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 (p-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 did have a higher likelihood of developing a secondary glioma compared to children with STR bs-PA and p-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, as a harbored sm-PA. Tumors in this location were also associated with an increased likelihood of non-BAF/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 toxicities, 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 5 years or younger 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-II. Time on therapy before decreased EF was 5 days to 21 months, median 2.8 months. Decreased EF developed in 5 of 13 patients considering of selenumtin 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 prior no systemic therapy (6), 2 (33%) had decreased EF while 11/25 (44%) of those who had received prior systemic therapy (selenumtin or trametinib) 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 spinal cord 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 T3–T11 and abnormal curvature of the thoracic spine to the right – 39-degree Cobb angle, after a few months – 71-degree. Blood and cerebrospinal fluid examination revealed 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, SNPA 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, SNPA karyotyping – normal. Conclusion: Intramedullary spinal tumours are overall rare in the pediatric population. Of note, PA accounts for 4% of spinal tumours. This 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 GLIOMA

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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 (40%, average age at diagnosis was 4 years 11 months. The most common sites of primary disease were optic pathway/chiasm (7/22, 32%) and suprassellar (5/22, 23%). Metastatic disease was most commonly noted in the leptomeninges (12/22, 55%); 16/22 patients (73%) received medical therapy with either chemotherapy or surgery. 14 patients (64%) had continued disease progression after initial surgery resection, the majority with carboplatin-based therapy; the remaining 6 patients received only surgery upfront. Only 2/22 patients (9%) did not progress after their initial treatment with an average follow-up of 42 months. 14 patients (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 the 2 most common MAPK alterations seen in pLGG.

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

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LGG-06. SELUMETINIB IN PEDIATRIC PATIENTS WITH NON-NEUROFIBROMATOSIS TYPE 1 ASSOCIATED, NON-OPTIC PATHWAY (OPG) AND NON-PILOCYTIC RECURRENT/PROGRESSIVE LOW-GRADE GLIOMA HARBORING BRAFV600E MUTATION OR BRAF-KIAA1549 FUSION: A MULTICENTER PROSPECTIVE PEDIATRIC BRAIN TUMOR CONSORTIUM (PBTC) PHASE 2 TRIAL
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BACKGROUND: A greater understanding of the Ras-MAP kinase pathway in pediatric low-grade glioma (LGG) paired with the availability of selective inhibitors has enhanced the ability to target this pathway with therapeutic intent. METHODS: The PBTC conducted a multi-institutional phase II study (NCT00109001) evaluating selumetinib (AZD6244, ARRY-142886), a MEK II inhibitor, in children with recurrent/progres-

LGG-08. MR IMAGING OF PEDIATRIC LOW-GRADE GLIOMAS: PRETHERAPEUTIC DIFFERENTIATION OF BRAF V600E MUTATION, BRAF-FUSED AND WILD-TYPE TUMORS IN PATIENTS WITHOUT NEUROFIBROMATOSIS-1
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OBJECTIVE: The prognosis and treatment of pediatric low-grade gliomas (pLGGs) is influenced by their molecular subtype. MRI remains the mainstay for initial work-up and surgical planning. We aimed to determine the relationship between imaging patterns and molecular subtypes of pLGGs.

METHODS: This is a bi-institutional retrospective study for patients diagnosed from 2004 to 2021 with pathologically confirmed pLGG, molecularly defined as BRAF-fusion (KIAA1549-BRAF), BRAF V600E mutation, or wild-type (negative for both BRAF V600E mutation and BRAF fusion). Two neuroradiologists, blinded, independently reviewed imaging parameters on the initial MRI and discrepancies were solved by consensus. Bivariate analysis was used followed by pairwise comparison of Wx, Steel, and Chi-square methods to compare the 3 molecular subtypes. Agreement between reviewers was assessed using Kappa (k). RESULTS: 70 patients were included: 30 with BRAF fusion, 19 with BRAF V600E mutation, and 21 wild-type. There was significant correlation between the two readers for overall image intensity (k=0.75). BRAF fusion tumors compared to V600E and wild-type had larger size (p=0.0022), greater mass effect (p=0.0053), and increased rate of hydrocephalus (p=0.0002). BRAF fusion tumors had increased frequency of diffuse enhancement compared with BRAF V600E and wild-type (p<0.0001). BRAF V600E-mutant tumors were more often located in a cerebral hemisphere (p<0.0001).