LOW GRADE GLIOMA

LGG-01. CHILDREN WITH SUPRATENTORIAL MIDLINE PILOCYTIC ASTROCYTOMAS EXHIBIT MULTIPLE PROGRESSIONS AND ACQUISITION OF NEUROLOGIC DEFICITS OVER TIME

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Pilocytic astrocytomas are the most common solid tumor of childhood and can arise anywhere in the central nervous system, including the posterior fossa (pf-PA), supratentorial midline (sm-PA; including optic pathway, hypothalamus, thalamus), and brainstem (bs-PA). Location (sm, bs) has been previously proposed as a prognostic factor for PA, but is difficult to separate from resection status on multivariate analysis. To overcome this limitation, we assembled a large cohort of children (n = 251) with biopsy-proved PA treated at St. Louis Children's Hospital from 2003 – 2021 and analyzed outcomes only in patients with subtotal resection (STR; n = 81). We excluded patients with NF1, as NF1-associated gliomas often display a more indolent clinical course than their counterparts. We identified that children with STR sm-PA had a higher likelihood of multiple progressions compared to children with STR bs-PA and pf-PA. This was associated with worsening neurologic deficits over time, consistent with the sm location as a poor prognostic factor. Furthermore, the only children in our cohort with leptomeningeal dissemination or death harbored sm-PAs. Tumors in this location were also associated with an increased likelihood of non-BRAF-fusion genetic alterations and multiple oncogenic mutations. Overall, these data support location as an independent prognostic factor for PA in cases in which a gross-total resection cannot be achieved. Treating neuro-oncologists may thus wish to consider early intervention rather than watch-and-wait strategies at first progression of STR sm-PA. These patients may also benefit from earlier consideration of molecularly targeted therapy.

LGG-02. CARDIAC TOXICITY IN PATIENTS RECEIVING SINGLE-AGENT MEK INHIBITION

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BACKGROUND: MEK inhibitor therapy is increasingly being utilized for the treatment of pediatric tumors, including low-grade glioma, plexiform neurofibroma and Langerhans cell histiocytosis. These drugs are well-tolerated but do have risk of toxicity, including cardiac toxicity. The purpose of this study is to better characterize MEK inhibitor-induced cardiac toxicity in pediatric patients. METHODS: Retrospective review of all patients who underwent MEK inhibitor mono-therapy for at least 3 months, 2015- 2021, age 25 years or less, at St. Louis Children's hospital and Cardinal Glennon Children's hospital. RESULTS: We evaluated 31 patients, 19 (61%) with brain tumors and 12 (39%) without. Of the thirty-one, fifteen (48%) had NF1, 1 had Tuberous sclerosis. Cardiac toxicity consisted of asymptomatic sinus tachycardia, bradycardia, or decreased ejection fraction (EF). Thirteen patients (42%) experienced an asymptomatic decrease in left-ventricular ejection fraction (EF), Grade I-III. Time on therapy before decreased EF was 5 days to 21 months, median 2.8 months. Decreased EF developed in 5 of 13 patients receiving selumetinib and 8 of 18 receiving trametinib. Of the patients who developed decreased EF, 11 (85%) had brain tumors, 6 (46%) had NF1, and 89% had received prior systemic therapy. Out of the patients who had received no prior systemic therapy (6), 2 (33%) had decreased EF, while 11/25 (44%) of those who had received prior systemic therapy did. Drug was held temporarily for 6 patients, with dose limiting toxicity for 5 patients. Drug was discontinued for 1 patient after EF continued to decline despite dose reduction. Patients showed improvement in EF as early as 2 weeks after holding therapy. CONCLUSIONS: Cardiac toxicity in our patients was limited to asymptomatic reduction in ejection fraction, sinus bradycardia and tachycardia, reinforcing the need for appropriate monitoring via echocardiography. Prior systemic therapy was associated with decreased EF.

LGG-03. PEDIATRIC SPINAL DEFORMITIES CONCOMITANT WITH SPINAL CORD PILOCYTIC ASTROCYTOMA

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INTRODUCTION: Childhood spinal cord tumours may lead to spinal deformity. Rapid scoliosis progression, a left thoracic curve and early onset scoliosis are associated with an increased risk of intraspinal anomalies, therefore magnetic resonance imaging (MRI) should be performed. CASE PRESENTATION: A 1-year-old girl presented with progressive early onset scoliosis. MRI of the spine showed diffuse intramedullary lesion at vertebral level T5 – T11 and abnormal curvature of the thoracic spine to the right – 39-degree Cobb angle, after a few moths – 71-degree. Blood and cerebrospinal fluid examination ruled out a neuroinfection and autoimmune diseases. Histology revealed BRAF V600E-mutant pilocytic astrocytoma (PA) (IDH non-mutant), DNA methylation profiling – PA, MGMT promoter methylation – not detected, SNP-A karyotyping – normal. Treatment with weekly vinblastin was started due to non-operable tumour and progressive scoliosis. Spinal deformity was managed using serial casting with only mild correction of curvature. In the second case report, a 14-year-old boy either presented with progressive scoliosis. Spine x-ray showed abnormal curvature of the thoracic spine to the left - 89-degree Cobb angle and after a few years - 120-degree. MRI of the spine detected intramedullary tumour masses located at vertebral level T3-T5. Surgical resection revealed BRAF V600E-mutant PA (IDH, ATRX, TERT non-mutant), DNA methylation profiling – PA, MGMT promoter status – not methylated, SNP-A karyotyping – non-specific trisomy of chromosome 5. The patient was followed-up by routine spine MRI. However, after 8 months new spinal cord masses appeared. It was decided to correct scoliosis only after the total tumour removal. CONCLUSIONS: Intramedullary spinal tumours are overall rare in the pediatric population. Of these, PA accounts for the majority, however treatment remains challenging. BRAF V600E mutation has relatively high frequency in PA. This mutation identification opens more treatment options such as targeted therapy with BRAF V600E and MEK inhibitors for progressive disease.

LGG-04. CLINICAL AND MOLECULAR CHARACTERIZATION OF METASTATIC PEDIATRIC LOW GRADE GLIOMAS

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BACKGROUND: Despite being the most common central nervous system tumor in children, ≤5% of pediatric low grade gliomas (pLGG) present with metastases. Due to their rarity, there is a paucity of clinical and molecular data in metastatic pLGGs. To address the need, we analyzed a cohort of 22 patients with pLGG followed at Texas Children's Hospital who presented with metastatic disease. RESULTS: The predominant histology was pilocytic astrocytoma (16/22, 73%); average age at diagnosis was 4 years 11 months. The most common sites of primary disease were optic pathway/chiasm (7/22, 32%) and suprasellar (5/22, 23%). Metastatic disease was most commonly noted in the leptomeninges (12/22, 55%). 16/22 patients (73%) were treated with up-front medical therapy following tumor biopsy/resection, the majority with carboplatin-based therapy; the remaining 6 patients received only surgery up-front. Only 2/22 patients (9%) did not progress after their initial treatment with an average follow-up of 42 months. 14 patients (14/22, 64%) had continued disease progression after at least 2 therapeutic interventions; however, only 3 patients (3/22, 14%) eventually received craniospinal radiation. 10 patients (10/22, 45%) received treatment with an agent targeting the mitogen-activated protein kinase (MAPK) pathway. 20/22 patients (91%) were alive at last follow-up (average 72 months). 4/21 patients (19%) harbored a BRAF V600E mutation while 7/20 (35%) had a BRAF::KIAA1549 duplication/fusion. 8/20 patients (40%) were wildtype for both analyzed molecular alterations in BRAF. 8 patients had germline whole exome sequencing performed and all were negative for pathogenic/likely-pathogenic variants related to their clinical phenotype. Methylation analyses are pending on patients with available tumor tissue. CONCLUSION: In our cohort of patients with metastatic pLGG, most tumors progressed despite numerous therapeutic regimens, but the overall survival was >90%. 40% of patients were wild type for the 2 most common MAPK alterations seen in pLGG.

LGG-05. A NINE-MONTH-OLD BOY WITH REGRESSION OF MILESTONES AND SEVERE CONSTIPATION: AN UNUSUAL CASE OF A SPINAL PILOCYTIC ASTROCYTOMA

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