Pediatric Neuroangiography: A Case-Based Approach

Time for Stroke Conference
November 1, 2013  3:15 PM

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Disclosures

- Chief Medical Officer: ChemoFilter
- Scientific advisory: Medina
- Consulting: Stryker, Silk Road
- Data Safety and Monitoring Committee: DAWN trial (Stryker)
- Core Imaging Lab: MAPS trial (Stryker), FRED trial (Microvention)
- Grant support: NIH-NIBIB, ASNR Foundation
- I will discuss off-label uses of drugs (tPA) and devices (stents, balloons, calcium channel blockers)
- Videos from vendors will be shown
- I have borrowed liberally from my colleagues and acknowledge their kind help: Christopher Dowd, MD, Joey English, MD, PhD, Daniel Cooke, MD, Peter Jun, MD, Van Halbach, MD, Randall Higashida, MD, Charles Stout, MD, PhD
Outline

• Techniques and special concerns
• Age specific pathology
• Illustrative cases
Techniques and Special Concerns

- Physically small
  - 4 Fr sheath, 4 Fr dx catheter
- Low blood volumes
  - Slow heparinized saline arterial drips
- Highly reactive arteries
  - Ultrasound guided puncture, nitropaste
- Inability to remain still
  - Anesthesia support
Age Specific Pathology

- Genetic syndromes
- Congenital AV fistulas
- Vascular dysplasias
- Traumatic injuries
- CNS neoplasms
Case 1
Pediatric Stroke

- Annual incidence: 2.3 to 13/100,000 children
- Neonatal incidence: 1/5000 live births
- Dx often delayed
- Over 50% cause long term sequelae
- 6-19% recurrence in first few years

Pediatric Stroke

• Etiologies
  – Arteriopathy (up to 80%)
    • Trauma, NF1, Moyamoya, trisomy 21
  – Infection (meningitis, endocarditis)
  – Congenital heart disease
  – Hypercoagulability, sickle cell disease

• Lack of adult risk factors (until what age?)
  – Smoking
  – Sympathomimetic drug abuse
# Pediatric vs Adult Aneurysms

<table>
<thead>
<tr>
<th>Pediatric</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-5%</td>
<td>95-97%</td>
</tr>
<tr>
<td>1-3M:1F</td>
<td>3F:1M</td>
</tr>
<tr>
<td>ICA bifurcation</td>
<td>AComA</td>
</tr>
<tr>
<td>Giant 20-40%</td>
<td>Giant uncommon</td>
</tr>
<tr>
<td>Rarely mult (except HIV)</td>
<td>15% mult</td>
</tr>
<tr>
<td>Post circ 20-40%</td>
<td>5.5%</td>
</tr>
</tbody>
</table>
Pediatric Aneurysm Presentation

- Headache: 45%
- Stroke: 18%
- Cranial Neuropathy: 16%
- Nausea/Vomiting: 15%
- Vision Changes: 13%
- Trauma: 12%
- Asymptomatic: 7%
- Seizure: 4%
- Pulsatile Tinnitus: 1%

28% Rupture

Hetts et al., AJNR 30:1315-24, 2009
Aneurysm Etiology and Location

Hetts et al., AJNR 30:1315-24, 2009
When Do New or Enlarging Aneurysms Arise?

Entire Cohort
- 81 patients
- Gender M39:F42
- Age Range 0.3–18 years
- Mean Age 12.2 ± 5.1 years
- Mean Follow Up 3.8 ± 4.4 years

New/Enlarging Subset
- 7 patients (9%)
- Gender M4:F3
- Age Range 4–17 years
- Mean Age 10.7 ± 4.6 years
- Mean Time to New Aneurysm 3.9 ± 3.7 years
- Range of Time to New Aneurysm 0.8-12 years

Hetts et al., AJNR 30:1315-24, 2009
Hetts et al., AJNR 32:2017-22, 2011
Comorbidities in Patients with New/Enlarging Aneurysms

- AIDS
- X-linked Severe Combined Immunodeficiency (SCID)
- Tricuspid Atresia
- Vascular Birthmark
- Microcephalic Osteodysplastic Primordial Dwarfism Type II (MOPD II)
- Hemiatrophy
Pediatric Aneurysms: Summary

• 9% of children with aneurysms develop a new or enlarging aneurysm an average of 4 years later (range: 10 mo to 12 yrs)
• Most children with new aneurysms have identifiable comorbidities
• Fusiform aneurysms are overrepresented
• New aneurysms may be in different vessel
• Close imaging and clinical follow up is warranted
Case 3
Angiographic evaluation of SAH

• What constitutes a complete angiogram?
• Internal carotid arteries (head)
• External carotid arteries (head)
• Vertebral arteries – including cervical segments
• Assess vessel origins with common carotid and subclavian arteriograms
Perimedullary AVF

- Type IV spinal vascular malformation
- Micro (group 1 and 2) and macro (group 3)
- Demographics (Antonietti et al., AJNR 2010)
  - Group 1: 54 y (40-65 y)
  - Group 2: 45 y (16-82 y)
  - Group 3: 17 y (2-40 y)
- Presentations: myelopathy, SAH
- Pathophysiology: venous hypertension, cord compression
Treatment Options

• Surgery – often best for micro AVF
• Embolization
  – Favorable for macro AVF or large varices
  – Favorable for young children
• Medical – alteration of coagulation or venous hypertension may temporize but not cure
Case 4
Look before you leap

- 3 day old girl
- Severe CHF, pulmonary HTN, “occipital infarct”
- Transferred for emergent embolization
- MRI scan obtained
Vein of Galen Malformations

- AV shunt to median vein of prosencephalon (midline Prosencephalic Vein of Markowski)
- Embryological precursor to vein of Galen
- Congenital
- Clinical
  - neonates: high output CHF
  - infants: hydrocephalus, ↑ head circumference
  - children: MR, seizure, ↑ facial/scalp vv., hemorrhage
VOGM Angioarchitecture

• True Vein of Galen Malformation

  ➢ **Choroidal**: persistent primitive choroidal aa; numerous small shunts (*neonates*; *ill*)

  ➢ **Mural**: direct AV fistulas to wall of median prosencephalic v.; fewer larger shunts (*infants*; *less ill*)

• “False” VOGM: dilated vein of Galen 2º to AVM/AVF; acquired vein of Galen ectasia drains AVM/AVF and normal brain.
VOGM Natural History

- **Cardiac**
  - L -> R shunt causes high output CHF, R heart failure, pulm. HTN, hepatic and renal failure, coagulopathy

- **Neurological**
  - “Hydrovenous disorder”
  - AV shunt + venous outflow restriction -> venous HTN -> atrophy -> DD and HCP
VOGM: Hydrocephalus

- Rarely 2º to aqueductal obstruction by varix
- ↑ venous pressures (often >30mm), ↓ CSF absorption, arachnoid granulation immaturity, ↑ CSF volume
- Avoid CSF shunting!
  - changes cerebrifugal medullary v. outflow to cerebripetal -＞ ↑ venous congestion -＞ sz, DD, hemorrhage
- Endovascular Rx of AVF to ↓ venous HTN
VOGM: Treatment

- No treatment
- Medical: CHF management
- Surgical: disconnection of AV shunts
- Endovascular:
  - Transarterial
  - Transtorcular
  - Transvenous
  - Transarterial → venous
  - Transvenous → arterial

*Complete cure not required, staged Rx preferable*
Outcomes: Pediatric VOGM

- Features associated with poor neurological outcomes:
  - Neonatal presentation, CHF, choroidal angioarchitecture

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Complete Occlusion</td>
<td>21/27 (77.8%)</td>
<td>118/216 (54.6%)</td>
</tr>
<tr>
<td>Death</td>
<td>4/27 (14.8%)</td>
<td>23/216 (10.6%)</td>
</tr>
<tr>
<td>No neurologic or developmental disability</td>
<td>14/27 (51.2%)</td>
<td>143/216 (66.2%)</td>
</tr>
</tbody>
</table>
NGAVF Early Presentation

Neonates - First month of life (8/23)

• (7/8) with CHF and large complex fistulas with multiple sites of AV shunting

• (1/8) scalp segmental cutis aplasia, enlarging scalp hemangioma, facial venous malformation, HCP, asymmetric facial weakness
NGAVF Delayed Presentation

After first month (15/23)

- Single hole fistulas predominated
- Associated symptoms
  - Seizure (8/15)
  - Headache (5/15)
  - Focal neurologic deficit (4/15)
  - Hemorrhage (3/15)

Single hole AVF with giant varix
Outcomes: Pediatric NGAVF

- NGAVFs are heterogeneous lesions with similar morbidity and mortality as VOGMs

<table>
<thead>
<tr>
<th>Outcome</th>
<th>NGAVF - Hetts et al. 2012</th>
<th>VOGM - Fullerton et al. 2003</th>
<th>VOGM - Lasjaunias et al. 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Occlusion</td>
<td>15/23 (65.2%)</td>
<td>21/27 (77.8%)</td>
<td>118/216 (54.6%)</td>
</tr>
<tr>
<td>Death</td>
<td>2/23 (8.7%)</td>
<td>4/27 (14.8%)</td>
<td>23/216 (10.6%)</td>
</tr>
<tr>
<td>No neurologic or developmental disability</td>
<td>11/23 (47.8%)</td>
<td>14/27 (51.2%)</td>
<td>143/216 (66.2%)</td>
</tr>
</tbody>
</table>
PEDIATRIC AVMs:
SPECIAL FEATURES

• Neonates/Infants:
  – Multiple pial AV fistulas (continuum with NGAVF)
  – Present with CHF

• Children:
  – Smaller nidus c/t adults
  – Increased frequency of hemorrhage
  – Increased frequency of IV hemorrhage
Recent AVM Research at UCSF

• To determine if clinical presentation and angioarchitectural features differ between children and adults with brain AVMs
Materials and Methods

• UCSF brain AVM database queried
  – Prospectively collected since 2001
• Patients with nidal AVMs were analyzed
  – VOGM, DAVF, NGAVF excluded
• Demographics and angioarchitecture abstracted and analyzed with logistic univariate and multivariable models
# Demographics and Presentation

<table>
<thead>
<tr>
<th></th>
<th>Children (0-18 y) (n=203)</th>
<th>Adults (≥19 y) (n=630)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Dx (yrs)</td>
<td>12 ± 5</td>
<td>43 ± 15</td>
<td></td>
</tr>
<tr>
<td>Female Gender</td>
<td>101 (50%)</td>
<td>321 (51%)</td>
<td>0.687</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td>0.014</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>88 (43%)</td>
<td>343 (54%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>11 (5%)</td>
<td>42 (7%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>71 (35%)</td>
<td>153 (24%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>31 (16%)</td>
<td>82 (13%)</td>
<td></td>
</tr>
<tr>
<td>Native American</td>
<td>1 (&lt;1%)</td>
<td>8 (1%)</td>
<td></td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>119 (59%)</td>
<td>256 (41%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Results: Demographics

- Children more likely to present with AVM hemorrhage than adults
  - OR 2.1 (95% CI 1.45 to 2.91)
- Overrepresentation of Hispanic children as compared to adults
# Angioarchitecture: Nidus and Feeding Arteries

<table>
<thead>
<tr>
<th></th>
<th>Children (n=203)</th>
<th>Adults (n=630)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nidus Size &lt;3 cm</td>
<td>95 (53%)</td>
<td>322 (55%)</td>
<td>0.069</td>
</tr>
<tr>
<td>Nidus Size 3-6 cm</td>
<td>68 (38%)</td>
<td>237 (41%)</td>
<td></td>
</tr>
<tr>
<td>Nidus Size &gt;6 cm</td>
<td>15 (8%)</td>
<td>23 (4%)</td>
<td></td>
</tr>
<tr>
<td>AVM Border Diffuse</td>
<td>38 (23%)</td>
<td>102 (19%)</td>
<td>0.218</td>
</tr>
<tr>
<td>Lobar Location</td>
<td>125 (71%)</td>
<td>430 (77%)</td>
<td>0.013</td>
</tr>
<tr>
<td>Central Location</td>
<td>78 (44%)</td>
<td>201 (36%)</td>
<td>0.075</td>
</tr>
<tr>
<td>Feeding Artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneurysm Related to</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shunt Flow</td>
<td>21 (13%)</td>
<td>151 (29%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
3 yo M with IVH
Corpus striatum AVM
Recurrent artery of Heubner feeding artery aneurysm
## Angioarchitecture: Venous

<table>
<thead>
<tr>
<th></th>
<th>Children (n=203)</th>
<th>Adults (n=630)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous Drainage</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Superficial</td>
<td>67 (37%)</td>
<td>322 (55%)</td>
<td></td>
</tr>
<tr>
<td>Deep</td>
<td>51 (28%)</td>
<td>83 (14%)</td>
<td></td>
</tr>
<tr>
<td>Superficial and Deep</td>
<td>61 (34%)</td>
<td>177 (30%)</td>
<td></td>
</tr>
<tr>
<td>Venous Ectasia</td>
<td>45 (35%)</td>
<td>228 (52%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Venous Stenosis</td>
<td></td>
<td></td>
<td>0.144</td>
</tr>
<tr>
<td>0-24%</td>
<td>75 (56%)</td>
<td>191 (44%)</td>
<td></td>
</tr>
<tr>
<td>25-49%</td>
<td>22 (16%)</td>
<td>71 (16%)</td>
<td></td>
</tr>
<tr>
<td>50-74%</td>
<td>24 (18%)</td>
<td>102 (23%)</td>
<td></td>
</tr>
<tr>
<td>75-99%</td>
<td>12 (9%)</td>
<td>59 (14%)</td>
<td></td>
</tr>
<tr>
<td>100% (occlusion)</td>
<td>2 (1%)</td>
<td>13 (3%)</td>
<td></td>
</tr>
</tbody>
</table>
Results: Angioarchitecture

- Size and diffuseness of AVM nidus did not differ between children and adults.
- Larger AVMs did present at younger ages (mean 26.8 y for >6 cm vs. 37.1 y for <3 cm).
- Location and venous drainage did differ:
  - Children more likely to have exclusively deep venous drainage than adults.
  - Children more often harbored deeply-located AVMs; adults more frequently had lobar AVMs.
Results: Angioarchitecture

- Venous ectasia and feeding artery aneurysms were underrepresented in children
  - ? due to hemodynamic stress
  - take time to develop
Discussion

• AVM presentation with hemorrhage in all patients:
  – Deep venous drainage, supply by perforators, nidal aneurysms, multiple aneurysms, supply by posterior circulation, basal ganglia location\(^1\)
  – Children more likely to present with hemorrhage than adults\(^2\)

• AVM presentation with hemorrhage in children:
  – Smaller AVM nidus, only deep venous drainage, infratentorial nidus location\(^3\)

\(^1\)Turjman *Neurosurg* 1995
\(^2\)Fullerton *Stroke* 2005
\(^3\)Ellis *JNIS* 2012
Discussion

• Subsequent AVM hemorrhage in all patients:
  – Small number of draining veins, venous ectasias, deep nidus location¹
  – Age (increasing), deep nidus location, only deep venous drainage²
  – Ethnicity: Hispanic patients more likely to have subsequent hemorrhage than white patients (OR 3.1, p = 0.013)³

• Subsequent AVM hemorrhage in children:
  – Children are less likely to have second hemorrhage during follow up than adults⁴

¹Stefani Stroke 2002
²Stapf Neurology 2006
³Kim Stroke 2007
⁴Fullerton Stroke 2005
Conclusion

- AVMs and their draining veins were more likely to be located deep within the brain in children
  - Do centrally-located AVMs arise earlier in development?
  - Or, do central AVMs have intrinsic features making them more likely to come to clinical attention early in life?
Conclusion

• Although children with brain AVMs were more likely to come to clinical attention due to hemorrhage than adults, certain high risk features (venous ectasia, feeding artery aneurysms) were underrepresented in children.

• Perhaps this helps explain the lower reported risk of hemorrhage during follow up in children.
PEDIATRIC DAVFs: SPECIAL FEATURES

- Congenital
- CHF, macrocephaly
- Higher flow rates, larger shunts
- Higher mortality
## Pediatric DAVF Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>UCSF Study</th>
<th>(Kincaid et al. 2001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete AVF Occlusion</td>
<td>6/21 (28.6%)</td>
<td>3/7 (42.9%)</td>
</tr>
<tr>
<td>No Neurological or Developmental Delay</td>
<td>4/21 (19%)</td>
<td>2/7 (28.6%)</td>
</tr>
<tr>
<td>Death</td>
<td>4/21 (19%)</td>
<td>2/7 (28.6%)</td>
</tr>
</tbody>
</table>
## Comparative Outcomes

### Comparison to other pediatric intracranial AVFs

<table>
<thead>
<tr>
<th>Outcome</th>
<th>UCSF DAVF 2012</th>
<th>UCSF NGAVF 2011</th>
<th>UCSF VOGM 2003</th>
<th>Bicetre VOGM 2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete AVF Occlusion</td>
<td>6/21 (29%)</td>
<td>15/23 (65%)</td>
<td>21/27 (78%)</td>
<td>118/216 (55%)</td>
</tr>
<tr>
<td>No Neuro Deficit or Devel Delay</td>
<td>4/21 (19%)</td>
<td>11/23 (48%)</td>
<td>14/27 (51%)</td>
<td>143/216 (66%)</td>
</tr>
<tr>
<td>Death</td>
<td>4/21 (19%)</td>
<td>2/23 (9%)</td>
<td>4/27 (15%)</td>
<td>23/216 (11%)</td>
</tr>
</tbody>
</table>
CNS Arteriovenous Shunting Lesions

- Vascular malformations
  - AVM
  - DVA
  - Cavernous malformation
  - Capillary telangiectasia
  - Transitional vascular malformation
- Dural AV fistula
- Traumatic AVFs

- Pediatric lesions
  - AVM
  - Pial NGAVF
  - Dural AVF
  - Vein of Galen malformation

- Spinal vascular lesions
  - AVM
  - Perimedullary AVFs
  - Spinal dural AVF
Retinoblastoma

- Loss of Rb tumor suppressor gene
- Unilateral, bilateral, or “trilateral” disease
- Traditional management of advanced dz
  - enucleation
  - combo: radiation, IV chemorx, cryo, laser
- IA chemotherapy first described 1958 (TEM)
- ICA chemotherapy (melphalan) Japan 1990s to 2000s with balloon inflated above OA
Intraarterial Chemotherapy for Ocular Retinoblastoma

- Small guide catheter (4Fr) to proximal ICA
- Small microcatheter (1.5 Fr) to OA origin
- Low dose x-ray settings, minimize angiograms
- Infuse weight based dose of melphalan over 30 minutes
- Early results: excellent regression of tumors
- Prevent enucleation or mets in 70% of eyes over 2 years of follow up (Gobin, 2011)
Conclusion

• Children are not small adults
• Age-specific diseases
• Assiduous technique
• X-ray and chemotherapy dose minimization
• Endovascular therapy for vascular and nonvascular conditions
Thank You

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