Haemorrhagic stroke in children

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Definition

- Acute neurological deficit secondary to focal haemorrhage in the brain.
What are we talking about?

• Hemorrhagic stroke (HS):
  – Intracerebral hemorrhage (ICH)
  – Subarachnoid hemorrhage (SAH)
  – Intraventricular hemorrhage (IVH)

• Excluding:
  – Hemorrhagic infarcts
  – Neonatal IVH
  – Subdural hemorrhage (SDH)
  – Epidural hemorrhage (EDH)
The Relative Importance of Hemorrhagic Stroke in Kids

Broderick, et al, J Child Neurol 1993
Background

• In adults haemorrhagic stroke (HS) – 15% strokes

• Children HS : 45% - 50% stroke

• Mortality rate HS x5 higher than ischaemic stroke

• High risk of serious life-long disability
  – Affecting multiple domains
Previous Studies

• Very little study of HS in children

• 10 times more ischaemic stroke publications than HS publications since 2000

• Sparse outcome data

• No population based outcome data
SOCS Study Area

Total population: 31 million

>27 days and < 16 years: 6 million

63% of children in England

65 cases in 12 month period

Incidence of 1.1 per 100,000 per year

Study of Outcome of Childhood Stroke
Pattern of Haemorrhage

• 153 haemorrhagic stroke cases

• Mean age: 11.8 years (SD 6.5)

Fullerton, Stroke, 2007
Clinical Presentation

- Headache: thunderclap
- Vomiting
- Syncope
- Seizures
- Focal deficits
- Altered mental status
- Hypertension
Diagnosis: CT sensitive for intracerebral hemorrhage
Diagnosis: CT also sensitive for subarachnoid hemorrhage

- But not 100%
- Gold standard is LP
- Consider when convincing story
Aetiology

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Percentage of Cases</th>
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<tbody>
<tr>
<td>AVM</td>
<td>50%</td>
</tr>
<tr>
<td>Aneurysm</td>
<td>10%</td>
</tr>
<tr>
<td>CCM</td>
<td>5%</td>
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<tr>
<td>Tumour</td>
<td>10%</td>
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<tr>
<td>Haematological</td>
<td>5%</td>
</tr>
<tr>
<td>Unknown</td>
<td>10%</td>
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</tbody>
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Etiologies of Pediatric HS

• Structural 53%

– Other 10%
  • Hypertension, drug use, thrombocytopenia, hemophilia, leukemia

Fullerton, *Stroke*, 2007
AVM: the most common cause
Arteriovenous Malformations (AVM’s)

• Def: collection of abnormal thin walled vessels connecting arteries to veins

• Over time, feeding arteries and draining veins dilate

• Later, veins can stenose (risk for hemorrhage)
AVM’s: Presentation & Dx

• Miller 1994, 56 children, newborns to 18yo:
  – hemorrhage (50%)
  – seizures (9%)
  – recurrent HA’s (3.5%)
  – hydrocephalus (9%)
  – CHF (18%)
  – Other, including progressive neuro deficits (11%)

• Diagnosis: conventional angiography
AVM presentation

- Children are more likely to present with ICH

Treatment of Brain AVMs

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

- **Surgical resection**—risk based on size, location, deep venous drainage; tx of choice for an AVM that has bleed

- **Radiosurgery** (Gammaknife)—delayed effect (6 mo to 3 years), reserved for high surgical risk or unruptured
Cavernous Malformations (Haemangiomas)

• Spherical collections of endothelial lined sinusoidal (cavernous) vascular spaces

• feeding arteries and draining veins have normal calibre
Cavernous malformations

• Presentation:
  – Seizures
  – Symptomatic hemorrhage
  – Incidental

• Diagnosis:
  – MRI
  – Most are angiographically occult
Cav mal: Management

• Management:
  – Surgical
  – Observation
  – Radiosurgery not effective

• Goals of surgery:
  – Prevention of hemorrhage
  – (Seizure control)

• Indications for tx:
  – Symptomatic hemorrhage
  – (Uncontrolled epilepsy)

• Risks of surgery vs natural history risk
Cav mal: Natural Hx
Annual Hemorrhage Risk

- LIMITED data: retrospective, ? definition of hemorrhage

- Depends on Presentation (Komata 95; Kondziolka 95)
  - Incidental: 0.4%/year
  - Hemorrhagic presentation: 4.5-23%/year

- Depends on location (Wallace 97; Zabramski 99)
  - “Deep” (BS, cerebellar nuclei, deep grey; mostly sx): 5-11%/year
  - “Superficial”: 0%
Pediatric Aneurysms
in the 2 cases. Case 1 has a collagenoma on the cheek ipsilateral to the aneurysm. Case 3 had an aneurysm in the right internal carotid artery detected at 38 years of age, which was diagnosed and treated in another institution, and brain images were not available for review. A female patient (case 4) with probable tuberous sclerosis complex had an aneurysm in the left middle cerebral artery (figure 3). She had lymphangioleiomyomatosis and hepatic and adrenal angiomyolipomas, but no tubers, subependymal nodules, or other manifestations of tuberous sclerosis complex.

Discussion

The prevalence of intracranial aneurysms in this cohort with definite tuberous sclerosis complex is 3 of 404 (0.74%; 95% confidence interval, 0.19%–2.34%), which seems slightly higher than the incidental finding of aneurysms on brain MRI in the general population (0.35%; 95% confidence interval, 0.13%–0.67%).

To the authors' knowledge, 31 cases of intracranial arteriopathy in patients with tuberous sclerosis complex have been reported in the literature (Table 2). Most of them are aneurysms, but other arterial abnormalities, such as stenosis, ectasia, tortuosity, or moyamoya syndrome, have been reported.

Assessment by conventional MRI can lead to the underestimation of intracranial arteriopathy in tuberous sclerosis complex, and in studies in the general population as well, because magnetic resonance angiography, which provides more sensitivity in the detection of more small lesions, is not usually performed as a routine examination. At the moment, there is not enough information to warrant a change in this practice, but...
Aneurysm Types

Berry

Fusiform

Dissecting

Also mycotic aneurysms
Aneurysms different in children

Paediatric
- 2-5%
- 1-3 M: F
- Internal carotid bifurcation
- Giant 20-40%
- Rarely multiple (except HIV)
- Posterior circulation 20-40%

Adult
- 95-97%
- 3F:1M
- Ant Communicating
- Giant uncommon
- 15% multiple
- Post circulation 5%
Aetiologies of Pediatric Aneurysms

- Childhood aneurysms are expressions of vessel wall dysfunctions, failure to repair wall
- Primary triggers: Trauma, infectious, autoimmune (vasculitis)
- Silent genetic disease: AD polycystic kidney disease, Ehlers-Danlos, Marfan’s syndrome, NF1, tuberous sclerosis, MOPD (microcephalic osteodysplastic primordial dwarfism) type 2, moyamoya syndrome

Treatment Options for Aneurysms

- Endovascular coiling
- Surgical clipping
Aetiologies of *Spontaneous ICH & SAH* in children

Fullerton, *Stroke*, 2007
Recurrence risk
Hemorrhagic Stroke Recurrence Kaiser Study

- Follow-up data on 152 of 153 (1 lost to f/u)
- Median f/u period 3.5 years (4 days - 12 years)
- 16 recurrent hemorrhagic strokes
- Median of 20 days (4 days – 5.7 years) after initial event

*Fullerton et al, Stroke, 2007*
Aetiology of Recurrences

- Structural 12/16
  - 3 AVM
  - 5 cavernous malformations
  - 3 brain tumors
  - 1 aneurysm
- Trauma 1/16
- Other 3/16
  - Hypertension and anticoagulation, thrombocytopenia, moyamoya secondary to SCD (initial SAH, f/u stroke AIS)
Cavernous malformation: Genetics

- Seen on MRI in 0.4% of asymptomatic patients
- Most are sporadic
- Can be inherited: AD
- Three genes identified:
  - Krit1 (role in cytoskeletal/plasma membrane interactions); mutation in 50% familial cases
  - MGC4607/CCM2
  - PDCD10/CCM3
Genetics of AVMs: Hereditary Haemorrhagic Telangiectasia

• 1 in 5000 individuals
• Aka Osler-Weber-Rendu syndrome
• Characterised by abnormal blood vessel formation in multiple organs
• Mutations in transforming growth factor – beta (TGF-β) signalling pathway
Genetics of AVMs: RASA1 mutations

- Port-wine stains (cutaneous capillary malformations) and brain or spine AVMs and AVFs
- Appears to be AD, variable penetrance
- Over-activation of mTORC1 pathway

Outcome
Parental Impressions

• International Pediatric Stroke Study Recovery and Recurrence Questionnaire

• Recovery from stroke
  – Fully recovered : 15 (26%)
  – Not fully recovered (alive) : 28 (48%)
  – Death (from stroke) : 11 (19%)
  – Death (not stroke) : 4 (7%)

• Dependency (daily activities)
  – No extra help needed : 26 (60%)
  – Extra help needed : 17 (40%)
Paediatric Stroke Outcome Measure

Percentage of Cases

PSOM

Full recovery, Mild, Moderate, Severe, Died Stroke, Died other

Study of Outcome of Childhood Stroke
Deficit Type

Study of Outcome of Childhood Stroke
Conclusions

• Haemorrhagic stroke not uncommon
• Significant acute management issues
• Half of children with HS dead or dependent at follow-up (significantly worse outcome than AIS)
• Significant recurrence risk
• HS is an important but under researched childhood condition
Should siblings be screened?

- **Cav mals**: mostly sporadic; consider only if multiple cav mals or strong family hx
- **AVMs**: mostly sporadic; consider only if pt or family hx suggestive of HHT (eg. nose bleeds) or RASA 1 mutations (port-wine stains)
- **Aneurysms**: sibs at increased risk, but normal MRI does not rule out aneurysm at later age
Questions

• What is the most common cause of haemorrhagic stroke in children?
• What is the overall recurrence risk for haemorrhagic stroke in children?
• If a child presents with subarachnoid haemorrhage alone – what is the most likely cause?
• Approximately what percentage of children with haemorrhagic stroke will make a full recovery?
• Name one of the genetic mutations associated with hereditary cavenous malformation?