Vascular Tumors in Children and Adults

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What are these lesions?

Arteriovenous malformation

Infantile hemangioma

Congenital hemangioma

(Marcelo Hochman, MD)
Clinical presentation, histopathology and molecular genetics

- Congenital hemangioma (NICH/RICH)
- Kaposiform hemangioendothelioma
- Angiosarcoma
# ISSVA classification for vascular anomalies

(Approved at the 20th ISSVA Workshop, Melbourne, April 2014)

<table>
<thead>
<tr>
<th>Vascular anomalies</th>
<th>Vascular tumors</th>
<th>Vascular malformations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benign</strong></td>
<td>Simple</td>
<td>Combined °</td>
</tr>
<tr>
<td></td>
<td></td>
<td>of major named vessels</td>
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<tr>
<td></td>
<td>Capillary malformations</td>
<td>CVM, CLM LVM, CLVM CAVM*</td>
</tr>
<tr>
<td></td>
<td>Lymphatic malformations</td>
<td>CLVM CAVM*</td>
</tr>
<tr>
<td></td>
<td>Venous malformations</td>
<td>CLAVM*</td>
</tr>
<tr>
<td></td>
<td>Arteriovenous malformations*</td>
<td>others</td>
</tr>
<tr>
<td></td>
<td>Arteriovenous fistula*</td>
<td></td>
</tr>
<tr>
<td><strong>Locally aggressive or borderline</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Malignant</strong></td>
<td></td>
<td>associated with other anomalies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>See details</td>
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<td>See list</td>
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</tbody>
</table>
### ISSVA Classification of Vascular Tumors

#### Benign vascular tumors

<table>
<thead>
<tr>
<th>Category</th>
<th>Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infantile hemangioma / Hemangioma of infancy</td>
<td>see details</td>
</tr>
<tr>
<td>Congenital hemangioma</td>
<td>**Rapidly involuting (RICH) ***</td>
</tr>
<tr>
<td></td>
<td><strong>Non-involuting (NICH)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Partially involuting (PICH)</strong></td>
</tr>
<tr>
<td>Tufted angioma</td>
<td>* °</td>
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<tr>
<td>Spindle-cell hemangioma</td>
<td></td>
</tr>
<tr>
<td>Epithelioid hemangioma</td>
<td></td>
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<tr>
<td>Pyogenic granuloma (aka lobular capillary hemangioma)</td>
<td></td>
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<tr>
<td>Others</td>
<td></td>
</tr>
</tbody>
</table>

#### Locally aggressive or borderline vascular tumors

<table>
<thead>
<tr>
<th>Category</th>
<th>Tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaposiform hemangioendothelioma * °</td>
<td></td>
</tr>
<tr>
<td>Retiform hemangioendothelioma</td>
<td></td>
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<tr>
<td>Papillary intralymphatic angioendothelioma (PILA), Dabska tumor</td>
<td></td>
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<tr>
<td>Composite hemangioendothelioma</td>
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<tr>
<td>Kaposi sarcoma</td>
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<tr>
<td>Others</td>
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</tbody>
</table>

#### Malignant vascular tumors

<table>
<thead>
<tr>
<th>Category</th>
<th>Tumors</th>
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</thead>
<tbody>
<tr>
<td>Angiosarcoma</td>
<td></td>
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<tr>
<td>Epithelioid hemangioendothelioma</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td></td>
</tr>
</tbody>
</table>
Congenital Hemangiomas
Congenital Hemangiomas
(distinct from infantile hemangiomas)

- Fully formed at birth
- More common in males
- Can occur at any body site, commonly on head and neck
- **Rapidly involuting congenital hemangiomas (RICH)** - can be gone by 12-18 months of age
- **Non-involuting congenital hemangiomas (NICH)**
- GLUT 1 negative
Rapidly-involuting congenital hemangioma (RICH)

Soon after birth

23 weeks in utero

Neck mass

17 months old

(Michele Ramien, MD, University of Ottawa)

8 months old
Rapidly involuting congenital hemangioma (RICH)

- Distinct hypercellular lobules with slit-like channels and enlarged central draining veins
- Fibrous tissue separating lobules
Rapidly involuting congenital hemangioma (RICH)

- Slit-like channels
- Fibrous tissue separating lobules
- Lobules with enlarged central draining vessels
Small vessels surrounding enlarged central draining vessels

Hobnail nuclei
Non-involuting congenital hemangioma (NICH)

- Lesion is **fully formed** at birth
- Does NOT involute as the child grows
Non-involuting congenital hemangioma (NICH)

Firm rubbery swelling with telangiectasia and a blue halo, warm to touch, non-compressible, non-tender mass
Color Doppler shows pulsatile arteries and veins within a well-circumscribed, non-compressible soft tissue mass
NICH

- Fibrous tissue separating large lobules

- Large lobules with enlarged stellate central draining vessels and curvilinear channels
Non-involuting congenital hemangioma (NICH)

Lobules of cells with dilated central vessels
Lobules of cells with dilated central vessels
Lobules of small vessels and large central draining vessels
Congenital hemangioma
GLUT-1 negative

Infantile hemangioma
GLUT-1 positive
Congenital hemangioma vs. Infantile hemangioma – Growth curves

Kaposiform hemangioendothelioma (KHE)
Kaposiform hemangioendothelioma

- Solitary firm tumor in the skin or soft tissue with red-purple ecchymosis
- Presents during infancy (58%) or early childhood (32%); rare in adults
- Present in head and neck, extremities, trunk, and extracutaneous sites (bone, mediastinum and retroperitoneum)
- A locally aggressive, borderline-malignant tumor; metastasis is very rare
- Major clinical complication is Kasabach-Merritt phenomenon – a severe DIC-like consumptive coagulopathy
Kaposiform hemangioendothelioma
Kaposiform hemangioendothelioma
Kaposiform hemangioendothelioma
Kaposiform hemangioendothelioma

CD31
Kaposiform hemangioendothelioma
D2-40
Angiosarcoma
Angiosarcoma

• Four groups
  1. Primary sporadic angiosarcoma - the head & neck in elderly men
  2. Post-radiation angiosarcoma
  3. Chronic lymphedema-associated angiosarcoma (Stewart-Treves syndrome)
  4. Exposure to vinyl chloride – liver angiosarcoma

• Poor prognosis, 5-year survival rate is 30-50%
• Epithelioid angiosarcoma has worse prognosis
Angiosarcoma
Angiosarcoma
Angiosarcoma
Angiosarcoma
Angiosarcoma

CD31+, ERG+, WT1+
Angiosarcoma

Large hemorrhagic zones
Genetic Mutations in Vascular Tumors

Receptor tyrosine kinase (VEGF, Tie2, PDGF)

**Infantile hemangioma**
- VEGFR-2/TEM8
- Angiosarcoma
  - VEGFR-2

**PTEN**

**PI3-K**

**Akt**

**mTOR**

**S6K**

**RAS/RAF**

**MAPK**

**Congenital hemangioma**
- GNAQ, GNA11
- KHE and tufted angioma
  - GNA14

**Angiosarcoma**
- KRAS, PTPRB, PLCG1
- TP53
- NUP160-SLC43A3 gene fusion
- MYC amplification (in 90% of post-radiation angiosarcoma)
Take Home Points

• Vascular malformations and tumors in children and adults represent a number of unique entities with diverse etiologies, many with distinctive clinical, imaging and histologic features.

• Some lesions continue to defy classification and are best viewed as complex biological processes yet to be defined. For these, it is best not to pigeon hole the lesion as a “hemangioma” but to describe it as accurately as possible and correlate the clinical, imaging and histologic features of the lesion.
Global Health Outreach in Southeast Asia
Vietnam Vascular Anomalies Center
Ho Chi Minh City, Vietnam

Infantile hemangioma - Treatment with pulsed dye laser and topical timolol

Since 2009, we have helped over 5,000 children in Vietnam!
www.VietnamVAC.org
Global Pathology, Ho Chi Minh City, Vietnam
Surgical pathology and dermatopathology

Slide review

CME conference
Telepathology – Multiple pathologists share skin biopsies in weekly video conference (Zoom)

Video conference each Wednesday

7 PM, Houston, USA 7 AM, Vietnam

Funding: AAD “Skin Care in Developing Countries” Grant
Global Pathology Program, Texas Children’s Hospital
Thank You!