accounting for the remaining 12%. The most common paediatric alterations in AYAs included BRAF p.V600E (11%) and FGFR alterations (6%) while BRAF fusions, H3 p.K27M and H3.3 p.G34R were rarely observed (4%, 4% and 1% respectively). BRAF fused tumours with non-canonical binding partners were enriched in AYAs. Analysis of BRAF-V600E gliomas between ages 0-40 revealed increased tendency for malignant tumours in patients >20 years suggesting malignant transformation possibly due to higher rate of secondary hits including TP53, CDKN2A and ATRX mutations. This resulted in worse overall-survival for AYA patients with BRAF-V600E glioma when compared to children under 20 years (p=0.0032). Ten-year OS of 100%, 90% and 95% was seen for BRAF fused, BRAF-V600E and FGFR-altered AYA low grade glioma respectively, compared to 14% and 25% for BRAF-V600E and FGFR-altered high grade glioma. In contrast, continuous decline was observed in the IDH-mutant gliomas with 10-year OS of 50% which declined to 29% at 15 years. CONCLUSIONS: Gliomas in AYA are enriched for paediatric-type alterations with distinct molecularly-based outcomes. As these tumours carry different outcomes than childhood glioma and may respond to targeted inhibitors, AYA gliomas would benefit from comprehensive diagnostic and therapeutic approaches.

LGG-42. THROMBOEMBOLIC TOXICITY OBSERVED WITH CONCURRENT TRAMETINIB AND LENALIDOMIDE THERAPY

Priya Chan[1], Ashley Sabus[2], Molly Hemenway[3], Kathryn Chatfield[3], Nicholas Foreman[3], Nathan Dahl[3]; [1]Department of Pediatrics, University of Utah, Salt Lake City, UT, USA. [2]Department of Pharmacy, Children's Hospital Colorado, Aurora, CO, USA. [3]Department of Pediatrics, Children's Hospital Colorado, University of Colorado Anschutz Medical Campus, Aurora, CO, USA

INTRODUCTION: Event-free survival of pediatric low-grade glioma (pLGG) is poor, and patients often require multiple treatment strategies. The hallmark of pLGGs are genetic aberrations of the mitogen-activated protein kinase pathway, which lead to constitutive pathway activation. MEK and