STROKE & NEUROVASCULAR DISORDERS

FP88

PERINATAL STROKE RISK FACTORS: SYNDROME-CONTROLLED ANALYSIS IN THE CANADIAN CEREBRAL PALSY REGISTRY

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Objectives: Perinatal stroke causes most hemiparetic cerebral palsy (CP). Pathophysiology is unknown with limited case-control studies. Comparisons to related disease states may provide unique insight. The population-based Canadian CP registry (CCPR) collects imaging and >70 risk factor variables. We hypothesized that perinatal strokes carry unique risk factor profiles within CP populations.

Methods: CCPR enrolls children across 13 Canadian centers. Systematic chart reviews and parental interviews acquire >150 variables including potential risk factors. Data current to June 2013 was extracted (RedCAP) and analyzed. Imaging reports for hemiparetic CP cases were classified as: (1) definitive stroke (arterial or venous), (2) probable stroke, (3) not stroke (alternate diagnosis), or (4) inconclusive. Risk factor variables were compared between definitive stroke and two disease control groups: (1) hemiparetic CP, not stroke and (2) all other CP. Univariate analysis informed multivariate logistic regression.

Results: Of 1168 children (57% male, median 42±23mos), hemiparetic was the most common CP phenotype (28%). Definitive perinatal stroke was common (158, 49%) compared to non-stroke (109, 34%) and 67% were arterial (33% venous). Comparing stroke to non-stroke hemiparetic CP found seven univariate associations but none persisted on multivariate analysis. Comparing stroke to other CP types demonstrated independent associations with preeclampsia (2.35;1.11-4.95;p=0.025), prematurity (0.165;0.093-0.293; p<0.001), maternal drug use (5.03;2.05-12.35;p<0.0001) and male gender (1.47;0.997-2.19;p=0.058).

Conclusions: CP registries are a valuable source of disease-specific etiologies including perinatal stroke. Stroke-specific risk factors may include previously (male gender) or inconsistently (preeclampsia) reported associations and novel factors (maternal drugs). Syndrome-controlled approaches may inform perinatal stroke pathogenesis.

FP89

PROFILE OF CHILDHOOD CEREBROVASCULAR OUTPATIENT CLINIC AT HOSPITAL IN THE SOUTH OF BRAZIL

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Introduction: Cerebrovascular disease in children has been increasingly diagnosed and studied, with advancements in technology and medical imaging. Its incidence ranges from 2 to 13 in 100,000 children and adolescents <18 years old and is 1 in 1,500-4,000 live births/year. Arterial ischemic stroke (AIS) is the most common childhood cerebrovascular disease. This issue has been extensively studied all over the world, especially during the last decade.

Methods: Data from the Childhood Cerebrovascular Outpatient Clinic at a public hospital were retrospectively reviewed, from March/2002 until September/2013. Patients with age varying from 0 to 18 years (at the moment of the stroke) were included.

Results: The sample is comprised of 133 cases of cerebrovascular disease, divided into three categories: 1) AIS, with 107 patients; 2) Hemorrhagic stroke, with 18 patients; 3) Sinovenous thrombosis, with 8 patients. Regarding age of the stroke, 36% occurred during neonatal period. In our sample, males were more affected than females (54.1%); as well as Caucasian children (86.4%). Six patients died due to cerebrovascular disease.

Discussion/Conclusion: In our sample, AIS was the most prevalent situation, in a slightly high percentage when compared with literature, probably because this specific disease was the first to be analyzed in our Center. The other results are in concordance with previous international studies. Our data show the relevance of cerebrovascular disease in neonates, children, and adolescents. These acute neurological situations must have to be remembered and diagnosed in the paediatric population, especially in the neonatal period.

FP90

NEUROLOGICAL INVOLVEMENT IN CHILDREN WITH E. COLI O104:H4-INDUCED HAEMOLYTIC URAEMIC SYNDROME

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Objectives: This study analyses the neurological involvement and the mid-term outcome in paediatric patients with haemolytic uraemic syndrome during the German epidemic 2011 caused by ***E. coli*** O104:H4.

Design, Setting, Patients: Data regarding clinical signs, magnetic resonance imaging (MRI) and electroencephalography (EEG) findings during the acute disease were analysed in 50 patients aged 1.3–17.5 years (median 11.9). Follow-up visits were performed after 3 and 6 months. In addition 25 children underwent neuropsychological testing (WISC IV) after 6 to 9 months of follow-up.

Results: Neurological involvement was observed in 14/50 (28%) patients, including stupor or coma in 11/50 (22%), seizures in 11/50 (22%), visual disturbances in 4/50 (8%), hemiparesis in 2/50 (4%), and myocloni in 3/50 (6%). One patient died and one developed residual hemiparesis. EEG was more frequently abnormal in patients with neurological involvement (12/14 vs. 13/25, p=0.03). Cranial MRI was obtained in 11 patients with neurological involvement with abnormal findings in 5. After 3 and 6 months, 28/42 (67%) and 17/39 (44%) of the patients complained about on-going reduced performance. Neuropsychological testing showed a slightly lower global intelligence quotient in patients with neurological involvement (113.4±2.8 vs. 119.4±1.8, p=0.07), mainly due to a reduced processing speed index.

Conclusions: Neurological involvement was frequent in paediatric patients with haemolytic uraemic syndrome caused by ***E. coli*** O104:H4, but there was a high incidence of pathological EEG-findings even in patients without clinical signs of neurological involvement in the acute phase. Major neurological sequelae were rare and neuropsychological outcome favorable after 6 months.

FP91

IS D-DIMER MEASUREMENT USEFUL IN PEDIATRIC CEREBRAL SINOVENOUS THROMBOSIS?

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Introduction: Pediatric CSVT diagnosis is dependent on neuroimaging (MRV/CTV). Biomarkers to suspect, quantify and prognosticate CSVT are lacking. D-dimer (DD) assay is useful in adults for diagnosis/prognosis.

Objectives: To determine frequency of elevated DD and its correlation with clot burden and outcome in paediatric CSVT.

Methodology: Children (29-days-18-years) with CSVT and DD assay from Sept'99-Dec'09 were identified. Patients with DD performed <7 before and <14 days after CSVT diagnosis were included. Clinical data, D-dimer (abnormal level: any value > institutional age-specific normative value, ng/mL) and neuroimaging data [high clot burden (>1 sinus with thrombus), haemorrhage, CSVT-propagation, recanalization] were analysed. Groups were compared by Fisher's exact/Chi-Square test. Logistic regression was used for outcome prediction.

Results: Ninety-three CSVT patients were identified. Sixty had DD. Forty-six (21 males) were included [mean age: 8-yrs, median time (in relation to CSVT-diagnosis) of DD-assay: 4+6.2-days]. DD was elevated in 32/46 (70%). No significant differences (with respect to age, gender, clinical/radiological features, risk factors, treatment) were found between those with and without elevated DD, except strong trends

with respect to high clot burden [97% with, 79% without elevated DD, (p=0.069)] and CSVT-propagation [25% with, 0% without elevated DD, (p=0.0845)]. Logistic regression analysis revealed 55% (p=0.1384; OR 1.55; 95% CI: 0.841-2.860) and 61% (p=0.1088; OR 1.61; 95% CI: 0.928-3.147) increased likelihood of clot propagation and poor neurological outcome respectively per 1000 unit DD increase.

Interpretation: D-dimer level is elevated in most children with CSVT and seems to correlate with CSVT burden, propagation and poor clinical outcome. Larger prospective study is warranted.

FP92

ROLE OF PROTHROMBOTIC RISK FACTORS (THROMBOPHILIA) IN NEONATAL ARTERIAL ISCHEMIC STROKE

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Introduction: Newborns constitute a large proportion of childhood arterial ischemic stroke (AIS). Relevance of prothrombotic risk factors in neonatal arterial ischemic stroke (NAIS) is unknown.

Objectives: To study the impact of prothrombotic risk factors on NAIS.

Methods: A single-centre retrospective analysis (July/1999-August/2009) of NAIS cases was conducted. Prothrombotic testing included protein-C(PC), protein-S(PS), antithrombin, anticardiolipin-antibodies(ACLA), lupus-anticoagulant, lipoprotein-(a), homocysteine, factor-VIII, factor-IX, factor-XI and Factor-V Leiden, prothrombin G20210A (PTG) and MTHFR gene mutations. Data on non-inherited coexisting risk factors [congenital heart disease (CHD), vasculopathy, head/neck disorders, systemic disease] and anti-thrombotic therapy (ATT) [Aspirin/anticoagulants] were collected. Stroke recurrence was defined as new ischemic lesion(s) on follow-up neuroimaging. Neurologic outcome was assessed by the validated Pediatric Stroke Outcome Measure (***any*** neurodeficit considered abnormal). Measures of association (Fisher's Exact) between risk factors, ATT and outcomes were studied.

Results: Seventy-six out of 88 NAIS cases (52 males) had prothrombotic testing. Of these 9(12%) had at least one prothrombotic risk factor [PC, ACLA, heterozygous PTG (2 each) and ACLA+factor-VIII, lipoprotein-a, MTHFR+elevated homocysteine (1 each)], and 62(85%) had at least 1 non-prothrombotic risk factor [majority: CHD (81%)]. ATT was administered in 37/88(43%). Stroke recurred in 8/88(13%). Presence of prothrombotic risk factor predicted stroke recurrence [OR 6.2(95%CI: 1.18-32.56); p=0.0485)] and trend towards poor outcome (median f/u: 2-yrs]) [(OR 6.97(95%CI: 0.82-59.34); p=0.069]. Neither presence of non-inherited risk factors nor ATT predicted outcome.

Conclusion: Prothrombotic abnormalities were encountered in a relatively small proportion of new-borns with AIS, but they were associated with unfavourable outcome. A larger prospective multicentre study is needed to corroborate these findings.

FP93

ROBOTIC QUANTIFICATION OF PROPRIOCEPTIVE DYSFUNCTION IN CHILDREN WITH PERINATAL STROKE

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Background: Perinatal stroke causes most hemiplegic cerebral palsy. Sensory dysfunction is an understudied contributor to disability in part due to limited objective measurement tools. Robotic technology can quantify complex sensory function in adult stroke but has not been applied to children. We hypothesized that proprioceptive dysfunction is measureable in children with perinatal stroke and correlates with stroke type and level of disability.

Methods: Children from the Perinatal Stroke Project had MRI confirmed unilateral perinatal stroke (arterial stroke or periventricular venous infarction) and upper extremity functional deficit. A bilateral exoskeletal robot (KINARM) tested planar upper limb movements in an augmented reality environment. Primary outcomes were two-dimensional variability, shift, and contraction/expansion scores of a position-matching task. Clinical measures of sensory function (touch, proprioception, graphesthesia, stereognosis) were scored. Matched controls (age/gender) were tested.

Results: Eight perinatal stroke children (median 15+/-2 years, 4 female) (3 PVI, 5 arterial) were compared to 9 healthy controls. Stroke children demonstrated marked impairment in position matching including variability (6.04±1.4 vs 3.93±0.6cm, p= 0.004) and shift (5.16±1.9 vs 1.91±1.1cm, p<0.001). Contraction/expansion ratios also appeared abnormal (0.56±0.27 vs 0.31±0.22; p=0.09). Deficits were greater in arterial lesions compared to PVI. Clinical sensory scores were lower in cases but correlated poorly with robotic measures and motor function. Assessments were well tolerated with no adverse events.

Conclusion: Robotic quantification of proprioception is feasible in perinatal stroke. Sensitivity and quantification appear superior to clinical exam. Disordered proprioception is an under-recognized component of disability and a novel therapeutic target.

FP94

HEMICEREBELLITIS: PRESENTATION OF THREE CASES

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Introduction: Cerebellitis is an acute syndrome characterized by inflammation of the cerebellum secondary to infections or vaccinations. Involvement of one hemisphere, hemicerebellitis, is rare.

Aim: To describe the clinical and imaging features and outcome of three patients with hemicerebellitis.

Methods: The clinical charts of patients with hemicerebellitis were reviewed.

Results: The patients presented with acute intense headache (2 occipital, 1 frontal) without a history of infection or vaccination. On physical examination only one patient was symptomatic showing diplopia and gait disturbance. In all patients CT scan showed hypodensity in one cerebellar hemisphere (with mass effect in one). Brain MRI revealed hemicerebellar hyperintensity on T2 and FLAIR with gadolinium enhancement. The following studies were normal: MR angiography of the brain and neck vessels, collagen disease test, thyroid profile, hemostasis and neurometabolic testing, echocardiography, and CSF cytochemistry. Opening pressure of CSF was normal. Only one patient had positive IgM antibodies to mycoplasma. Response to pulse methylprednisolone was good in all cases. The patients remained asymptomatic on subsequent control visits. Neuroimaging at 6 months after onset showed sulcal widening in two patients.

Conclusion: The presentation of acute intense headache and scarce or absent cerebellar symptoms without any other signs of intracranial hypertension was remarkable. Hemicerebellitis is a self-limiting entity which generally has a good prognosis, however, given the risk of potentially lethal complications (brain herniation) careful clinical and imaging follow-up is warranted during the acute phase of the disease.

FP95

MALIGNANT MIDDLE CEREBRAL ARTERY INFARCTION IN CHILDREN

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Background: Large hemispheric strokes have a high risk of fatal cerebral edema and brain herniation also known as "Malignant infarction of the middle cerebral artery" (MIMCA), this is a severe complication of arterial ischemic stroke seen in the adult population. The description of malignant MCA stroke syndrome in the paediatric population is very scarce (1, 2).

Aim: Describe the most common clinical, radiological and electrographic features associated with malignant MCA syndrome at the Hospital for Sick Children

Methods: Patients with a diagnosis of arterial ischemic stroke. A retrospective review of the clinical and radiological findings was performed, from a prospectively collected patients throughout the stroke database at the Hospital for Sick Children.

Results: We identified 117 children carrying the diagnosis of stroke at the Stroke Program at the Hospital for Sick Children in Toronto, ON Canada from January 2005 to September 2012.. Among these, 69 (58%) had MCA territory involvement. We identified 12 (17%) patients that developed malignant MCA syndrome. The mean age was 6.7 years (range from 0.08 to 15).

Conclusion: Malignant cerebral edema, is a severe complication of infarcts involving the middle cerebral artery territory. These patients have a more severe deficit on presentation and prolonged seizures. Large territorial infarcts, and proximal artery occlusion is seen in these patients. The early recognition of these findings could be helpful for clinicians in order to identify patients at risk.

FP96

SHINGLES OF THE BRAIN - RECURRENT HERPES ZOSTER OPHTHALMICUS CAUSING ARTERIOPATHY AND BASAL GANGLIA INFARCTION

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Introduction: *Varicella zoster* is thought to lie quiescent in the trigeminal ganglion following an episode of chicken pox. Viral reactivation occurs with retrograde infection of the first division of the trigeminal nerve and the clinical phenomenon of Herpes zoster ophthalmicus (HZO). Direct and indirect mechanisms affecting the neurovascular bundle are implicated in the aetiology of post-varicella angiopathy arterial ischaemic stroke (AIS) although pathological evidence is limited to.

Case: A five year old girl with a history of chicken pox at four weeks of age was diagnosed with HZO of the left eye (Fig 1). This remained indolent in the left eye despite treatment. Ten weeks after initial diagnosis, she presented with right sided choreoathetosis. MRI and MRA demonstrated left basal ganglia signal change, narrowing of the terminal left internal carotid artery (ICA), proximal anterior and middle (MCA) cerebral arteries (Fig 2). Ultrasound angiology revealed abnormal velocities of the left MCA and ICA. Protein S and C levels were transiently low. Further investigations were normal. She received a second course of HZO treatment and Dipyridimole. Choreoathetosis and MRI changes resolved however there was persistent narrowing of the vessels.

Conclusion: We propose HZO related AIS is the clinical equivalent to shingles of the brain supporting a peri-infectious, immune mediated inflammatory basis for the condition. We suggest pathology targeted treatments such as Acyclovir and corticosteroids be considered and that further research is required in this area.

FP97

ISOLATED BILATERAL CAROTID ARTERITIS PRESENTING WITH STROKE IN CHILDHOOD

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Introduction. Most arterial ischemic strokes in children are attributable to acquired vasculopathies, a significant subset of which are inflammatory in nature. The cervical carotid system in particular is often involved in Takayasu arteritis (TA), a systemic vasculitis that classically affects the aortic arch and its major branches. We discuss the case of a 16 year old girl with stroke and transient ischemic symptoms due to isolated inflammatory occlusive lesions of both carotid arteries.

Case Report. Our patient presented with stuttering onset of right-sided weakness and was found to have an acute ischemic stroke in the left basal ganglia and internal capsule. Labs were notable for elevated serum inflammatory markers. Vascular imaging demonstrated severe occlusive disease of both common carotid arteries, without involvement of the aortic arch or other branches. Her disease initially progressed, but stabilized with anticoagulation, antiplatelet therapy, corticosteroids, methotrexate, and cyclophosphamide. She subsequently presented with transient left-sided symptoms correlated with decreased perfusion in the territory of the right internal carotid artery.

Discussion. The common carotid arteries are among the most frequently affected vessels in TA. In children, approximately 52% of patients have common carotid involvement (1). However, isolated involvement of aortic branch vessels occurs in only 5% of cases (2), and isolated involvement of the common carotid arteries has not been reported to our knowledge.

Conclusions. Isolated inflammation of the common carotid arteries occurs in children and may present with ischemic stroke. A combination of aggressive antithrombotic, anti-inflammatory and immune-modifying therapy appears to halt disease progression.

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LONG-TERM NEUROPSYCHOLOGICAL OUTCOME AFTER CHILDHOOD CEREBRAL SINOVENOUS THROMBOSIS

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Introduction: Clinical outcome from childhood cerebral sinovenous thrombosis (CSVT), particularly in younger children, is poor. Most studies report "general" neurological outcomes; few describe neuropsychological outcomes.

Aim: To study the spectrum of neuropsychological deficits following childhood CSVT.

Methods: Retrospective analysis of neuropsychological testing (NPT) performed in children with CSVT from 1995-2011. NPT included IQ [Wechsler Intelligence Score for Children (WISC-IV), Wechsler Preschool & Primary Scale of intelligence (WPPSI-III)], executive function [Behaviour Rating Inventory of Executive Function (BRIEF)] and attention [Test of everyday attention (Tea-Ch)]. Full scale IQ (FSIQ) included verbal comprehension (VCI), perceptual reasoning (PRI), working memory (WMI) and processing speed (PSI) index.

Results: NPT [mean age: 5.4-years (neonatal CSVT), 8.5-years (non-neonatal CSVT)] was performed in 48/206 patients. Forty-one (34 males) were included [exclusions: cavernous sinus thrombosis (5), prematurity (1), co-existing arterial stroke (1)]. NPT revealed some abnormality in 87% [across one (29%)/multiple (58%) domains] compared to normative population. FSIQ was abnormal in 64% [VCI-69%, PRI-80%, WMI-71%, PSI-79%). FSIQ (p=0.026), VCI (p=0.608), PRI (p= 0.032), WMI (0.124) and PSI (p=0.007) scores were lower. No differences were seen in FSIQ between groups [neonates/non-neonates (p=0.827), single/multiple sinus thrombosis (p=0.2), present/absent parenchymal lesions (p=0.991)] except gender. Males had lower FSIQ (p=0.006) [PRI (p=0.004), WMI (p=0.002), PSI (p=0.002)], BRIEF [metacognition (p=0.061), executive composite (p=0.0950)] and Tea-Ch (p=0.046) scores.

Conclusions: Many childhood CSVT survivors (males > females) have significant residual cognitive deficits detectable only by NPT on long-term follow-up. NPT is indicated for more accurate CSVT outcome assessment.

FP99

HYPOTHERMIA IN HYPOXIC ISCHEMIC ENCEPHALOPATHY PRELIMINARY RESULTS IN NEURODEVELOPMENTAL OUTCOME

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Introduction: Perinatal **as**phyxial encephalopathy (PAE) is associated with high morbidity and mortality rates worldwide and is a major burden for the patient, the family, and society. The objective of the study was to evaluate neurodevelopmental outcome of newborn babies who underwent a protocol of Hypothermia in the first 72 hs of life. Taking into consideration that the incidence for PAE has not changed in the last 20 years, there is an urgent need to improve outcomes in affected infants.

Methods: To present our preliminary experience from two Institutions with 30 cases of clinical application of therapeutic corporal hypothermia for PAE. Systemic hypothermia temperature to 33.5ºC was begun and continued for 72 hours. Normalization of temperature is by 0.5ºC per hour. We included in a protocol all babies filling criteria.

Results: Cooling was well tolerated with no adverse reactions. Neurodevelopmental follow up of the surviving infants from 3 months to 40 months. There was considerable reduction on mortality and reduce on moderate PAE neurological disability. None developed feeding problems, oculomotor abnormalities, spasticity or seizures on follow up-

Conclusions: Induction of hypothermia to 33.5ºC central temperature for 72 hours in infants who had PAE improved neurologic outcomes in survivors. Hypothermia is beneficial on neurodevelpomental outcome in PAE babies. Our preliminary experience with this modality in a large neonatal service is consistent with the clinical findings of published trials. Decreasing motor, sensory and cognitive handicap and disability. Whether hypothermic therapy improves neurodevelopmental outcomes in long term is uncertain.