Update on Vascular Tumors

Deepti Gupta, MD
Assistant Professor
Department of Pediatrics and Division of Dermatology
Seattle Children’s Hospital
University of Washington School of Medicine
PHOTOGRAPHY & VIDEOTAPING ARE STRICTLY PROHIBITED 
IN ALL EDUCATIONAL SESSIONS 

CELL PHONES MUST BE PLACED ON VIBRATE OR TURNED OFF 
Violations of this policy will result in removal from the session and possible revocation of meeting registration. 
Session directors will be closely monitoring such occurrences.

FOTOGRAFIA E FILMANDO SÃO ESTRITAMENTE 
PROIBIDOS EM TODAS AS SESSÕES EDUCACIONAIS 

TELEFONES CELULARES DEVEM SER COLOCADOS EM VIBRAR OU DESLIGADOS 
Violações desta política resultará na remoção de sessão e possível revogação do registo da reunião. 
Diretores de sessão irão acompanhar de perto tais ocorrências.
DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

UPDATE ON VASCULAR TUMORS

DISCLOSURES
Pierre Fabre, Advisory Board
QLT, Data Safety and Monitoring Board
Objectives

• Diagnose and categorize pediatric vascular tumors
• Discuss new and emerging therapeutics for vascular tumors
• Recognize associations with different vascular tumors
ISSVA classification of vascular anomalies

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

## Benign vascular tumors

<table>
<thead>
<tr>
<th>Kind</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infantile hemangioma / Hemangioma of infancy</td>
<td><a href="#">see details</a></td>
</tr>
</tbody>
</table>

### Congenital hemangioma

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapidly involuting (RICH)</td>
<td>*</td>
</tr>
<tr>
<td>Non-involuting (NICH)</td>
<td></td>
</tr>
<tr>
<td>Partially involuting (PICH)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Kind</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tufted angioma</td>
<td>* °</td>
</tr>
<tr>
<td>Spindle-cell hemangioma</td>
<td></td>
</tr>
<tr>
<td>Epithelioid hemangioma</td>
<td></td>
</tr>
<tr>
<td>Pyogenic granuloma (aka lobular capillary hemangioma)</td>
<td></td>
</tr>
</tbody>
</table>

### Others

<table>
<thead>
<tr>
<th>Kind</th>
<th>Description</th>
</tr>
</thead>
</table>
| Locally aggressive or borderline vascular tumors
| Kaposiform hemangioendothelioma | * ° |
| Retiform hemangioendothelioma | |
| Papillary intralymphatic angioendothelioma (PILA), Dabska tumor | |
| Composite hemangioendothelioma | |
| Kaposi sarcoma | |
| Others | |

<table>
<thead>
<tr>
<th>Kind</th>
<th>Description</th>
</tr>
</thead>
</table>
| Malignant vascular tumors
| Angiosarcoma | |
| Epithelioid hemangioendothelioma | |
| Others | |
Infantile Hemangiomas of the Breast

- Mammary gland modified apocrine sweat gland
  - Development 5th week gestation through infancy → arrest → puberty
- Deep or Mixed IH
- May not be apparent until puberty
- Breast hypoplasia (hyperplasia?)
- Early treatment with propranolol

Theiler et al. Ped Derm 2016
Rebound Growth and Hemangiomas

• After cessation of propranolol
  • 25% experienced rebound growth (15% systemic therapy)

• Predictive factors
  • Age at discontinuation (< 9 months vs. 12-15 months)
  • Deep component IH
  • Female Gender
  • Head and Neck location
  • Segmental pattern

• Duration of therapy

Congenital Hemangiomas

- Fully formed at birth
- No postnatal growth
- GLUT-1 negative, WT-1 positive
- Ultrasound- show fast flow, draining veins/prominent vessels
- Previously thought to belong to 2 subgroups \(\rightarrow\) 3 subgroups

Nasseri et al. JAAD 2014
Non-involuting Congenital Hemangiomas (NICH)

- Do not regress over time
- 2 distinct morphologies
  - Patch
  - Nodular Plaque
  - Pallor, coarse dark-red telangiectasias, bluish areas, warm
- Over time
  - Fading color
  - Protuberant
  - Soft tissue atrophy
  - Prominence of veins
- Pain
  - Vasoconstriction/ local tissue ischemia
  - Post surgery

Enroljas et al. *Plast Reconstr Surg* 2011
Lee et al. *JAAD* 2014
Rapidly Involuting Congenital Hemangiomas (RICH)

- Regresses between 6 and 14 months
- Raised, gray-violaceous, fine telangiectasias, pale halo, ectatic veins
- Resolution: atrophy, dilated veins
- Complications: ulceration, bleeding, transient coagulopathy
- Coagulopathy mild and resolves over weeks
RICH Complications and Ultrasound Findings

• Complications of RICH
  • Bleeding
  • Ulceration
  • Cardiac Failure

• Ultrasound Findings (N=24)
  • Cardiac failure-venous lakes
  • Bleeding and Ulceration-Venous ectasia and Venous lake
  • Cardiac failure all with AV shunting

• RICH associated with venous lakes may warrant closer monitoring/treatment

Waelti et al. Pediatr Radiol 2018
Partially Involuting Congenital Hemangiomas

- Initially course similar to RICH
- Partial regression over 12 months
- Stabilization and persistence
- Similar ultrasound and histologic features to RICH and NICH
- Treatment: Excision could be considered
  - PDL not as effective

Nasseri et al. JAAD 2014
Somatic Activating Mutations in GNAQ and GNA11 found in Congenital Hemangiomas

- Mutations found in GNAQ c.626A>T and GNA11 c.626A>T
- Same mutation found in RICH and NICH
- Difference in behavior due other genetic, epigenetic, environment factors
- Implications for future treatment

Tufted Angioma and Kaposiform Hemangioendothelioma Spectrum

- Rare
- Potentially life-threatening
- Kasabach-Merritt Phenomenon
- Work-up suspected TA or KHE
  - CBC w/plt
  - Coagulation studies (PT, PTT, fibrinogen, D-dimer)
  - MRI with or without contrast
  - Tissue biopsy (if diagnosis uncertain)
- Course
  - Spontaneous Regression- TA
  - Persistence without symptoms
  - Chronic Coagulopathy
  - KMP recurrent

Drolet et al. Pediatr 2013
Treatment of TA and KHE based on presentation

<table>
<thead>
<tr>
<th>Archetype</th>
<th>Suggested first-line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fulminant KHE with KMP* (neonate/young infant)</td>
<td>Multi-agent therapy often necessary. Consider consultation with a Vascular Anomalies Center for patient tailored recommendations.</td>
</tr>
<tr>
<td>KHE/TA with KMP*</td>
<td>Vincristine 0.05 mg/kg IV weekly AND prednisolone 2 mg/kg/day OR Methylprednisolone 1.6 mg/kg/day</td>
</tr>
<tr>
<td>KHE without KMP</td>
<td>Stable or minimally invasive lesion: Observation Lesion growth or symptoms: Prednisolone 2 mg/kg/day +/- antiplatelet therapy with aspirin 2 to 5 mg/kg/day</td>
</tr>
<tr>
<td>Symptomatic TA</td>
<td>Consider trial of an antiplatelet agent such as aspirin +/- ticlopidine</td>
</tr>
</tbody>
</table>

- Avoid Platelet transfusions
- Cryoprecipitate and platelet transfusions can be considered when procedure/intervention

*Drolet et al. *Pediatr* 2013*
Topical Rapamycin for Tufted Angiomas

Escuadero-Gongora et al. Actas Dermosifiliogr 2017
### Treatment of TA and KHE based on presentation

<table>
<thead>
<tr>
<th>Archetype</th>
<th>Suggested first-line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fulminant KHE with KMP* (neonate/young infant)</td>
<td>Multi-agent therapy often necessary. Consider consultation with a Vascular Anomalies Center for patient tailored recommendations.</td>
</tr>
<tr>
<td>KHE/TA with KMP*</td>
<td>Vincristine 0.05 mg/kg IV weekly AND prednisolone 2 mg/kg/day OR Methylprednisolone 1.6 mg/kg/day</td>
</tr>
<tr>
<td>KHE without KMP</td>
<td>Stable or minimally invasive lesion: Observation Lesion growth or symptoms: Prednisolone 2 mg/kg/day +/- antiplatelet therapy with aspirin 2 to 5 mg/kg/day</td>
</tr>
<tr>
<td>Symptomatic TA</td>
<td>Consider trial of an antiplatelet agent such as aspirin +/- ticlopidine</td>
</tr>
</tbody>
</table>

*Sirolimus

*Topical Sirolimus?

- Avoid Platelet transfusions
- Cryoprecipitate and platelet transfusions can be considered when procedure/intervention

Drolet et al. *Pediatr* 2013
Take away Points

• Propranolol treatment for deep or mixed IH of the breast due to breast hypoplasia
• Rebound growth can be seen in IH when therapy is discontinued or tapered at a younger age (<9 months) and short treatment duration
• Congenital hemangiomas can mimic other vascular tumors
• Transient and mild coagulopathy can be seen in RICH
• Aspirin can be a treatment for Tufted angiomas and potentially topical rapamycin
Thank you!