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Surgery consists in the mainstay of treatment in most gliomas, but in many cases, a resection is not feasible. Liquid biopsy is an ideal tool providing a minimally invasive method through plasma or CSF sampling to aid in detecting ctDNA (exosomal DNA). Here, we describe our experience of detecting DNA in plasma exosomes (exoDNA) extracted from glioma patients and further investigate its use in identifying molecular alterations. Exosomes were isolated from 2ml of plasma from 24 patients (13 LGG, 8 HGG, 3 DIPG) and fully characterized by nanoparticle tracking analysis and transmission electron microscopy. DNA was extracted from 13 samples (exoDNA) so far. Five patients had confirmed point mutations in the primary tumor (3BRAFV600E, 1FGFR1N546K, 1H3.3), additionally, 3 samples were collected from clinically diagnosed DIPG patients to inquire H3K27M mutations. DNA was extracted successfully from all exosome samples; a pre-amplification step was needed and direct sequencing was carried out for BRAFV600E. FGFR1N546K and H3K27M mutations were sought in patients with positive tumors. Wildtype BRAF fragment was identified in 12/13 samples (1 patient failed sequencing). However, none of the five tumor positive patients nor the DIPG patients had mutations detected at the exoDNA level. There is growing evidence that CSF may be the ideal source of ctDNA in brain tumor patients, therefore although we could not detect mutations in plasma DNA we are currently analyzing CSF exoDNA and cell-free DNA to evaluate if this proves a successful strategy and we ther exoDNA is more representative of the tumor content.

PATH-31. THE IMPACT OF MOLECULAR PROFILING OF PEDIATRIC CNS TUMORS ON TUMOR DIAGNOSIS AND MANAGEMENT - A SINGLE CENTER EXPERIENCE
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BACKGROUND: Next generation sequencing (NGS) plays a role in neuro-oncology research and in clinical diagnosis and management. Here, we describe how NGS for pediatric CNS tumors impacted clinical diagnosis and subsequent management. METHODS: NGS was performed on the UCSF 500 Gene Panel (targeted sequencing platform covering about 500 cancer associated genes). Patients were selected for NGS based on tumor pathology need to identify therapeutic targets. We collected data on patient demographics, tumor histology/pathway alterations/therapeutic targets/ therapy and used descriptive statistics for data analysis. RESULTS: Between January 2016 and July 2019, about one-third of patients with CNS tumors seen at our institution (N=29) were interrogated. NGS revealed pathway alterations in 20/29 patients. Treatment recommendations/modifications based on pathway alterations impacted the therapy of 18 patients. Patient groups: Medulloblastoma (N=6), alterations in WNT, SHH, and TP53 pathways (Vismodegib recommended for SHH pathway alteration but not used). High-grade glioma (N=4), alterations (with treatment changes) included, NFI (Tamoxifen, Everolimus); MSH2/ MLH1(4Nivolumb); CDKN2A/CDKN2B/CDKN2C (Abemaciclib); EGFR (Osimertinib, Atefinatim); H3K27M (Panobinostat/ONC201); BRAFV600E (Dabrafenib, Trametinib); ATRT (N=1) SMARCB1; Low Grade Glioma (N=10); BRAFV600E/Vemurafenib); NRASQ61H/1349 fusion (Trametinib); PIK3CA; DIPG (N=5), H3K27M/BCOR/PS5/ACVR/PIK3CA (LY3032414, Everolimus)/PDGFR (Dasatinib); Ependymoma (N=3), PAF/P/REL Fusion. Seven patients were treated with targeted therapy + conventional therapy. In 8 patients targeted therapy remains an option but not yet pursued. CONCLUSIONS: NGS of pediatric brain tumors is widely available and contributes to the diagnosis/therapy of pediatric CNS tumors. Optimal chemotherapyn/targeted therapy combinations are areas of study.

NEUROPSYCHOLOGY/QUALITY OF LIFE

QOL-01. LONGITUDINAL COMPARISON OF NEUROCOGNITIVE TRAJECTORIES IN PEDIATRIC MEDULLOBLASTOMA PATIENTS TREATED WITH PROTON VERSUS PHOTON RADIOTHERAPY
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PURPOSE: By reducing dose to normal brain tissue, proton radiotherapy (PRT) may lessen neurocognitive risk traditionally associated with photon radiotherapy (XRT). We examined change in neurocognitive scores over time in pediatric medulloblastoma patients treated with proton versus XRT. METHODS: Neurocognitive scores from 79 patients (37 PRT, 42 XRT) were examined. Patients were treated between 2007–2018 on the same treatment protocols that differed only by craniospinal modality (PRT versus XRT). Change in scores over time since diagnosis were compared between groups. RESULTS: Groups were similar on most demographic/ clinical variables: sex (67.1% male), age at diagnosis (mean 8.6 years), CSI dose (median 23.4 Gy), length of follow-up (mean 4.3 years), and parental education (mean 14.3 years). Boost dose (p<0.001) and margin (p<0.001) differed between groups. Adjusting for covariates, the PRT group exhibited superior outcomes in global IQ, perceptual reasoning, and working memory versus the XRT group (all p<0.05). The XRT group exhibited significant decline in global IQ, working memory, and processing speed (all p<0.05). The PRT group exhibited stable scores in all domains except processing speed (p=0.003). Posterior fossa syndrome imparted risk independent of modality. CONCLUSION: This is the first study comparing neurocognitive trajectories between pediatric patients treated with medulloblastoma with PRT versus XRT on comparable, contemporary protocols. PRT was associated with more favorable neurocognitive outcomes in most domains compared to XRT, although processing speed emerged as vulnerable in both groups. This is the strongest evidence to date of an intellectual sparing advantage with PRT in the treatment of pediatric medulloblastoma.

QOL-02. PERCEPTIONS OF LATE EFFECTS CARE NEEDS AMONG SURVIVORS OF PEDIATRIC BRAIN TUMOURS
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OBJECTIVES: Pediatric brain tumour survivors are at risk of long-term consequences of therapy. Comprehensive late effects care may mitigate these effects. The aim of this study was to describe the care experience and quality of life (QOL) of pediatric brain tumour survivors at the McMaster Children’s Hospital joint adult/pediatric Neuro-Oncology clinic. METHODS: Cross-sectional survey data were collected. Care needs were assessed with the Cancer Care Experience Questionnaire (CCEQ); Cancer Worry Scale (CWS), and Self-Management Skills Scale (SMSS). Quality of life was measured utilizing the PedsQL Brain Tumor Module. Data were analyzed descriptively. RESULTS: Thirty-two childhood brain tumor survivors and/or their parents participated. Their malignancies included embryonal tumors (medulloblastoma/ATRT) (62%), ependymoma (22%), and germ cell tumours (16%). Among 77%, therapy included chemotherapy, surgery and radiation. Most respondents reported high quality cancer care, although some could not recall discussions of late effects risks and health promotion. Mean cancer worry scores were low (71.8 [± 28.4]), survival 68.2 (±16.6), CONCLUSION: In contrast to other childhood cancer survivor cohorts, this group of long-term brain tumour survivors appear to have similar QOL, fewer cancer worries, and increased need for aid with self-management. Given this, along with the positive care experience reported, this clinic model of care appears to meet the needs of this population.

QOL-04. INFLUENCE OF FAMILY, SCHOOL, AND HOSPITAL SYSTEMS IN SUPPORTING SURVIVORS OF PEDIATRIC BRAIN TUMORS WITH NEUROCOGNITIVE LATE EFFECTS
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OBJECTIVE: Pediatric brain tumor survivors (PBTS) are at risk for developing neurocognitive late effects that may interfere with academic and adaptive functioning. To mitigate the potential impact, some PBTS may implement strategies independently, while others may rely on system-level support from family, school, or hospital systems. Given the limited knowledge on survivor and family perspectives of these supports, we conducted a mixed-methods study involving PBTS and their caregivers to examine the...
QOL-05. TUMOR LOCATION IS LESS INFLUENCE ON COGNITIVE DYSFUNCTION IN CHILDREN
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INTRODUCTION: Though several factors are known to influence on long-term cognitive function in children with brain tumor, the impact of tumor localization to specific cognitive function was not well known. Here we investigated the influence of localization of the tumor, postoperative cognitive outcome in school-aged children. METHODS: Participants were seven pediatric patients who underwent craniotomy for tumor resection in our hospital (mean age, 13.9 years). Their diagnoses were WHO grade 1 or 2 glioma (n=6) and hemangiomat (n=1). Tumor were mainly located in following regions; frontal, n=2; parietal, n=2; temporal, n=3 (These lesions included hippocampus or were located very close to it). Temporal assessments for cognitive function of several functional domains were performed at the time of tumor resection and postoperatively 1 year. Based on preoperative cognitive function, we estimated cognitive dysfunctions and compared them to observational symptoms. RESULTS: Preoperative cognitive function was normal in all patients. Cognitive dysfunctions estimated from resected area were as follows: (cognitive domain number) memory on working memory disorder, n=4; visuospatial cognitive disorder, n=3; disorder of processing speed, n=2; facial or topographical agnosia, n=2; Gerstmann syndrome, n=1. Just after surgery, cognitive function was declined in two functional domains of two patients, which were only 16.7% of estimated deficit from resected region. They recovered completely before 5 months postoperatively, and returned to their previous life without any deficits. CONCLUSIONS: In pediatric lower-grade tumor, focal cognitive symptom was unlikely to be induced by local resection.

QOL-06. QUALITY OF LIFE IN MEDULLOBLASTOMA SURVIVORS IN WESTERN MEXICO
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BACKGROUND: Treatment of children with medulloblastoma (MB) can lead survivors to lidiate with long term sequelae and affect their quality of life (QoL). This study evaluates QoL in long term MB survivors. DESIGN/METHODS: Clinical files of MB survivors from 1997 to 2016 were retrospectively analyzed. QoL was defined by Schipper Criteria in a five dimensional evaluation: clinical data, physic effects of treatment, academic develop, functional state and self welfare report. RESULTS: Clinical data: Twelve survivors were identified, mean age at review was 18 years; median follow up was 106 months. Functional state: Last visit Karfonsky/ lansky were 90 to 80% in 25% of patients. Physic effects of treatment: Cerbellar Mutism or ataxia were present in 25% of cases. Two patients required external dispositive. Audiometry detected an auditory toneal decrease in 25% of cases. An endocrine disfunction was present in 46% of cases, 32% required hormone replacement and 28% having short size. Renal damage without dialysis was detected in 7% and 10% had a transient tubulopaty. One case had bilateral amaurosis and 14% uses glasses. Three patients had a life partner. One female has offspring and two males had azoospermia. Academic develop: While 90% attends to school, 35.7% complained of learning difficulties and 18% needed special education. Self welfare report: Difficultes in social environment were described in 21% and 14% still feeling sick during years. CONCLUSIONS: Survivors of MB had adverse physical effects, followed by academic development, functional state and self welfare report and all this has a negative impact in their QoL.

QOL-07. CORTICAL VOLUME AND THICKNESS IN ADULT SURVIVORS OF CHILDHOOD POSTERIOR FOSSA TUMORS
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PURPOSE: A brain tumor treatment including cranial radiotherapy has previously been associated with long-term neurocognitive sequelae. Since underlying neurological mechanisms remain inconclusive, we investigated cortical features in childhood posterior fossa tumor survivors. METHODS: T1-weighted MRI (MPRAGE, resolution=98x98x1.2mm) was acquired to investigate the cortical structure in adult survivors of childhood infratentorial tumors (n=19, 15males, 16.4–34.8 years old, 2-years after treatment). These scans were compared to age- and gender- matched controls. Supratentorial cortical volume and thickness were investigated using voxel-based morphometry (VBM) and surface-based morphometry (SBM), respectively. We compared patients and controls, irradiated (n=13) versus non-irradiated patients, and investigated the age at radiotherapy (peak level: p<0.001). RESULTS: Lower GM volumes were encountered in multiple brain areas of patients compared to controls, i.e. the right and left occipital and temporal lobes. Non-irradiated patients showed lower GM volumes then non-irradiated patients in the superior and middle frontal gyrus, the right supramarginal gyrus and precuneus. Age at radiotherapy was associated with GM volume in the inferior frontal gyrus. SBM yielded larger cortical thickness in patients in the left precuneus, inferior temporal and fusiform gyri. The opposite effect was only marginally significant, in the left temporal lingual gyrus. Age at radiotherapy was not associated with cortical thickness, but radiotherapy was associated with the left parietal lobe. CONCLUSION: Widespread differences in cortical volumes and thickness were observed in posterior fossa tumor survivors. Both radiotherapy and age at radiotherapy could be suggested as risk factors for long-term cortical development.

QOL-09. WHOLE-BRAIN WHITE MATTER NETWORK CONNECTIVITY IS DISRUPTED BY PEDIATRIC BRAIN TUMOR TREATMENT
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INTRODUCTION: Treatments for pediatric brain tumors (PBT) are neurotoxic and lead to long-term deficits that are driven by the perturbation of underlying white matter (WM). It is unclear if and how treatment may impact WM connectivity across the entire brain, and return to normal post treatment. METHODS: Magnetic resonance images from 41 PBT survivors (mean age: 13.19 years, 53% M) and 41 typically developing (TD) children (mean age: 13.32 years, 51% M) were analyzed. Image reconstruction, segmentation, and node parcellation were completed in FreeSurfer. DTI maps and probabilistic streamline generation were completed in MRtrix3. Connectivity matrices were based on the number of streamlines connecting two nodes and the mean DTI (FA) index across streamlines. We used graph theoretical analyses to define structural differences between groups, and random forest (RF) analyses to identify hubs that reliably classify PBT and TD children. RESULTS: For survivors treated with radiation, betweenness centrality was greater in the left insular (p < 0.000) but smaller in the right pallidum (p < 0.05). For survivors treated without radiation (surgery-only), betweenness centrality was smaller in the right interparietal sulcus (p < 0.005). RF analyses showed that differences in WM connectivity from the right pallidum to other parts of the brain reliably classified PBT survivors from TD children (classification accuracy = 77%). CONCLUSION: The left insular, right pallidum, and right inter-parietal sulcus are structurally perturbed hubs in PBT survivors. WM connectivity from the right pallidum is vulnerable to the long-term effects of treatment for PBT.