Cerebral Vascular Malformations in Hereditary Hemorrhagic Telangiectasia

June Yowtak, MD, PhD
Georgia Neurosurgical Society Meeting
December 8, 2013
Acknowledgments

M. Neil Woodall, MD
Ian Heger, MD
Cargill H. Alleyne, Jr., MD
James Gossage, MD

No Disclosures
Hereditary Hemorrhagic Telangiectasia (HHT)

- Osler-Weber-Rendu disease
- Affects 1.4 million people world-wide
- Mucocutaneous telangiectasias, visceral arteriovenous malformations, epistaxis
- Inherited in autosomal dominant fashion
  - HHT1 = Endoglin (ENG) gene
  - HHT2 = Activin-like kinase receptor 1 gene
  - JPHT = SMAD4 gene
Cerebral Vascular Malformations (CVM)

- 5-20% of people with HHT
- Cerebral arteriovenous malformations (AVM), spinal AVM, ischemic stroke, brain abscess, intracerebral hemorrhage, migraines, seizures
- Annual spontaneous hemorrhage rate of sporadic AVM is ~ 2-4%
- Current guidelines: screen children in the 1st 6 months of life (or time of Dx) with MRI

HHT Foundation

- GRU is one of 16 US centers (35 worldwide)
- Jim Gossage (Dir. of Pulm. Vasc. Dis. At GRU) is Med. Dir. of HHT Foundation
- Multidisciplinary program
  - Pulmonology
  - Genetics
  - Interventional radiology
  - Gastroenterology
  - Otolaryngology
  - Neurosurgery
Characterization of CVM in HHT

• Retrospective review of database from 8/2002 – 10/2009
• 167 pediatric patients < 21 years of age
• Data collection:
  – History, physical exam, radiographic studies
  – 3 Tesla MRI/MRA with and without gadolinium with gradient echo sequences
• AVMs analyzed with regard to size, location, eloquence of cortex
Results

• Average age of referral 9.6 years (range 0.1 to 20.7 yr)
• 76 patients with definite HHT, of these 68 had screening MRI/MRA brain
• CVM in 11 patients
  – 7 cerebral AVM
  – 2 developmental venous anomalies
  – 1 cavernous malformation
  – 1 capillary telangiectasia
## HHT AVM Characteristics

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Size</th>
<th>Location</th>
<th>Eloquence</th>
<th>Venous Drainage</th>
<th>Treatment</th>
<th>Outcome</th>
<th>DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 F</td>
<td>&lt;3cm</td>
<td>Cerebellum</td>
<td>No</td>
<td>Superficial</td>
<td>None</td>
<td>Thrombosed</td>
<td>No</td>
</tr>
<tr>
<td>5 M</td>
<td>&lt;3cm</td>
<td>R Temporal</td>
<td>No</td>
<td>Superficial</td>
<td>Embo x 2 + Surgery</td>
<td>Recurred, Obliteration</td>
<td>ENG</td>
</tr>
<tr>
<td>7 M</td>
<td>&lt;3cm</td>
<td>R Frontal</td>
<td>No</td>
<td>Superficial</td>
<td>Embo + Gamma</td>
<td>Obliteration</td>
<td>ENG</td>
</tr>
<tr>
<td>8 F</td>
<td>&lt;3cm</td>
<td>R Temporal</td>
<td>No</td>
<td>Superficial</td>
<td>Embo</td>
<td>Obliteration</td>
<td>ENG</td>
</tr>
<tr>
<td>8 F</td>
<td>&lt;3cm</td>
<td>L Frontal</td>
<td>Yes</td>
<td>Superficial</td>
<td>Surgery</td>
<td>Obliteration</td>
<td>ENG</td>
</tr>
<tr>
<td>12 M</td>
<td>&lt;3cm</td>
<td>R Frontal</td>
<td>No</td>
<td>Superficial + Deep</td>
<td>Embo</td>
<td>Obliteration</td>
<td>ENG</td>
</tr>
<tr>
<td>15 F</td>
<td>&lt;3cm</td>
<td>R Frontal</td>
<td>No</td>
<td>Superficial</td>
<td>Gamma</td>
<td>Obliteration</td>
<td>No</td>
</tr>
</tbody>
</table>
HHT AVM Characteristics

• 5 AVMS were Spetzler-Martin Grade 1
• 2 AVMS were Spetzler-Martin Grade 2
• Treatment:
  – Gamma knife (1)
  – Surgery (1)
  – Embolization (3)
  – Embolization and gamma knife (1)
  – Autothromboosed on follow up (1)
Cerebral AVMs in a Family with HHT

Family with HHT - 1 (Endoglin Positive)

- Nosebleeds + Brain AVM
- + Pulmonary AVM - Brain AVM
- + Pulmonary AVM - Brain AVM
- - Brain AVM + Brain AVM + Brain AVM
Patient #1

- 5 y/o M with epistaxis since age 1 or 2, which occurs several times per week
- No overt signs of HHT
Screening MRI
Initial Cerebral Angiogram
Initial Cerebral Angiogram
Treatment with Glue Embolization
Follow Up Angiogram 2 yrs
Retreatment with Glue Embolization
Residual AVM
Surgery for Residual AVM
Final Angiogram
Patient #2

- 7 y/o M with epistaxis from 2 years, which have been fairly mild. The epistaxis typically occurs less than once per month, and he has occasional HA
- No other overt manifestations of HHT
Screening MRI
Initial Cerebral Angiogram
Glue Embolization
Gamma Knife Treatment
Follow Up MRI 1 yr
Conclusions

- 14.5% HHT patients had CVM
- 9.2% HHT patients had AVM
- 2.6% HHT patients had DVA
- 1.3% HHT patients had a cavernous malformation
- 1.3% HHT patients had a capillary telangiectasia
- HHT AVMs were found to be small in size and superficial in location
Future Directions

Determine the natural history of CVM in HHT in order to guide treatment decisions

Determine whether routine screening and treatment for CVM in HHT is better than the natural history
Thank you