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Pediatric Low-grade gliomas (PLGGs) are extremely heterogeneous tumors and account for approximately 35% of childhood brain tumors. This retrospective study on 55 newly diagnosed children (<14 ys) with pathologically confirmed LGG from 2006 to 2016 aimed to review demographic data, clinical and therapeutic aspects and treatment outcome of PLGGs in children in Saudi Arabia. RESULTS: 33 (60.0%) males,22 (40.0%) females, median age at diagnosis 68 months. Pilocytic astrocytoma was the most common pathological diagnosis 42 (76.4%) location of tumor was Infratentorial in 30 patients (54.0%) and Supratentorial in 24 patients (43.2%), 19 patients (34.6%) had total surgical excision, 10 (18.2%) subtotal resection, 20 (36.4%) partial excision and 6 (10.9%) had biopsy only; After initial Surgery 30 patients (54.5%) required adjuvant chemotherapy of whom 14 patients (46.7%) experienced a treatment failure event, 25 patients (45.5%) who were initially observed post surgery 6 patients (24%) of them had relapse /progression and required further therapy. Only 2 patients (3.6%) received radiotherapy due to uncontrolled progression first line chemotherapy carboplatin and vincristine (CV) regimen was tolerated, Carboplatin allergic reactions developed in 21.1% of patients. Median follow-up of 6.49 years, the median time of relapse/ progression was 2.85 years The 5-year overall survival (OS) rates and progression free survival for all patients were 92.2 %, and 63.3% respectively. This study was to document the outcome of pediatric LGG in Saudi Arabia and to serve as a guideline for the future management with incorporation of molecular studies on pediatric LGGs which may help improve the outcome for Saudi children with LGG.

LGG-16. PILOMYXOID ASTROCYTOMA OF THE CERVICAL SPINAL CORD IN A 7-YEAR-OLD ARMENIAN BOY: A CASE REPORT

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BACKGROUND: Pilomyxoid astrocytoma (PMA) is a glial tumor that occurs predominantly in the hypothalamic-chiasmatic region and rarely in spinal cord. It has similar features as pilocytic astrocytomas, with some distinct histological characteristics and worse prognosis. The 2007 WHO recognized PMA as a Grade II glioma due to its aggressive behavior and dissemination tendency, but according to 2016 version grading of the pilomyxoid variant is under research. Here we report a case with a rare location, aggressive behavior and rapid progression. CASE PRESENTATION: A 7-year-old boy presented with headache, nausea, vomiting. Imaging revealed an intramedullary tumor extending from C2 to C6 with hydrocephalus. A ventriculo-peritoneal shunt and complete surgical resection were performed with significant improvement in the patient's condition. Histopathological findings were consistent with pilomyxoid variant of pilocytic astrocytoma, with negative BRAF V600E and MGMT. Three months later, the follow-up imaging revealed disease recurrence with leptomeningeal metastases, for which the patient received standard-dose craniospinal irradiation 35.2 Gy with boosts to tumor bed and metastatic sites 49.6 Gy and 54 Gy respectively. 11 months later tumor progression was revealed with new metastatic lesions in the bones. Patient received 6 cycles of chemotherapy with TMZ and Avastin, but continued to suffer disease progression on therapy and he succumbed to his disease at 24 months from diagnosis. CONCLUSION: Given the rarity of documented patients with spinal pilomyxoid astrocytoma with rapid progression, as well as the lack of certain WHO classification and treatment guidelines, this case report might be useful for development of more efficient treatment strategies.

LGG-17. SYNERGISTIC ACTIVITY OF MAPK INHIBITOR CLASSES REVEALED BY A NOVEL CELL-BASED MAPK ACTIVITY PEDIATRIC LOW-GRADE GLIOMA ASSAY

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Pilocytic astrocytomas (PAs) and other pediatric low-grade gliomas (pLGGs) exhibit aberrant activation of the MAPK signaling pathway caused by genetic alterations, most commonly KIAA1549:BRAF fusions, BRAF V600E and NF1 mutations. In such a single-pathway disease, novel drugs targeting the MAPK pathway (MAPKi) are prime candidates for treatment. We developed an assay suitable for pre-clinical testing of MAPKi in pLGGs, aiming at the identification of novel MAPK pathway suppressing synergistic drug combinations. We generated a reporter plasmid (pDIPZ) expressing destabilized firefly luciferase driven by a MAPK-responsive ELK-1-binding element, packaged in a lentiviral vector system. We stably transfected pediatric glioma cell lines with a BRAF fusion (DKFZ-BT66) and a BRAFV600E mutation (BT-40) background, respectively. Measurement of MAPK pathway activity was performed using the luciferase reporter. pERK protein levels were detected for validation. We performed a screen of a MAPKi library and calculated Combination Indices of selected combinations. The MAPKi library screen revealed MEK inhibitors as the class inhibiting the pathway with the lowest IC50s, followed by ERK and second generation RAF inhibitors. Synergistic effects in both BRAF-fusion and BRAFV600E mutation backgrounds were observed following combination treatments with different MAPKi classes (RAFi/MEKi, > RAFi/ERKi > MEKi/ERKi). We have generated a novel reporter assay for medium- to high-throughput pre-clinical drug testing of MAPKi in pLGG cell lines. MEK, ERK and next-generation RAF inhibitors were confirmed as potential treatment approaches for KIAA1549:BRAF and BRAFV600E mutated pLGGs. Synergistic suppression of MAPK pathway activity upon combination treatments was revealed using our assay in addition.

LGG-18. EVEROLIMUS TREATMENT IN PEDIATRIC PATIENTS AFFECTED BY LOW-GRADE GLIOMAS (PLGG) NON-TSC, BRAF V600-WT

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BACKGROUND: MAPK pathway is the hallmark of pediatric low grade gliomas (pLGGs); hyperactivation of mTOR (mammalian target of rapamycin) might be a suitable biomarker for therapeutic response. We investigated the feasibility of Everolimus, mTOR inhibitor, in patients affected by pLGGs. METHODS: Patients 1 to 18 years old, diagnosed with pLGG, with a positive tumor biopsy for mTOR/phospho-mTOR and radiological and / or clinical disease progression, treated at Bambino Gesù Children's Hospital in Rome were evaluated. Tumor DNA methylation analysis was performed in 10 cases. Exclusion criteria included: Tuberous Sclerosis patients, Sub Ependymal Giant Astrocytoma. Everolimus was administered orally at a dose of 2.5 mg or 5 mg daily based on body weight. Patients were evaluated with brain MRI every 4, 8 and 12 months after treatment start and every six months thereafter. RESULTS: 16 patients were enrolled from September 2014 and 2019. The median age was 7.5 years old. All patients had at least one adverse event. Events rated as severe (grade 3/4) were reported in 6 patients. Stomatitis was the most frequent adverse event. One patient discontinued treatment due to grade 4 toxicity (ulcerative stomatitis and fatigue). The median duration of treatment was 21 months (4–57 months). Brain MRI evaluations have showed disease stability in 11 patients, partial response in 2 patients and disease progression in 3 patients. CONCLUSIONS: Everolimus has proven to be well tolerated and effective treatment in terms of disease stability in patients with pLGGs. It's also an excellent example of chemo-free personalized approach.

LGG-19. SPINAL LOW-GRADE GLIOMAS IN CANADIAN CHILDREN: A MULTI-CENTRE RETROSPECTIVE REVIEW

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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 1990–2015 was undertaken to examine the clinical features, pathological 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 least 6 months after symptoms developed. Two patients had 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 surgery-only and the others received chemotherapy and/or focal radiation. 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, 0.5–20.4 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 final 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 worse regardless of 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-associated 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 LASER 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. Standardly, these patients are treated with sequential lines of chemotherapy, while delaying as long as possible radiation. Magnetic resonance-guided laser interstitial 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 underwent treatment. Despite sequential trials of thioguanine/procarbazine/lomustine/vincristine, carboplatin/vincristine, dabrafenib, and combination dabrafenib/trametinib, 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 improved 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 optic tracts. The tumor progressively shrank over the year 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)

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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 2000–2017. Here we evaluate this cohort and one additional patient using quantitative multiple immunofluorescence (qmIF) and next generation sequencing (NGS) using the Columbia Combined Cancer Panel (CCCP). For qmIF, 4 micron immuno-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 CCCP failed in 2 cases. CCCP 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 1.5%). Non-cytotoxic T cells (CD3+CD8-) comprised 60.7–100% of the T cell compartment. There was no difference 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-cytotoxic 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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In-operable 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 hypothalamic/optic chiasm region. She presented with ataxic gait, bi-temporal hemianopia, 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 positive for BRAF-V600E mutation, she was started on Dabrafenib monotherapy, resulting in dramatic improvement in her clinical symptoms (able to stand, improved vision), and a 60% reduction in tumor size at 3-months. At 6-months, follow up MRI showed slight increase in the solid portion of the tumor, with no clinical symptoms. We plan to add MEK inhibitor (Trametinib) and continue with Dabrafenib. Our experience and literature review suggests that LGG with