Child Neurology (CACN)

C.1

Utility of genetic testing in the pre-surgical evaluation of children with drug-resistant epilepsy

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Background: All patients with drug-resistant focal epilepsy, should undergo an evaluation to determine if non-medical options, including surgical intervention, are appropriate. This evaluation involves a thorough work-up, typically including some or all of neuropsychological evaluation, prolonged video EEG monitoring, and advanced neuroimaging. The utility of genetic testing as part of this evaluation has not been thoroughly investigated. Methods: In this retrospective study, we reviewed the charts of pediatric patients referred for epilepsy surgery evaluation over a 5-year period. We extracted and analyzed results of genetic testing as well as clinical, EEG, and neuroimaging data. Results: 125 patients were referred for epilepsy surgical evaluation, 86 of whom had some form of genetic testing. Of these, 18 had a pathogenic or likely pathogenic variant identified. Genes affected included *NPRL3*, *TSC2*, *KCNH1*, *CHRNA4*, *SPTAN1*, *DEPDC5*, *SCN2A*, *ARX*, *SCN1A*, *DLG4*, and *ST5*. One patient had ring chromosome 20, one a 7.17p12 duplication, and one a 15q13 deletion. A specific medical therapy choice was allowed due to genetic diagnosis in three patients who did not undergo surgery. Conclusions: Obtaining a molecular diagnosis may dramatically alter management in children with drug-resistant focal epilepsy. Genetic testing should be incorporated as part of standard investigations in the pre-surgical work-up of such patients.

C.2

An in-depth analysis of pediatric inflammatory myopathies: findings from a comprehensive tertiary care hospital

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Background: Pediatric inflammatory myopathies (PIM) are a rare, heterogenous group of disorders requiring prompt diagnosis and treatment to reduce complications and improve long-term outcome. This study reviews the clinical characteristics, management, and outcomes in PIM. Methods: A retrospective analysis of pediatric patients diagnosed with PIM at CHEO from January 2009 to December 2023 was performed. Patient data, including age at symptom onset, diagnostic testing performed, treatment, and follow-up durations, were evaluated. Results: A total of 25 patients with juvenile dermatomyositis (JDM), overlap syndromes, and necrotizing myopathy (HMG-CoA reductase and anti-SRP myositis) were identified. Symptoms began at an average age of 8.37 years (1.10-14.11), with formal diagnosis occurring at 8.57 years (2.02-16.11). Initial symptoms included skin changes, muscle weakness, joint pain, and fatigue. Diagnosis involved laboratory testing (CK, myositis antibodies), muscle MRI, electromyography, and/or muscle biopsy. Treatments included corticosteroids, IVIG, and steroid-sparing agents (methotrexate, mycophenolate mofetil, rituximab, hydroxychloroquine). Follow-up averaged 4.23 years (range: 0.5 to 13). Most patients displayed only mild residual symptoms with the exception of an anti-SRP myositis patient who became wheelchair-dependent, requiring ventilatory support. Conclusions: Inflammatory myopathies require prompt treatment to prevent complications. Most patients require multiple treatment modalities, however with early diagnosis and treatment the majority of patients' symptoms resolve.

C.3

Retrospective study of sulthiame in treatment of pediatric epilepsy

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Background: This retrospective study assessed the efficacy and tolerability of sulthiame as a treatment in children with epilepsy. In Canada, sulthiame is only available through Health Canada's Special Access Program. Methods: Patients who received sulthiame at the Montreal Children's Hospital from April 2012 to March 2023 were included. Patients' medical charts were reviewed, and clinical data was extracted from neurology clinic notes and electroencephalogram (EEG) reports. Efficacy was assessed by comparing seizure frequency and frequency of EEG epileptiform abnormalities before and after initiating sulthiame, while also noting any reported changes in cognition or behaviour. Results: Sixteen patients were included (10 males, 6 females), all of whom had drug-resistant epilepsy and continuous spike-wave in sleep (CSWS) on EEG. Sulthiame starting dose ranged from 0.74 to 6.75 mg/kg/day. Improvement, either in terms of seizure control, cognition, or reduction in EEG epileptiform abnormalities, was reported in 8/16 children (50%). Two patients (13%) became seizure free, while three more (19%) had reduced seizure frequency. Three other patients (19%) had reported improvements in concentration, learning abilities or behaviour. No serious adverse event was reported. Conclusions: These data indicate that sulthiame is effective and well-tolerated in children with CSWS, regardless of the etiology and type of epilepsy.

C.4

Neurologic injury in pediatric patients cannulated for rescue extracorporeal life support

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Background: Historical literature suggests the risk of neurologic injury in children supported by extracorporeal life support (ECLS) is between 10-20%, however recent studies suggest the

incidence may be much higher. Methods: The Alberta Children's Hospital (ACH) Rescue ECLS program cannulates patients who are then transferred to the partner program at Stollery Children's Hospital. Data was systematically collected from all patients cannulated for Rescue ECLS at ACH October 2011 and May 2023. Neuroimaging (CT, MR) performed after cannulation was reviewed for evidence of ischemic and hemorrhagic strokes and hypoxic-ischemic brain injury. Results: Seventy-one patients were included in the Rescue ECLS cohort. Median age at cannulation was 1.74 years (range 0-17.6 years, 51% female). Survival to hospital discharge was 65%. Primary indication for ECLS included cardiac (42%), respiratory (33.3%), extracorporeal cardiopulmonary resuscitation (ECPR; 23.2%) and trauma (1.4%). Seventy four percent of the cohort underwent neuroimaging, of whom 67% had evidence of neurologic injury including stroke (ischemic 67%; hemorrhagic 50%) or hypoxic-ischemic injury (33%). Risk of neurologic injury did not differ by indication for ECLS. Conclusions: Neuroimaging abnormalities are present in most pediatric patients imaged post-cannulation for Rescue ECLS. Further research into modifiable risk factors for specific ECLS-related brain injuries may help to improve outcomes for survivors.

C.5

Altered inflammatory profiles in critically ill children with neurologic involvement

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Background: More than 1 in 4 children admitted to the pediatric ICU (PICU) have suspected neuroinflammation for a variety of reasons. While often beneficial, uncontrolled inflammation can lead to secondary neurologic injuries and interfere with repair mechanisms. Methods: A prospective cohort study was initiated at Alberta Children's Hospital to evaluate neuroinflammation in children admitted to the PICU. Forty-eight cytokines, chemokines and growth factors collected at multiple pre-determined timepoints were analyzed along with data on clinical trajectory. Preliminary exploratory analyses of patients enrolled January 2022-July 2023 were completed. Results: Fifty-three patients were included in the initial analysis. Encephalopathy (18.9%), hypoxia (17%) and TBI (15.1%) were the most common reasons for enrollment. All groups had temporal alterations in serum cytokines, with primary inflammatory brain diseases having the highest levels of innate inflammation (cytokine storm) on admission and day one compared to other subgroups. There was a trend towards normalization of cytokine levels over time. Conclusions: Temporal profiling of cytokine levels can inform on neuroinflammatory pathways contributing to the clinical course in critically ill children. Further analysis is ongoing with the entire cohort to evaluate longitudinal and between-group differences. Improved understanding of altered neuroinflammatory pathways in this population may assist with rationalizing targeted immunotherapies to improve outcomes.

C.6

Sex differences in neurodevelopmental outcomes and brain development from early-life to 8-years in preterm males and females

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Background: Sex is associated with differences in early outcomes with preterm males at greater risk for mortality and morbidity. The objective of this study was to examine preterm sex differences in neurodevelopmental outcomes and brain development from early-life to 8-years. Methods: A prospective cohort of preterm infants born 24-32 weeks gestation were followed to 8-years with standardized measures. MRI scans were performed after birth, term-equivalent age and 8-years. Associations between sex, risk factors, brain volumes, white matter fractional anisotropy (FA) and outcomes were assessed using generalized estimating equations. Results: Preterm males (N=83) and females (N=72) had similar risk factors, brain injury and pain exposure. Sex was a predictor of cognitive scores (P=0.02) and motor impairment (P=0.03), with males having lower cognitive scores and higher motor impairment over time. There was a sex effect for FA (P=0.04), with males having lower FA over time. There were significant sex-brain injury and sex-pain interactions for cognitive and motor outcomes. Conclusions: In this longitudinal study, preterm males had lower cognitive scores and greater motor impairment, which may relate to differences in white matter maturation. Effects of brain injury and pain on outcomes is moderated by sex, indicating a differential response to early-life adversity in preterm males and females.

Clinical Neurophysiology (CSCN)

D.1

Efficacy, safety, and tolerability of subcutaneous efgartigimod in chronic inflammatory demyelinating polyneuropathy: results from the ADHERE trial

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Background: Efgartigimod, a human immunoglobulin G (IgG)1 antibody Fc fragment, blocks the neonatal Fc receptor,