Childhood Stroke: Challenges and Opportunities

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Disclosures

- Member of Clinical Event Committee for the Berlin Heart trial for pediatric ventricular assist devices.
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How does it start?

- Healthy 8 yr/o boy is playing with friends
- Suddenly has severe left eye pain
- Then slurred speech
- And weakness of the right arm and leg
- What now?
Arrives to ED, where main complaint is severe headache
- Right hemiparesis & speech deficit present but fluctuating
- Triaged as probable complicated migraine
- Head CT “negative”

- Gets IVFs & analgesic for HA
- After initial improvement, about to be discharged when hemiparesis becomes worse & he is completely aphasic.
Stroke in Childhood

CHALLENGES ↔ OPPORTUNITIES

- Specific and timely diagnosis
- Acute Treatment
- Secondary Prevention
- Recovery: rehabilitation, reintegration
- Advocacy and Education
**Background: How big is the problem?**

**Incidence:**
- Ischemic stroke 3-13/100,000/yr (similar to brain tumors)
- Intracranial hemorrhage 1-3/100,000/yr
- Cerebral sinovenous thrombosis 0.7/100,000/yr

**Modifiers of incidence:**
- Age: neonates ~30% of all childhood stroke
- Geography: the “stroke belt” exists for children
- Gender: M:F = 60:40
- Race, ethnicity (AA > others)
Background: How big is the problem?

**Mortality:** 0.1-0.5/100,000 person years
- Among top 10 causes of death in children in US
- Case fatality rate ~ 5% for CSVT, ~2-5% for AIS

**Outcome:**
- Outcomes: ~60% have long-term disability
- Factors which predict or modify outcome are poorly understood
- Children “grow into” their impairments – full effects on cognition, learning, social function evolve over years
Causes and Risk Factors for Ischemic Stroke in Children

Coagulation

Vasculature

Heart & Aorta

Cardiac-Aortic Embolism
- “Trans-cardiac” – right-to-left shunts w PFO, CHD
- Intracardiac clots – myocarditis, cardiomyopathy, arrhythmias, CHD
- Peri-procedural – heart surgery, catheterization
- Valvular disease - SBE
- Device-related – VAD, ECMO, artificial valves
- Intracardiac tumors
Causes and Risk Factors for Ischemic Stroke in Children

**Coagulation**

- Genetic thrombophilias (factor deficiencies, folate defects, mutations in fibrinolytic pathways)
- Autoimmune thrombophilias (APLAS)
- Hematologic disorders (Hgb SS, Fe-deficiency anemia)
- Drugs (IV Ig, L-asparaginase, contraceptives)
- Protein-losing conditions (enteropathies, nephropathies, liver failure)

**Vasculature**

**Heart & Aorta**
Causes and Risk Factors for Ischemic Stroke in Children

Arteriopathies:
- Genetic/syndromic (e.g. NF, alagille)
- Traumatic (dissection)
- Degenerative (post XRT)
- Inflammatory (infectious, autoimmune)
- Compressive (tumors)
- Sickle cell vasculopathy
- Unknown (e.g. moyamoya, focal arteriopathy)
Causes and Risk Factors for Ischemic Stroke in Children: What do we know?

*Ganesan et al, 2003  Results of 20-yr UK Cohort study N=212

Stroke Risk Factor Known At/Before Onset of Stroke*?

- YES ~45%
- NO ~55%

Risk factors in symptomatic AIS
- Menin-Gitis
- Brain Tumor
- Neuro-cutan
- Other Heme
- Immunol
- Other
- Cardiac 31
- Hemoglobinopathy, 35

Risk factors in cryptogenic AIS
- Thrombophilia
- Other heme
- Cardiac
- Vasculopathy
Challenge #1: Recognition

- Many “stroke mimics” → need MRI for dx:
  - Demyelinating, infectious/post-infectious, hypertensive encephalopathy, tumor, post-ictal paralysis, migraine, MELAS, psychogenic, infection
- Children can’t articulate symptoms
- Adult caregivers: “Children don’t have strokes”
- Infants fail to localize – newborns, infants with heart disease – have seizures, altered mental status
ED Presentation: Characteristics of Childhood Stroke vs. Stroke Mimics

Common Presenting Signs & Symptoms

![Bar chart showing frequency of signs and symptoms.]

- **Focal signs alone**
- **Focal signs + other**
- **Altered LOC**
- **Seizure**
- **HA**

- **AIS**
- **Mimics**

Frequency (% of group)
ED Presentation: Timeline to Diagnosis

A tertiary care pediatric hospital*

Time from onset of symptoms (hrs)

0 4 8 12 16 20 24 28 32

Dx confirmed

Initial imaging

Arrive to hospital

Seek medical help

*Rafay et al 2009
Challenge #2: Acute Treatment

- General support: normovolemia, normothermia, normoglycemia, aspiration & DVT precautions
- Reperfusion therapy:
  - IV tPA ?
  - IA tPA ??
  - Angioplasty???
- Managing seizures???
- Neuroprotection????
Use of alteplase in childhood AIS: IPSS experience 2003-2007*

687 children with AIS enrolled in IPSS 2003-2007

tPA given to 15 (2%):
9 IV at 3.3 hrs (2-52 hrs)
6 IA at 4.5 hrs (3.8-24 hrs)

Outcome
- Death in 2 (13%)
- Neurologic deficit at discharge in 12/13 survivors
- ICH in 4/15, none symptomatic

*Amlie-Lefond, 2008 Lancet Neurology
Eligibility for Thrombolysis in Children with Arterial Ischemic Stroke

Eligibility Assessment (CHOP registry 2008)

All cases, n= 70

Cases ineligible for tPA:
- Recent surgery, n=10
- Moyamoya disease, n=6
- Bacterial meningitis, HIV arteritis or vasculitis, n=6
- Malignancy, n=5
- Hemoglobinopathy, n=3
- Intracranial hemorrhage, n=4 (3 extra-axial, 1 infarct)
- Other (TBI, sepsis, prior AIS)

Potentially eligible, n= 33

PedNIHSS score < 10, n= 26

Presented > 3 hrs after symptom onset, n=13

Meet all eligibility criteria, n = 4 (6%)

RECEIVED tPA, n = 2
The role of tPA in children: Many unknowns

- Safety margin of tPA for systemic clots in children is narrow
- Timeline in adults is narrow, undefined in children
- Safety & dosing of tPA for childhood stroke is unknown
- Outcome prediction from stroke severity in 1st 6 hrs is unknown
Challenge #3: Secondary Prevention

- How big is the problem?
- Recurrence risk factors and natural history
- Current practices
- Unanswered questions & the need for research
Stroke Recurrence in Children: How often and when?

- CHOP registry data 2005-2009, N=90
- Mortality: 3 (3%) from underlying disease.
- Follow-up: available for 85 of 90 survivors, at median 16 months (1-72)
- Recurrence: in 12 patients (13%)
  - 6 events before stroke diagnosis was confirmed and treatment initiated
  - 7 events (in 6 pts) at median 9 days (4-96 days) after diagnosis confirmed and treatment initiated
Incidence: 3.9/100 person-years
Stroke recurrence-free survival at 1 year 92%. 
Risk Factors for Recurrence: Focus of current research

- Arteriopathy
  - 40-70% of childhood AIS
  - Interactions with thrombophilia and infection
- Thrombophilia
  - 10-20% of childhood AIS
  - Often multiple
  - Usually combined with other risk factors
Acute treatments:
- anticoagulation alone in 171 patients (27%),
- antiplatelet therapy alone in 177 (28%),
- antiplatelet and anticoagulation in 103 (16%),
- no antithrombotic treatment in 189 (30%).
Goldenberg 2009
AHA Scientific Statement

Management of Stroke in Infants and Children
A Scientific Statement From a Special Writing Group of the American Heart Association Stroke Council and the Council on Cardiovascular Disease in the Young

E. Steve Roach, MD, FAHA, Chair; Meredith R. Golomb, MD, MSc; Robert Adams, MD, MS, FAHA; Jose Biller, MD, FAHA; Stephen Daniels, MD, PhD, FAHA; Gabrielle deVeber, MD; Donna Ferriero, MD; Blaise V. Jones, MD; Fenella J. Kirkham, MB, MD; R. Michael Scott, MD, FAHA; Edward R. Smith, MD

Stroke. 2008;39:2644-2691
Challenge #4 The road to recovery: options for interventions

- Acute in-patient rehab
- Post-acute out-patient rehab: the promise of CIMT & other technologies
- Importance of family & psychosocial involvement
- Reintegration: the central importance of extending “rehab” into the school environment
Management: A Team Approach

Community awareness, field triage, early referral

Transport, Emerg Med, Nursing

RECOGNITION & INITIAL RX

Neuro, NroRad, ICU, Heme, Cardiol, Nsg, IR

COMPLETE DX, STROKE-SPECIFIC RX

PM&R, SW, Neuro, Heme

IN-PT REHAB, 2º PREVENTION

PM&R, SW, Educ Neuropsych, Neuro, Heme

OUT-PT REHAB, BACK TO HOME, SCHOOL

RECOVERY

SYMPTOM ONSET

Stroke Team: Neuro Fellow, Attnd Neuro, RN, SW
Stroke Care for Children: The importance of Nursing

- “Eyes & ears”
- Family & patient education & support
- Team leadership & integration
- Research
- Community outreach & education
Challenge #5: Advocacy & Public Awareness

- Family & Individual patient level: outreach to school
- Community level: teachers, school nurses, athletic team coaches
- Health care providers: PCPs, ED providers, EMTs
- National organizations: AHA, CHASA, other family-oriented support org
- Government: CHILDREN NEED ACCESS TO CARE
Children Don’t Have Strokes?
Just Ask Jared
By JONATHAN DIENST

“EMERGENCY Jared Dienst had walked to a park with his mother after school let out one day in June 2008 when he complained of a headache. He soon began to stumble, and his speech was slurred. ....”

Alex di Suvero for The New York Times
First and last – it's about children.....
– and their families.....