RARE TUMORS/OTHER

RARE-01. ASSESSING THE SYMPTOM DIAGNOSTIC INTERVAL FOR CHILDREN WITH CENTRAL NERVOUS SYSTEM TUMOURS

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Background: Diagnostic delays in pediatric neuro-oncology is a subject of distress for families and providers. We aimed to evaluate the symptom diagnostic interval (SDI) and influencing variables for children with CNS tumors. Methods: This retrospective study analyzed 210 patients diagnosed from 2001-2018 and managed at the tertiary care facility in Halifax, Canada. SDI was defined as time from first symptom until tissue diagnosis or, if not available, imaging diagnosis. Non-parametric tests were used to compare SDI between groups. Results: Median SDI was 12.4 weeks (IQR 4.3–30), longer than 7 other studies of 1308 children reporting medians of 0.80–3.51 weeks. Longer SDI was associated with younger age (p<0.01), male sex (p=0.03), greater socioeconomic status (p=0.03), and distance to the tertiary care facility. Conclusion: SDI at our centre is longer than previously reported studies. SDI is linked to tumor biology and its relevance within specific tumor groups deserves further investigation given it doesn’t appear to predict tumor progression/recurrence, yet families and providers feel distress when delays in diagnosis are perceived.

RARE-02. POLYAMINE PATHWAY INHIBITION AS A POTENT NOVEL THERAPEUTIC STRATEGY AGAINST DIFFUSE INTRINSIC PONTINE GLIOMA

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Diffuse intrinsic pontine glioma (DIPG) is an aggressive paediatric brainstem tumor with a median survival of less than 1 year. Polyamines are intracellular polycations that control important aspects of cell growth and are often upregulated in cancer. Difluoromethylornithine (DFMO) is a FDA-approved inhibitor of the enzyme ornithine decarboxylase (ODC1) which is a key driver of polyamine synthesis. We investigated the efficacy of polyamine pathway inhibition as a therapeutic strategy against DIPG, Brain Tumor Atlas initiative to comprehensively define the molecular landscape of pediatric brain tumors. The initiative contains multi-modal analyses of research- and clinical-trial based DNA and RNA sequences from nearly 1,000 children (with 1,236 tumors) along with their longitudinal clinical data. The OpenPBTA’s open science framework for analysis tests the capacity of crowd-sourced collaborative architectures to advance more rapid, iterative and integrated discovery of the underlying mechanisms of disease through integrative multi-modal analyses. The OpenPBTA project, OpenPBTA has collaboratively created reproducible workflows for integrated consensus SNV, CNV, and fusion calling, enabled RNA-seq-based classification of medulloblastoma subtypes, and more than 25 additional DNA- and RNA-based analyses. The open-science platform and associated datasets and processed results provide a continuously updated, global view of the integrated cross-disease molecular landscape of pediatric brain tumors. Such biospecimen- and clinically-linked scalable data resources provide unprecedented collaborative opportunities for precision-based, personalized therapeutic discovery and drug development. Further integration of proteomic sample data (N>300) and drug response datasets, additionally diversifying the multimodal discovery potential of crowd-sourced approaches for accelerated impact for children with brain tumors.
We found that there were high over-expression levels of polyamine synthetic enzymes from DIPG primary patient samples and neurosphere cultures. Using alamar blue cytotoxicity and soft-agar clonogenic assays, we found that polyamine inhibitors, and that dual blockade of polyamine synthesis and transport is a promising novel therapeutic strategy. AMXT 1501 is currently in clinical development, and following completion of an adult Phase 1 trial, a clinical trial of AMXT 1501 + DFMO for DIPG patients is planned through the CONNECT consortium.

RARE-03 CENTRAL NERVOUS SYSTEM TUMORS IN CHILDREN WITH NEUROFIBROMATOSIS TYPE 1, A COHORT FROM A NATIONAL PEDIATRIC ONCOLOGY CENTER

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Approximately 15% of the children with Neurofibromatosis type 1 (NF1) develop a central nervous system (CNS) tumor, predominantly optic pathway gliomas. Without early recognition, these brain tumors are also frequent, resulting in an intrinsically multi-system nature of treatment toxicity. With an appreciation of the intrinsically multi-system nature of treatment toxicity, educational initiatives be developed and delivered to the interdisciplinary neuro-oncology treatment team in an effort to bridge both learning and practice gaps. With an appreciation of the intricately multi-system natural of NF1, which necessitates a longitudinal treatment approach encompassing the totality of the multidisciplinary team, CEC Oncology designed and tailored targeted NF1 educational activities to improve confidence, advance knowledge, and promote enhanced utilization of targeted medical therapies among pediatric neuro-oncologists, neuro-oncologists, and neurosurgeons who manage patients with NF1. We conducted two independent satellite symposia, one at the 2020 Society for Neuro-Oncology (SNO) Annual Meeting, and one at the CNS SPECTRUM Neuro-Oncology Symposium, to achieve robust educational outcomes across multiple learning levels. With a focus on evidence-based education, an appreciation of the multi-system nature of treatment toxicity, and an effort to bridge both learning and practice gaps, we utilized this approach to improve confidence, advance knowledge, and promote utilization of targeted medical therapies in NF1, thereby optimizing patient outcomes.

RARE-04 IMPACT OF LIVE, VIRTUAL EDUCATIONAL SYMPOSIUM ON PEDIATRIC NEURO-ONCOLOGIST, NEURO-ONCOLOGIST, AND NEUROSURGEON CONFIDENCE, KNOWLEDGE, AND INTENTION TO EMPLOY TARGETED MEDICAL THERAPIES FOR THEIR PATIENTS WITH NEUROFIBROMATOSIS TYPE 1

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Historical treatment options and management strategies for neurofibromatosis type 1 (NF1) have been limited, with a relative paucity of clinical studies and the traditional paradigm focused on an ineffectual, and possibly even harmful, trimal blood combination of radiation, surgery, and sur- veillance. Fortunately, an emerging preponderance of trial data supporting the use of targeted medical therapies, including MEK inhibitors and multi- kinase inhibitors, is expanding the standard of care for NF1 patients. Given the profound novelty of this paradigmatic shift in NF1 management, it is imperative that timely, adaptive, and evidence-based educational initiatives be developed and delivered to the interdisciplinary neuro-oncology treatment team in an effort to bridge both learning and practice gaps. With an appreciation of the intricately multi-system natural

RARE-05 ANAPLASTIC ASTROCYTOMA AND OLIGODENDROGLIOMA PRESENTING AS SIMULTANEOUS PRIMARY BRAIN TUMORS IN A PEDIATRIC PATIENT: THE FIRST KNOWN REPORT OF A RARE CONDITION

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Multiple metastatic brain tumors and multiple histologically identical primary brain tumors have been reported in adults and children. The concurrent presence of multiple histologically distinct primary brain tumors is rare. Here, we report a case of simultaneous anaplastic astrocytomas and glioblastomas being rare. We report a case of simultaneous anaplastic astrocytoma and grade II oligodendroglioma in a pediatric patient. A previously healthy 6-year-old female presented with persistent headaches. Initial magnetic resonance imaging (MRI) demonstrated enhancing right frontal lobe and left peritrigonal lesions without mass effect. Serial MRIs showed progression of both lesions, prompting frontotemporal biopsy, which revealed a grade II oligodendroglioma. The patient was started on standard low-grade glioma chemotherapy, which was stopped due to an allergic reaction. Following chemotherapy, the lesions increased in size, and the peritrigonal lesion demonstrated new heterogeneous enhancement. The patient underwent gross-total resection of the peritrigonal lesion and repeat biopsy of the frontal lobe lesion. Pathology confirmed the frontal lobe lesion to be a grade IV glioblastoma, and the peritrigonal lesion to be an anaplastic astrocytoma. The patient responded well to cranial radiotherapy and standard high-grade glioma chemotherapy. To the best of the authors’ knowledge, this is the first case of simultaneous anaplastic astrocytoma and oligodendroglioma in a child, increasingly unique given the histological and molecular rarity of the tumors in pediatric patients.