MD CONFERENCE EXPRESS

Issues in Pediatric Stroke

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Cerebral arteriopathy is the strongest predictor of recurrent arterial ischemic stroke (AIS) in childhood [Fullerton HJ et al. *Pediatrics* 2007]. Catherine Amlie-Lefond, MD, Medical College of Wisconsin, Milwaukee, WI, presented results from the International Pediatric Stroke Study (IPSS), which suggest a role for infection in the pathogenesis of cerebral arteriopathy.

The objective of the IPSS was to determine the prevalence/predictors of arteriopathy and, in particular, focal cerebral arteriopathy (FCA) in childhood. The study population included subjects aged 29 days to 19 years with AIS. FCA was defined as stenosis on vascular imaging that otherwise was not classified as dissection, moyamoya, sickle cell arteriopathy, vasculitis, or another specific diagnosis.

Of 667 subjects, 525 had known vascular imaging results; 277 of those had an arteriopathy**.** FCA/transient cerebral arteriopathy (25%), moyamoya (22%), and arterial dissection (20%) accounted for two-thirds of all subjects.

Independent predictors of arteriopathy were age 5 to 9 years (OR, 2.04; 95% CI, 1.25 to 3.34; p=0.004), sickle cell disease (OR, 3.06; 95% CI, 1.27 to 7.39; p=0.013), and upper respiratory infection (URI) (OR, 2.36; 95% CI, 1.05 to 5.27; p=0.037; Table 1). Predictors of FCA were determined by comparing the 69 subjects with FCA with the 456 without FCA. Recent URI was the only independent predictor of FCA (OR, 2.82; 95% CI, 1.29 to 6.22; p=0.01).

Table 1. Independent Predictors of Arteriopathy.

Demographics-Age Group		
29 days-4 years	reference	p value
5-9 years	2.04 (1.25-3.34)	0.004
10-14 years	1.12 (0.68-1.86)	0.647
15-19 years	1.10 (0.61-1.97)	0.749
Past Medical History		
Cardiac disease	0.37 (0.24-0.57)	<0.0001
Sickle cell disease	3.06 (1.27-7.39)	0.013
Recent Infection		
Sepsis	0.34 (0.13-0.88)	0.026
Meningitis	0.27 (0.05-1.36)	0.112
Upper respiratory infection (includes sinusitis and OM)	2.36 (1.05-5.27)	0.037

Additional support for infection as a risk factor for AIS comes from the Kaiser Pediatric Stroke Study (KPSS). Nancy K. Hills, PhD, University of California, San Francisco, CA, presented data from a nested case control study in a subset of patients from the KPSS, showing that minor infection is a significant risk factor for childhood stroke (32% of subjects with AIS vs 8% of controls; OR, 7.9; 95% CI, 3.7 to 16.8; p<0.0001).

Children with AIS had a variety of infections, and those in the controls were mostly acute otitis media and URI. Subjects with AIS also had a significantly (p<0.001) higher median number of medical visits for infection during the 2 years prior to stroke onset.

Despina Eleftheriou, PhD, Institute of Child Health, London, UK, presented the results of a retrospective study that showed that circulating endothelial cells (CECs) can be used to

track cerebral arteriopathy-associated vascular injury and to differentiate progressive versus nonprogressive disease in children with AIS.

The study included subjects aged >28 days with radiological confirmation of AIS. Progressive disease (n=7) was defined as recurrent clinical strokes ≥6 months after initial presentation and/or progressive arterial or parenchymal disease. Nonprogressive disease (n=18) was defined as no clinical or radiological recurrence over ≥6 months of follow-up.

The median concentration of CECs in the progressive group was 232 CECs/ml versus <50 CECs/ml in the nonprogressive group.

Antithrombotic treatment of neonates with cerebral sinovenous thrombosis (CSVT) is inconsistent. Lori C. Jordan, MD, Johns Hopkins University School of Medicine, Baltimore, MD, presented the results of a study that aimed to determine frequencies/predictors of antithrombotic treatment. The study was based on a subset of data from the IPSS and included 84 subjects with isolated CSVT.

Univariate analysis showed only 2 significant predictors of nontreatment: thrombus that was limited to the deep venous system (p=0.05) and presence in the United States (OR, 0.2; 95% CI, 0.1 to 0.5; p=0.001). After multivariate analysis, only geographic location (US versus non-US) remained significant. Dr. Jordan suggested that the high rate of nontreatment of neonatal CSVT may reflect uncertainty with regard to safety and the lack of evidence either for or against treatment.

Lauren A. Beslow, MD, University of Pennsylvania, Philadelphia, PA, presented results that showed that poor outcome in subjects with intracerebral hemorrhage (ICH) is associated with ICH >2% brain volume (RR, 3.9; 95% CI, 1.1 to 13.7; p=0.02) and early altered mental status (RR, 3.5; 95% CI, 1.3 to 9.9; p=0.01).

This prospective study included 26 subjects (median age 11.3 years; 50% female). Twenty of the hemorrhages were parenchymal (mostly in the cerebral lobes); 6 were subarachnoid. Mean hemorrhage volume was 1.9% of total brain volume. Subjects were followed for a median of 7 months. Although death was rare, residual deficits—mostly cognitive problems—affected >50% of subjects.

Coriene E. Catsman, MD, Erasmus Medical Center, Rotterdam, The Netherlands, presented results from a prospective study in subjects (aged 1 month to 17.1 years) with AIS, showing that poor outcome (modified Rankin Scale [mRS] score 3 or 4) is associated with right MCA stroke, fever at presentation, and younger age at onset.

The study was conducted in 76 children (46% male; median age 2.5 years). Follow-up data (median 2.6 years) were available for 66 subjects. Symptoms at presentation were similar to those seen in the literature. Risk factors included infection (39.5% of patients), arteriopathy (34.2%), cardiac disease (26.3%), prothrombotic disease (16.4%), cancer-related disease (6.6%), metabolic disease (6.5%), and others (2.6%).

Approximately 66% of the children had only 1 risk factor; 26% had >1 risk factor, and 8% had no risk factors. The most common impairments were motor (80%), cognition/behavior (~50%), aphasia (24%), and epilepsy (20%). On the mRS, 46% had mRS 1/2 and 54% had mRS 3. Eight patients died (mRS 4). Subjects <2 years at onset had lower scores on physical functioning, and those >6 years at onset had more cognitive deficits. Almost 50% of survivors were severely disabled (mRS ≥3); mortality was 11%.