A MULTICENTRE RETROSPECTIVE REVIEW

Arabia, *Genomics Research Department, Saudi Human Genome Project, King Fahad Medical City and King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia

Pediatric Low-grade gliomas (PLGGs) are extremely heterogeneous tumors and account for approximately 35% of childhood brain tumors. This retrospective study on 33 newly diagnosed children (1-14 yrs) with pathologically confirmed PLGG from 2011 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 (17%) is the most common pathological diagnosis. 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 (54.3%) 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 allogeneic 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- and 7-year 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 PLGG 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.

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

Anna Avagyan1-4, Lilit Sargsyan2-4, Julia Hoveyan3, Samvel Iskanyan4, Samvel Bardakchyany2,3, Samvel Danielyan1,2, Gevorg Tamanyan1-3,1 Yerevan State Medical University and GH Urology, Yerevan, Armenia, 2Pediatric Cancer and Blood Disorders Center of Armenia, Hematology Center after Prof. R. Yeleyan, Yerevan, Armenia, 3Hematology Center after Prof. R. Yeleyan, Yerevan, Armenia

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 examination of the resected tumor tissue was 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 cranio-spinal irradiation 33.2 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.

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

Diren Usta1,2, Romain Sigaud1-2, Juliane L. Buhl1,2, Florian Selt2, Viktoria Mitrakos1,2, David Puck1-3,4, Nathan Vrabc1, Jonas Ecker2,3, Thomas Hielshcer1, Johanna Vollmer2,3, Alexander C. Sommerkamp3,4, Tobias Rubner1, Darren Hargrave1, Cornelis M. van Tilburg1,2, Stefan M. Pfister1,2,3, David T.W. Jones1,2,3, Marc Remke1,2,3,4, Florian Münzel1,2,3,4, Olaf Wentrup1,2,4, and Angela Wikimedia1,2,3. Children’s Cancer Center Heidelberg (KiTZ), Heidelberg, Germany, 2Department of Pediatric Oncology, Hematology, and Clinical Immunology, Medical Faculty, University Hospital, Heidelberg, Germany, 3Department of Pediatric Neurooncology, Oncogenomics, German Cancer Consortium (DKTK), Düsseldorf, Germany, 4Department of Neurology, Heidelberg University Hospital, Heidelberg, Germany

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 if inhibitors targeting the MAPK/ERK pathway would be more efficient than inhibitors targeting mTOR and if BRAFV600E mutation could be used as a driver for therapeutic decision. 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 to 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-22. EVALUATION OF IMMUNE AND GENOMIC CHARACTERISTICS IN PEDIATRIC OPTIC NERVE GLIOMA (ONG)
Ashley A. Campbell1,2, Andrew M. Silverman3, Hanna Moisander-Joyce4, Cheng-Chia Wu5, Mahesh Mansukhani6, George Zanazzi3, Andrew Turk7, Peter D. Canoll3, James H. Garvin1, Michael Kaur1, Andrew M. M. Gartrell-Corrado3, Stephen Wu4, Michael Campbell5, Rozovsky6
1Stollery Children's Hospital, Edmonton, AB, Canada, 2London Health Sciences Centre, London, ON, Canada

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 2007 and 2015 was undertaken to examine the clinical, radiological, 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 chemotherapy and/or radiation 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
Koji Yoshimoto1, Nobuhiro Hata2, Nayuta Higa3, Hajime Yonezawa3, Hiroyuki Uchida4, Tatsuki Oyoshi5, and Masahiro Mizoguchi6
1Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan, 2Department of Neurosurgery, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

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 decription. However, a subgroup of OHA patients show resistance to chemotherapy and 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 showed good prognosis only by biopsy or partial resection. By regarding Dodge 3 tumor, patient prognosis is irrespective 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. In one additional patient, we treated only with biopsy and Dodge 3 tumor, patient prognosis is irrespective of chemotherapy and radiotherapy. 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 decription in the early phase when a large tumor does not respond to chemotherapy.

LGG-21. MR-GUIDED LASER INTERSTITIAL THERMAL THERAPY FOR IN-OPERABLE AND SYMPTOMATIC PEDIATRIC LOW GRADE GLIOMA
David Kram1, Jessica Benjamin-Eze, Roy Strowd2, and Stephen Tatter1
1Wake Forest School of Medicine, Winston-Salem, NC, USA

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. Traditionally, these patients are treated with standard-of-care regimens with advancements in the field of pediatric LGGs, particularly in the use of immunotherapy. 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 supratentorial, hypothalamic LGG, BRAF V600E mutation positive. The patient was unresectable, and due to progressive vision loss and headaches, a suprasellar, hypothalamic LGG, BRAF V600E mutation positive. The patient continued to experience 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 appetite. The patient was discharged on 1 mg of lumbar 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 progression. CONCLUSION: We report a case of a pediatric patient with an inoperable low grade glioma who underwent LITT with excellent clinical and radiographic effects. LITT should be considered for children with inoperable and morbid LGGs that fail to respond to more conventional therapies.

LGG-23. EXCELLENT CLINICAL / RADIOLOGICAL RESPONSE TO BRAF INHIBITION IN A YOUNG CHILD WITH IN-OPERABLE SUPRA-SELLAR PILOCYTIC ASTROCYTOMA
Stacy Chapman1, Demitre Serletis2, Colin Kazina3, Mubeen Rafay3, Sherry Krawitz1, Katya Rozovsky2, and Magnusian Izzan Vanagi1
1Cancer Care Manitoba / University of Manitoba, Winnipeg, Manitoba, Canada, 2Neurosurgery, University of Manitoba, Winnipeg, MB, Canada, 3Neurology, University of Manitoba, Winnipeg, MB, Canada

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 2007 and 2017. Here we evaluated immunohistochemistry and next generation sequencing (NGS) in a young child with optic nerve glioma (ONG). QmIF and CD68+ cells were not different between groups (p=0.49 and p=0.27, respectively) 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-24. OUTCOMES OF LARGE PINNACLE POINTS FROM IMMUNO-HISTOCHEMISTRY TO BRAF INHIBITION IN A YOUNG CHILD WITH IN-OPERABLE PILOCYTIC ASTROCYTOMA
Koji Yoshimoto1, Nobuhiro Hata2, Nayuta Higa3, Hajime Yonezawa3, Hiroyuki Uchida4, Tatsuki Oyoshi5, and Masahiro Mizoguchi6
1Department of Neurosurgery, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan, 2Department of Neurosurgery, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Large PINs of pediatric pilocytic astrocytomas were not infiltrated by CD3+ T cells or CD68+ cells. The large PINs were infiltrated by both CD3+ and CD68+ cells in the SETD2 mutation in the added case. Qualitative analysis showed immune infiltration across cases included macrophages (CD68+, 1.6–6.5% of all cells) and T cells (CD3+, 0.4% to 1.3%). Non-cytotoxic T cells (CD3+CD8-) comprised more than 100% of the T cells in patients. Also, there is a strong correlation between 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+ 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.