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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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