P.103

Imaging neuron-glioma cell interactions in freely behaving animals with a novel implantable mini-microscope

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Background: High grade gliomas (HGG) are diffusely infiltrative brain tumours with dismal prognosis. Recent studies from our lab have demonstrated that glioma cells form synapses with surrounding neurons, and proliferate in response to neuronal input. How these neuron-glioma networks develop, and are influenced by experience, is currently unknown. We aimed to develop a novel imaging tool to study neuron-glioma cell interactions in freely behaving animals. Methods: Several patient-derived HGG cell lines were transfected to express the green calcium indicator GCaMP6s. These cells were xenografted into the premotor cortex of mice, along with a virus expressing the red calcium indicator jRGECO1a under a neuronspecific synapsin promotor to allow dual-color imaging of neurons and glioma cells. The Inscopix mini-microscope system was implanted into the cortex to allow real-time live calcium imaging in freely behaving animals. Results: Several HGG cell lines effectively expressed the GCaMP6s calcium indicator. In vivo, we were successfully able to image both neurons and glioma cells simultaneously in freely behaving mice in real time. Conclusions: The Inscopix system has been modified for studying cancer cells for the first time. This technology will be used to study how pharmacological agents and neuronal experience shape neuron-glioma circuit dynamics, to develop new therapeutic strategies for HGG.

P.104

Grade 3 meningioma survival, recurrence and functional outcomes in an international multicenter cohort

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Background: Meningiomas are the most common intracranial tumor, graded from 1 (benign) to 3 (malignant). The aim of this study was to identify clinical features associated with overall survival (OS), progression-free survival (PFS) and functional status for malignant meningiomas. Methods: Demographic, clinical and histopathological data from grade 3 intracranial meningioma cases were identified in the clinical databases from seven sites in North America and Europe from 1991-2022. Summary statistics and Kaplan-Meier OS and PFS curves were generated. Results: We identified 108 patients, with a median age 65 years (IQR: 52, 72) and 53.7% were female. Median OS was 109 months (95% CIs: 88, 227), and 5-year OS rate was 65% (95% CIs: 56, 76). Median PFS was 38 months (95% CIs: 24, 56) and 5-year PFS rate was 37% (95% CIs: 28, 49). OS and PFS

were significantly lower in patients aged ≥65 years. Median preoperative KPS score was 80 (IQR: 70, 90), postoperatively KPS was 90 (IQR: 70, 98) and 1-year follow-up KPS was 70 (IQR: 50, 80). Conclusions: This study provides robust survival, recurrence and functional data for grade 3 meningiomas in North America and Europe over a 30-year period.

P.107

Endocrine and vision outcomes following 90Yttrium therapy for cystic sellar lesions: a prospective cohort study

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Background: Due to high risk of recurrence and complications associated with microsurgical resection or aspiration of enlarging cystic sellar lesions, stereotactic intracavitary irradiation with ⁹⁰Yttrium (⁹⁰Yt) has been proposed as an alternative to mitigate these challenges. Long-term efficacy data for this procedure is lacking. Methods: We conducted a Health Canada approved, single-centre, prospective cohort study to assess the effect of ⁹⁰Yt therapy on cyst volume, visual field (VF) testing and endocrine function. All patients underwent right frontal stereotactic insertion of ⁹⁰Yt colloid (200 Gy cyst wall). Results: 22 patients [mean age = 63.5 (± 15.4) years] received ⁹⁰Yt therapy. Mean follow-up was 52 (5-113) months. Cysts included: craniopharyngioma (86%), Rathke's cleft cyst (9%) and cystic prolactinoma (5%). Mean cyst volume reduction was 77% at 12-months (5.2 \pm 4.5 cc to 1.2 \pm 1.5 cc; p = 0.002). Rate of pre- and post-op hormonal dysfunction was 59% and 68%, respectively (p = 0.50). Pre-operative VF deficits were found in 68% of patients, of which 32% normalized and 36% remained stable (p = 0.180). Worsened vision was detected in 9% of patients post-operatively. Conclusions: 90Yttrium therapy significantly reduces sellar cyst size without having a deleterious effect on vision and endocrine function.

P.109

Meningioma with intraparenchymal abscess: a case report and review of the literaure

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Background: Intracranial intratumoural abscesses are rare occurrences typically treated with antibiotics and possible surgical resection. This study describes a meningioma-associated abscess and a review of the literature. Methods: Medical records and investigations were reviewed. A literature search of PubMed was completed. Results: A 56-year-old male presented with septic shock and dysuria. Urine culture isolated E. Coli, and he was treated with Ertapenem prior to discharge. A CT scan was ordered during hospitalization for unrelenting headaches, revealing a meningioma. Conservative management with follow-up as an outpatient was decided. However, he returned within two weeks with a fever and progressive left-sided weakness. A right frontal craniotomy for tumour resection was performed, and culture of necrotic-appearing tissue within the

Volume 50, No. S2 – June 2023 S85

tumour revealed E. Coli. He was treated with Meropenem for six weeks, and at follow-up, the patient was asymptomatic. Our scoping review illustrated that 18 meningioma-associated abscesses have been reported in the literature since the first report in 1994. Conclusions: This case highlights the hematogenous spread of a urinary infection, resulting in an intratumoural abscess. Review of the literature indicated that, similarly, 39% of cases had recent or concurrant urinary tract infections. Future studies should seek to determine conclusive guidelines for diagnosing intratumoural abscesses.

P.110

The use of 5-Aminolevulinic acid (5-ALA) in high-grade glioma surgery, a single Canadian center experience

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Background: 5-Aminolevulinic acid (5-ALA) is a prodrug used to selectively illuminate high-grade glioma (HGG) tissue intra-operatively, shown to nearly double complete resection rates in a 2006 multicentre, phase III clinical trial. Here, we review the history of the 2020 approval of 5-ALA in Canada and present some of the first preliminary results on resection rates, survival analysis, and adverse effects from a single Canadian center. Methods: We enrolled 76 patients (median age 61 years, 42 male) with suspected HGG amenable to surgical resection between June 2020 and January 2023. Gross total resection was defined by the absence of enhancing lesions on postoperative MRI. We compared the survival distributions of confirmed HGG cases with complete vs. incomplete resection using a log-rank test and Kaplan-Meier statistic. Results: 52 patients were confirmed as having a HGG based on a pathological diagnosis. In 32 of these patients (60.3%) a gross total resection was achieved. 82.76% were still alive at 180 and 270 days, and 72.73% at 360 days. 47.8% had a survival of 600 or more days. Conclusions: 5-ALA fluorescence-guided surgery resulted in high complete resection rates, and improved overall survival comparable to the literature with no notable adverse side effects.

P.111

5-ALA guided surgical resection of newly diagnosed high grade gliomas at Health Sciences North (HSN) in Sudbury, Ontario

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Background: Since its approval by Health Canada in 2020, several neurosurgical centres across Canada have used 5-ALA, an oral drug that assists with surgical resection of malignant gliomas by causing tumour cells to fluoresce under the microscope. The study's objective is to prospectively evaluate the extent of resection (EOR) and clinical outcomes in 5-ALA-guided surgery at HSN compared to historical controls. Methods: A retrospective analysis was performed of patients with

malignant gliomas having undergone surgery at HSN from 2011 to December 2020, assessing the EOR (contrast-enhanced tumour on post-operative CT/MRI), progression-free survival (PFS), overall survival (OS). Results: 235 patients underwent surgery for malignant glioma including 51 newly-diagnosed patients felt to be surgically resectable and with post-operative imaging. 25/51 (49%) had no residual tumour. The median PFS and OS were 7.1 and 11.5 months respectively. To date, 3 patients have successfully undergone 5-ALA-guided surgery with complete resection of contrast-enhancing tumour and no new focal neurological deficit post-operatively. Conclusions: We continue to recruit and follow prospectively patients having undergone 5-ALA-guided resection of malignant gliomas at HSN. Patients living in Northern Ontario may derive significant benefits from the use of 5-ALA-guided surgery, particularly since other technologies, such as intraoperative MRI and ultrasound, are costly and not available.

P.112

Location pattern of recurrence of WHO Grade 1 Meningiomas

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Background: Meningiomas can lead to significant morbidity and mortality and have recurrence potential despite their benign classification. The precise location of the recurrence has not been delineated. The objective of this study was to determine any spatial clustering of recurrence for surgically treated Grade 1 meningiomas. Methods: Patients diagnosed with Grade 1 meningiomas and treated with surgical resection with recurrence were reviewed. Patient demographics, presentation, extent of resection, time to recurrence, and location were established by medical records. Outcomes were the time to recurrence and location relative to the original surgical bed. Results: Among the 42 cases that met the study inclusion criteria, 12 were male and 30 were female. The mean age at treatment was 49.7 years, and the mean years until recurrence was 5.2 years. 33 (68.8%) tumours recurred locally, 12 (25.0%) recurred at the periphery (<1cm of the surgical bed), and 3 (6.3%) recurred distal to the resection site. Conclusions: A sizeable portion of cases may benefit from therapy directed beyond the resection margin. It may be more successful to prevent recurrence in these patients by performing a more aggressive resection of the dural attachment surrounding the tumour and/or focusing adjuvant therapy on the area surrounding the resection cavity.

P.113

Impact of 5-ALA on rates of complete high grade glioma resection: a Canadian perspective

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Background: The relationship between glioblastoma extent of surgical resection (EoR) and survival is well documented. ¹⁻³ The