Advances in Pediatric Stroke

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What’s New in Pediatric Stroke?

• Epidemiology: more common than we thought
• Risk Factors: the role of infection (&vaccination)
• Hyperacute Treatment
• (A few) Pediatric Stroke Syndromes

Stroke in Children: How often does that happen?

• Incidence:
  - 4.6 per 100,000 children/year in US
  - 1 per 3,500 neonates
  - About 5,000 US kids/year

Agrawal, Stroke, 2009

Stroke Subtype

Broderick, J Child Neuro, 1993
Etiologies of Childhood Stroke: The Typical Laundry List

- **Cardiac**
  - Congenital heart disease
  - Bacterial endocarditis
  - Rheumatic heart disease
  - Arrhythmias

- **Vascular disease**
  - Transient Cerebral Arteriopathy
  - Moyamoya
  - Arterial dissection
  - FMD

- **Hematologic**
  - Sickle cell disease
  - Leukemia
  - Polycythemia

- **Hypercoaguable state**
  - Acquired: sepsis, nephrotic syndrome, liver failure, SLE, anti-phospholipid syndrome, cancer
  - Inherited: protein C/S deficiency, AT III deficiency, Factor V Leiden, MTHFR, prothrombin 20210

- **Infection**
  - Meningitis/encephalitis
  - Chicken pox

- **Drugs**
  - Cocaine
  - OCP's
  - Chemotx (L-asp)

- **Metabolic/Genetic**
  - Homocystinuria
  - Fabry's
  - Organic acidemias
  - Majewski's Osteopetrosis
  - Leukemia
  - Neurocutaneous disorders: NF1, TS

What triggers stroke in a chronic disease?

Hedley A. Emsley, J CBF&Metabolism, 2011

Results: Infection

Infection ≤ 1 week prior to stroke/interview date conferred a 6.5-fold risk of AIS (p<0.0001).

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Infection & Stroke in Adults

- Peripheral inflammation
- Arteriosclerosis
- Stroke
- Systemic infection
- Hypothalmus and cytokines
- Systemic symptoms
- Microvascular injury
- Blood brain barrier

Hedley A. Emsley, J CBF&Metabolism, 2011

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Odds Ratios with 95% confidence intervals
Results:

- **Published seroprevalence** (IgG)
  - 20% by age 5 years
  - plateaus during later childhood
  - 40-60% in young adulthood (20-40 years)

- **After adjusting for age:**
  - OR 9
    (95% CI 3.1, 39; p=0.0004)

Results: Vaccination

Children reported to have had some/few/no routine vaccinations had 7 times the risk of stroke compared to those receiving all or most of their routine vaccinations.

OR = 6.6
(95% CI 2.3, 19.2), p=0.001

**Odds Ratios for Stroke by Vaccination Type**

**Hyperacute therapy in pediatric stroke: when to consider?**
**IV tPA: Cost/Benefit Ratio**

- **Adults:**
  - Cost: 10x risk of ICH
  - Benefit: Improved neuro outcome

- **Kids?**
  - Cost: Risk of ICH
  - Benefit: 

**TIPS Trial:** Thrombolysis in Pediatric Stroke
- Safety & dosing study only
- Closed due to lack of enrollment

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**Special Considerations in Children**

- Very limited data (case reports)
- Acute hemiparesis more likely to be non-stroke (migraine, seizure)
- Delayed stroke diagnosis
- Predominantly large vessel stroke
- Immature coagulation system—? tPA dosing

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**When We Consider Hyperacute Tx**

- Not very often—not standard of care
  - Older teenagers
  - Basilar artery thrombosis
  - Dominant MCA strokes

- But only with full disclosure to family of limited data in children, potential risks
(A few) Pediatric Stroke Syndromes

Childhood arteriopathies are important to recognize and diagnose because...

Arteriopathies predict recurrent ischemic stroke in children

Kaplan-Meier survival estimates, by abvascim_x_occl

Normal vascular imaging, n=30
Abnormal vascular imaging, n=22

P<0.0001 by log-rank

66% (95% CI 43-87%)

7 y.o. girl, previously healthy, R HP & aphasia

“Transient” Cerebral Arteriopathy (TCA)

• Natural history:
  – Monophasic disease
  – Initial progression (2-6 months)
  – Nonprogression after 6 months
  – Improvement or stabilization; rarely normalization
  – Chabrier & Sebire, J Child Neurol 1998; Danchaivijitr, Ann Neurol 2006

• Tx: aspirin

Courtesy of G. DeVeber
3 y.o. girl with “blown pupils” & left HP

- PMHx:
  - Congenital mydriasis
  - Patent ductus arteriosis
  - “Large bladder,” recurrent UTIs

ACTA 2 Mutations

- De novo (parents not affected)
- Arg179His (most common), Arg179Leu, Arg179Cys, Arg39Cys
- Affect smooth muscle function
  - Vascular disease: “moyamoya,” aortic aneurysms, aortic dissections, PDA, pulmonary hypertension
  - Congenital fixed dilated pupils (mydriasis)
  - Hypotonic bladder
  - Gut malrotation, delayed gastric emptying, constipation
- Tx: cautious revascularization (high surgical morbidity)
6 y.o. boy with recurrent posterior circulation ischemic strokes

Right Vertebral

R vertebral, Neutral

Head turned 45 degrees, left

Right Vertebral

Head turned 60 degrees, left

“Vertebral Artery CRIMP” Syndrome

- Cervical
- Rotational
- Injury
- Embolism
- Posterior circulation

- Chronic mechanical injury to the vertebral artery at C1/C2
- Progressive occlusion with head turning at the level of injury
- Tx: surgical decompression or endovascular vertebral occlusion

Stout C, et al, under review
Take Home Points

• Children have strokes (≈5,000 US kids per year)
• Infection can act as an acute trigger
  – Vaccinations are probably protective
• No answers on safety or efficacy of tPA in children
  – Not standard of care, but reasonable to consider in older teens with full disclosure to family on lack of data
• Arteriopathies in children are
  – Common
  – Strongest predictor of recurrence
  – Heterogeneous, with variable treatment approaches

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