Abstracts

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PURPOSE: Primary spinal low-grade gliomas (LGGs) are rare, can be difficult to treat, and can result in significant morbidity. The management of pediatric spinal LGGs remains controversial. METHODS: A national multi-centre retrospective review of spinal LGGs diagnosed in children less than 18 years of age between 1981 and 2015 was undertaken to examine the clinicopathological subtypes, and treatment outcomes. RESULTS: Forty-three patients from five institutions were included. The median age of diagnosis was 5.2 years. All patients were symptomatic at diagnosis. Forty-four percent of patients were diagnosed at 6 months after symptoms developed. Two patients were metastatic disease at diagnosis. The most common histology was pilocytic astrocytoma (48.8%). Molecular information was available for 15/43 patients: 6 patients had BRAF fusions and 4 patients had BRAF V600E mutations. Gross-total resection was achievable in only 6 patients. Twenty-seven patients were treated with chemotherapy and/or radiation, and the others with surgery. Eleven patients were irradiated. No patients were registered in clinical trials for first-line therapy. Twenty-three patients experienced relapse or progression. Patients were followed for a median of 8.3 years (range, 0.3–20.4 years). Five-year progression-free survival (PFS) and overall survival (OS) rates were 48.3% (95% CI, 32.3% to 62.5%) and 89.7% (95% CI, 74.6% to 96.1%) respectively. CONCLUSION: There is significant heterogeneity in surgical outcomes and treatment modalities of pediatric spinal LGGs. The PFS and OS rates remain suboptimal, likely due to tumor location. The low clinical trial enrollment rate highlights the paucity of available trials for spinal LGGs.

LGG-20. CLINICAL FEATURES AND TREATMENT RESULTS FOR PEDIATRIC OPTICO-HYPOTHALAMIC ASTROCYTOMA

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Current consensus for the treatment of optico-hypothalamic astrocytoma (OHA) is a chemotherapy-first policy, limiting the role of surgery for histopathological diagnosis and partial decompression. However, a subgroup of OHA patients show resistance to chemotherapy and have a worse prognosis. In this study, we retrospectively analyzed our clinical experiences of the treatment of patients with OHA in two university hospitals. We have extracted and analyzed the medical charts of 15 pediatric OHA patients treated in two university hospitals since 1990. NF-1-associated OHA patients were excluded. Patient ages ranged from 10 months to 21 years (median 7 years). Out of 15 cases, 12 patients had a tumor larger than 3 cm and classified as Dodge 3. The histopathological diagnosis was pilocytic astrocytoma in 13 cases. Three patients with tumors classified as Dodge 1 or 2 show good prognosis only by biopsy or partial resection. However, regarding Dodge 3 tumor, patient prognosis is generally regarded as chemotherapy and radiotherapy. After the initial surgery, chemotherapy was administered in 11 cases and radiotherapy in 5 cases. Multiple surgeries are needed for tumor control in 7 patients. Four patients died of tumor progression or treatment-related complications. When the initial tumor is large enough to cause neurological deterioration, a chemotherapeutic tumor suppressive effect might be limited in a subset of large OHA cases. Therefore, it is important to consider the proper timing of safe surgical decompression in the early phase when a large tumor does not respond to chemotherapy.

LGG-21. MR-GUIDED LATERAL INTERSTITIAL THERMAL THERAPY FOR UNRESECTABLE AND SYMPTOMATIC PEDIATRIC LOW GRADE GLIOMA

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BACKGROUND: Pediatric low-grade gliomas (LGG) not amenable to resection, while often indolent, represent a significant source of cancer-related morbidity and an unmet therapeutic need. Typically, these patients are treated with multimodal therapy with advancements in chemotherapeutic and radiation therapy. The potential for minimally invasive percutaneous thermal therapies is often limited in the inoperable pediatric population. Magnetic resonance-guided laser interstitial thermal therapy (LITT) is a minimally invasive procedure that utilizes real-time MR thermography to ablate brain lesions. METHODS: A 15-year-old girl was diagnosed with a suprasellar, hypothalamic LGG, BRAF V600E mutation positive. The tumor was unresectable, and due to progressive vision loss and headaches, the patient continued to experience debilitating headaches, malnutrition, school absenteeism, and overall poor quality-of-life. Using real-time, sequential MRI-thermometry and the Neuroblate cooled directional laser catheter, the bulk of the enhancing tumor was heated to a killing temperature. RESULTS: At 1-year post-LITT, the patient’s symptoms were dramatically improved, including greatly im-

proved headaches, malnutrition, school absenteeism, and overall quality of life. LITT was generally well tolerated, though the patient had slight progressive left homonymous hemianopia, thought secondary to LITT impact on the pregressively shrank over time. Post-LITT to a peak of 42% volume reduction. CONCLUSION: We report a case of a pediatric patient with an unresectable low grade glioma who underwent LITT with excellent clinical and radiographic effects. LITT should be considered for children with unresectable and morbid LGGs that fail to respond to more conventional therapies.

LGG-22. EVALUATION OF IMMUNE AND GENOMIC CHARACTERISTICS IN PEDIATRIC OPTIC NERVE GLIOMA (ONG) ASHLEY A. Campbell1,2, Andrew M. Silverman1, Hanna Moisander-Joyce1, Cheng-Chia Wu1, Mahesh Mansukhani1, George Zanazza1, Andrew Turk1, Peter D. Canoll1, James H. Garvin1, and Robyn D. Gartrell-Corrado1

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Pediatric optic nerve glioma (ONG) is a rare, sight-threatening tumor. We previously reported clinical, radiologic, histopathologic, and molecular characteristics of pediatric ONG patients treated at Columbia University Medical Center between 2008-2017. Here we evaluated the greatest additional patient using quantitative multiplex immunofluorescence (qmIF) and next generation sequencing (NGS) using the Columbia Combined Cancer Panel (CCCCP). For qmIF, 4 micron immunomark-blank slides were stained for CD3, CD8, CD68, CD163, HLA-DR, and Olig2. qmIF images were analyzed and data were processed in R studio and compared based on tumor mutation and treatment history. QmIF failed in 1 case and CCGP failed in 2 cases. CCGP confirmed KIAA1549:BRAF fusions in 2 patients, identified NF1 in 2 patients, and demonstrated both a KIAA1549:BRAF fusion and SETD2 mutation in the added case. Qualitative analysis showed immune infiltrate across cases included macrophages (CD68+, 1.6-6.5% of all cells) and T cells (CD3+, 0.4% to 1.3%). Non-lytotoxic T cells (CD3+CD8-) comprised more than 100% of the T cell compartment and have a worse prognosis when comparing mutation groups. However, patients who previously received radiation had increased CD3+, specifically CD3+CD8+ cells compared to non-irradiated patients (p=0.01 and p<0.01, respectively) while CD3+CD8+ and CD68+ cells were not different between groups (p=0.49 and p=0.27, respectively). In summary, qmIF analysis showed increased tumor infiltration by non-lytotoxic T cells in previously irradiated pediatric ONG patients compared to non-irradiated patients, while there was no difference in macrophages of cytotoxic T cells. This type of analysis may be useful in designing immunotherapeutic strategies for pediatric ONG.

LGG-23. EXCELLENT CLINICAL / RADIOLOGICAL RESPONSE TO BRAF INHIBITION IN A YOUNG CHILD WITH IN-OPERABLE SUPRA-SELLAR PILOCYTIC ASTROCYTOMA

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Inoperable low grade gliomas (LGG) in the pediatric population continue to present a treatment dilemma. Due to the low-grade nature of these tumors, and variable response to chemotherapy / radiation, the choice of adjuvant treatment is difficult. Overall survival is directly related to the degree of surgical resection, adding complexity to these inoperable tumors. Current chemotherapeutic regimen for these inoperable tumors includes vincristine (VCR) and carboplatin (Carbo). With advancements in the molecular characterization of gliomas, the role of targeted therapy has come into question. We present a 2-year-old female with biopsy proven Pilocytic Astrocytoma (positive BRAF-V600E mutation) involving the hypothalamus/optic chiasm region. She presented with ataxic gait, at-hemiparesis, obstructive hydrocephalus and central hypothyroidism, which progressed to altered consciousness, and right hemiparesis due to location/ mass effect of the tumor. She was initially treated with chemotherapy (VCR/ Carbo) but her tumor progressed at 6 weeks of treatment. As her tumor was pos-

itive for BRAF-V600E mutation, it was started on dabrafenib monotherapy, resulting in dramatic improvement in her clinical symptoms (able to stand, im-

proved vision), and a 60% reduction in tumor size at 3-months. At 6-months,

resulting in dramatic improvement in her clinical symptoms (able to stand, im-

proved vision), and a 60% reduction in tumor size at 3-months. At 6-months,
BRAF-V600E mutations may benefit from upfront targeted therapy. Prospective clinical trials comparing the efficacy of BRAF inhibitors versus standard chemotherapy in LGG with BRAF mutations are urgently needed.

LGG-24. CARBOPlatin-INDUCED HEMATURIA IN A PEDIATRIC PATIENT WITH LOW-GRADE GLIOMA AND REVIEW OF LITERATURE
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OBJECTIVE: In this case report, we present a pediatric patient with gross hematuria and hydroureteronephrosis associated with high dose carboplatin. Given the paucity of literature on the subject, we also conduct and present a review of cases. CASE PRESENTATION: A 6-year-old Caucasian female with history of Type 1 neurofibromatosis was undergoing treatment for a low-grade glioma with monthly high dose carboplatin (560 mg/m²). After 8th dose out of 13, the patient developed severe nausea and vomiting and was admitted for dehydration. She was noted to have microscopic hematuria. After 9th dose, the patient again developed severe nausea, vomiting and gross hematuria with clots. She was admitted and treated with IV hydration. Renal ultrasound showed further increased size of the right kidney. Urine cultures and viral studies were normal. Literature review revealed only 4 reported cases of carboplatin-induced hematuria, including only one pediatric case that occurred in a patient with concurrent thrombocytopenia. Carboplatin may exhibit toxicity to the transitional epithelial cells of the urinary tract causing hematuria from the renal pelvis and ureters. If untreated, this may lead to urinary outflow obstruction and subsequent obstructive nephropathy. CONCLUSION: We present a rare toxicity, gross hematuria caused by high-dose carboplatin treatment. Providers should be aware of this rare toxicity and provide timely hydration and supportive care to prevent development of obstructive kidney injury and/or renal failure.

LGG-25. A PHASE 2 STUDY OF TRAMETINIB FOR PATIENTS WITH PEDIATRIC GLIOMA WITH ACTIVATION OF THE MAPK/ERK PATHWAY. TRAM-01
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BACKGROUND: Pediatric low-grade gliomas (PLGG) are the most frequent brain tumors in children. It is now known that the majority of PLGG have activation of the MAPK/ERK pathway. We hypothesize that we will observe responses in recurrent/refractory PLGG treated with trametinib. METHODS: This is a multicenter phase II including three pediatric PLGG groups: NF1 patients, KIAA1549-BRAF fusion patients and patients with other activation of the MAPK/ERK pathway (excluding V600E). Patients will receive daily oral trametinib for a total of 18 cycles of 28 days. A total of 104 patients will be enrolled in seven Canadian centers. Secondary objectives include the assessment of safety, tumor response, overall survival and progression-free survival, tolerability of trametinib, serum levels of trametinib and evaluation of quality of life during treatment. RESULTS: As of January 7, 2020, 28 patients have been enrolled (NF1: 6 patients, KIAA1549-BRAF fusion: 17, other: 5 including 3 patients FGFR1 alteration). Median age is 8.5 years (range 2.5–25.4 years). Median follow-up is currently 4.6 months (range 0.16–14.7 months). Twenty patients are currently evaluable. Best response includes: 1 complete response (5%), 3 partial response (15%), 4 minor response (20%), 8 stable disease (40%), 4 progressive disease (14%), 8 patients (28.5%) discontinued treatment: 4 for progressive disease, 3 adverse event (alanine aminotransferase increase), 1 withdrew. CONCLUSION: Trametinib is potential effective targeted therapy for patients with refractory/refractory PLGG. Overall treatment is well tolerated. This ongoing trial will continue to gather data on response rate, duration of response and safety of trametinib for PLGG.

LGG-26. DIFFUSE LEPTOMENINGEAL GLIONEURONAL TUMOR (DLGNT) IN CHILDREN: DIFFERENT CLINICAL PRESENTATIONS AND OUTCOMES
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Diffuse leptomeningeal glioneuronal tumor (DLGNT) is an extremely rare disease, newly recognized in the 2016 WHO classification of tumors of the CNS. Most DLGNTs are low-grade neuroepithelial tumors with variable elements of neuronal/neurorocytic and glial differentiation, have diffuse leptomeningeal, and typically harbor BRAF V600E fusions. Other alterations, such as the BRAF V600E substitution, are less common. Here, we present three cases of DLGNT with different presentations and outcomes. The first patient is a 2y-old male with KIAA1549-BRAF fusion, and was treated with Carboplatin chemotherapy after a biopsy, with resultant ongoing stable disease for 3.5 years. The second patient, an 8y-old male had the BRAF V600E point mutation and was treated with conventional chemotherapy (VCR/carboplatin). On progression, he received the BRAF inhibitor vemurafenib, achieving a complete response which lasted 14 months. The third patient, a 27 month old male, harbored a KIAA1549-BRAF fusion and was treated at diagnosis with the MEK inhibitor trametinib. The tumor has been radiographically stable in the context of clinical improvement for 21 months since the treatment initiation ongoing 24 month. In summary, we present further evidence of MAPK pathway alterations in children with DLGNT. We describe a range of molecular presentations and clinical outcomes, including one patient presented with conventional chemotherapy with further stabilization of disease during 3.5 years and two patients who were successfully treated with targeted therapy.

LGG-27. TARGETED THERAPY FOR PEDIATRIC LOW-GRADE GLIOMAS AND PLEXIFORM NEUROFIBROMAS WITH TRAMETINIB
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BACKGROUND: Targeted therapy aimed at modulating the RAS/RAF/MEK/ERK pathway is of increasing interest for patients with plexiform neurofibromas and low-grade gliomas. Trametinib is an FDA-approved MEK inhibitor that has little published pediatric experience to date. METHODS: A retrospective chart review of patients treated with trametinib for low-grade gliomas (LGG) and/or plexiform neurofibromas (PN) between 2015–2018 was conducted at Children's Hospital Colorado. Data collected included patient demographics, lesion location, Neurofibromatosis type 1 (NF1) status, best response of PN/LGG to trametinib, duration of trametinib therapy, and reported toxicities at least possibly at trametinib. RESULTS: Thirty (57% male; 73% NF1) patients were identified. Sixteen (53%) patients had PN only, 12 (40%) had LGG only, and two (7%) patients had both PN and LGG. The most common LGG location was the optic pathway/hypothalamus (72%). The most common location of PN was the face (63%). Two-thirds (8/12) of patients with LGG had a BRAF alteration or NF1 mutation. The median age at start of trametinib therapy was 9.9 years (range, 2.0 – 18.8 years). The median duration of trametinib therapy was 0.8 years (range 0.1 – 2.9 years). The most commonly reported adverse event was rash. No patients developed retinotoxicity or cardiotoxicity. Only two (7%) patients discontinued trametinib therapy one (3%) for progressive disease. CONCLUSIONS: Trametinib can be administered without significant toxicity to children with PN or LGG. Clinical benefit is noted in this cohort; however, prospective clinical trials are necessary to characterize efficacy formally.