Advances in Pediatric Stroke Management

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Outline: Pediatric Stroke

- Presentation
- Diagnosis
- Management
  - Ischemic Stroke
  - Hemorrhagic Stroke
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

Children

Ischemic

Hemorrhagic

Adults

Ischemic

Hemorrhagic

Broderick, J Child Neuro, 1993
Types of stroke

- **Ischemic**
  - *Arterial Ischemic*
    - Large vessel
    - Small vessel
  - *Venous Sinus Thrombosis*

- **Hemorrhagic**
  - *ICH (intracerebral hemorrhage)*
  - *SAH (subarachnoid hemorrhage)*
Clinical Presentation: Arterial Ischemic Stroke

- **Most common presenting feature:**
  - *Hemiparesis 45-100%*
  
- **Onset of deficit (n=47, ischemic):**
  - *Abrupt 51%*
  - *Progressive over hours 36%*
  - *Waxing/waning 13%*

- **Seizures as presenting feature:** *26%*

  Mancini, J Child Neurol 1997; Abram J Child Neurol 1996

  Dusser, J Child Neurol 1986

Dusser, J Child Neurol 1986
Clinical Presentation in Children

Venous Sinus Thrombosis
• Headache: subacute
• Encephalopathy
• Seizures
• Focal deficits (less often)
• Pseudotumor cerebri

Hemorrhagic Stroke
• Headache: thunderclap
• Syncope
• Seizures
• Focal deficits
• Hypertension
Diagnosis: CT sensitive for intracerebral hemorrhage

White (bright) on CT:
- Blood
- Contrast
- Calcium
- Metal
Diagnosis: CT also sensitive for subarachnoid hemorrhage

- But gold standard is LP
- Consider when convincing story
Diagnosis: Ischemic Stroke

- CT insensitive in first 6-12 hours

- MRI highly sensitive
  - DWI positive within minutes, up to approx 10 days
Hyperacute Management
ICU Mgmt: Ischemic Stroke

- Goal #1: *Reperfuse brain by removing clot*
  - *Only case reports in kids*
  - *IV tPA (tissue plasminogen activator)*
    - Time window: within 4.5 hrs fr last seen normal
  - *IA tPA*
    - Time window: within 6 hrs for anterior circulation, 12 hrs for posterior circulation
  - *Clot retrieval*
    - 8 hrs for ant circ; no real time limit for basilar artery thrombosis
Thrombectomy: Merci retriever
IV tPA: Cost/Benefit Ratio

- Adults:

  Cost: 10x risk of ICH

  Benefit: Improved neuro outcome
IV tPA: Cost/Benefit Ratio

- Kids?:

  - ? Cost: Risk of ICH
  - ? Benefit
Special Considerations in Children

- Acute hemiparesis more likely to be non-stroke (migraine, seizure)
- Delayed stroke diagnosis
- Predominantly large vessel stroke
- Immature coagulation system -- ? tPA dosing
When We Consider Hyperacute Tx

- Older teenagers
- Basilar artery thrombosis
- Dominant MCA strokes

- *But only with full disclosure to family of limited data in children, potential risks*
ICU Mgmt: Ischemic Stroke

- Goal #2: Minimize the injury
- Protect the ischemic penumbra
  - “permissive HTN”
    - At least keep normotensive
    - 2X maintenance fluids
    - Pressors if necessary (esp if sedated for ICP mgmt)
      - Avoid significant HTN $\rightarrow$ risk of hemorrhage
- Avoid hyperglycemia & hyperthermia
ICU Mgmt: Ischemic Stroke

- Goal #3: observe for neurologic decompensation
- Mass effect/herniation:
  - max at 3-4 days
  - Hemorrhagic transformation
- Subfalcine herniation
  - ACA strokes
- Uncal herniation
ICU Mgmt: High Intracranial Pressure

- Osmotherapy
- Hyperventilation (short term benefit)
- Sedation/Coma

- Decompressive surgery
  - Cerebellar stroke
  - Malignant MCA
    - hemicraniectomy
ICU Mgmt: Ischemic Stroke

• Goal #3: Prevent recurrent stroke

• 2 main predictors:
  – **Age:** non-neonatal
  – **Etiology:** arteriopathy
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 Osteop dysplastic Primordial Dwarfism, type II
  - Collagen vascular (e.g., Ehlers-Danlos)

- **Neurocutaneous d/o’s**: NF1, TS
Kaiser Pediatric Stroke Study: Etiologies in a Population of Children

Idiopathic Vasculopathy
Infection
Prothrombotic
Other

Neonatal

Idiopathic
Vasculopathy
Infection
Prothrombotic
Other

Later Childhood

Idiopathic
Vasculopathy
Infection
Prothrombotic
Cardiac
Other

Recurrence: rare in babies, but occurs in up to 20% of older kids with stroke

Neonates, n=84

Older children, n=92

P=0.0003 by log-rank

19%
(95% CI 12-30%)

Fullerton, Pediatrics, 2007
Kids with diseased blood vessels to the brain are at higher risk of recurrence

P<0.0001 by log-rank

66%
(95% CI 43-87%)

Fullerton, Pediatrics, 2007
Treatment to prevent recurrent stroke depends on the cause of the first stroke
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

- **Tx:** aspirin
Arterial Dissection

- Tear in the wall of a blood vessel to the brain
- Caused by trauma, or spontaneous
- Tx: Anticoagulation (or aspirin)
- Fullerton, *Neurology*, 2001
6 y.o. boy with recurrent posterior circulation ischemic strokes

R vertebral, Neutral
Right Vertebral

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
Chronic, bilateral arteriopathies in children

Munot, Ganesan, *Brain* 2012
Moyamoya disease/syndrome

- Slow narrowing of the tops of the internal carotid arteries in the brain
- Seen in kids with sickle cell disease, Down syndrome, neurofibromatosis, brain cancer
- Tx: Surgical bypass
  - *Indirect*: EDAS
  - *Direct*: EC-IC bypass
Cardioembolic: Intracardiac Thrombus

- Tx: anticoagulation
- Duration x months or until clot resolves
Hemorrhagic Stroke Management
ICU mgmt: Intracerebral Hemorrhage (ICH)

- BP control
  - *Allow mild HTN*---improve cerebral perfusion
  - *Prevent significant HTN*---extend bleed
- Indications for ICP monitor
  - *Altered mental status: pathologic or iatrogenic*
- Manage elevated ICP
- Seizure prophylaxis? – consider for large bleeds with high herniation risk
- Observe for neurological decompensation: get worse (48-72 hrs) before they get better
ICU mgmt: ICH

- Neurosurgical management:
  - Large ICH, ICP refractory to medical therapy
  - Cerebellar ICH
  - Rare for neonates
ICU mgmt: ICH

• Prevent recurrent bleed—look for etiology
  – Check/correct plts, PT, PTT
  – MRI brain:
    • Cavernous malformation
    • Brain tumor
  – Vascular imaging: MRA and/or conventional angiography
    • AVM—most common cause in children
    • Aneurysm
    • Arteriovenous fistula
Brain Arteriovenous Malformations (AVM)

- Congenital malformations of blood vessels in the brain
- High flow
- Arteries feeding a nidus (tangle of abnormal vessels), draining into enlarged veins
Angiogram Of a Brain AVM
Treatment of Brain AVMs

- Embolization—usually just to decrease surgical risk, but not curative

- Surgical resection—risk based on size, location, deep venous drainage

- Radiosurgery (Gammaknife)—delayed effect (6 mo to 3 years), reserved for high surgical risk or unruptured
Brain Arteriovenous Fistula (AVF)

- Direct connection of artery to vein
- Can be congenital in children
- Tx: endovascular (embolization) first choice, or surgical
Cavernous Malformation

- congenital or acquired
- can be familial
- low flow lesion
- not seen on angiograms
- tends to cause smaller bleeds
- Tx: surgical resection
Subarachnoid Hemorrhage
Pediatric Aneurysms
Aneurysm Types

Also mycotic aneurysms
Pathophysiology of Pediatric Aneurysms??

Figure 1. Graphic representation of the concept that pediatric and adult aneurysms may result from different blends of intrinsic and acquired factors.

- **Intrinsic Vascular Factors**
  - Aneurysms in *children*
  - Aneurysms in *adults*

- **Acquired Vascular Factors**

**Connective Tissue Abnormalities**
- HTN
- Smoking
- EtOH

UCSF Benioff Children's Hospital
San Francisco
ICU mgmt: SAH/IVH

- Unsecured aneurysm: prevent rebleeding
- Rebleed rate: 5% at 24 hrs, 20% at 2 wks

- Keep patient normotensive
  - PRN anti-hypertensives
  - Analgesics for headache
  - Consider prophylactic anti-epileptics
    - Load with Fosphenytoin 20 mg/kg IV
ICU mgmt: SAH/IVH

- Identify source:
  - Aneurysm or AVM
  - MRI/MRA
  - Conventional angiogram
Treatment Options for Aneurysms

- Endovascular coiling
- Surgical clipping
ICU mgmt: SAH/IVH

• “Secured” aneurysm or AVM:
  – Liberalize BP (allow HTN)
  – Stop seizure prophylaxis

• Manage/Prevent complications of SAH
  – Hydrocephalus
  – Vasospasm
  – Hyponatremia
ICU mgmt: SAH/IVH

• Hydrocephalus
  – May occur acutely or delayed (up to weeks)
  – Indications for EVD:
    • Evidence of hydrocephalus on CT
    • Obtundation
      – ie, you don’t have an exam to follow
ICU mgmt: SAH/IVH

• Vasospasm
  – *Usually occurs at 4-6 days (range 3 days to 3 weeks)*
  – *Nimodipine 30 po/FT q 2hrs*
    • Neuroprotectant
    • Start immediately, continue x 21 days
    • SE: hypotension
  – *Tx:*
    • HTN, hypervolemia
    • angioplasty
ICU mgmt: SAH/IVH

- **Hyponatremia**
  - *Cerebral salt wasting (as opposed to SIADH)*
  - *Follow Na BID initially, then q 6 hours if low*
  - *Replace with po NaCl (N/V) or IV 3% NaCl*

- **Central (neurogenic) fever**

- **Diabetes insipidus--uncommon**
Summary

• Pediatric stroke is heterogeneous
• Significant ICU issues
• Vigilance to prevent secondary injury
• High risk of recurrence
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