History and Examination

Historian: mother

HPI: 10 week old black female presented with reddish lesions on her face first noted at birth, and the lesions have been gaining “depth” over time. Patient’s mother also noted some new lesions recently in the forehead area. The right eye does not open as much as the left eye. The child is alert, active, and gaining weight appropriately. There is no significant gestational/birth history.
History and Examination

- PMH: none
- PSH: none
- POH: none
- Meds/All: none
- SH: none
- FH: none
- Birth/Development: normal
History and Examination

- **PLE:**
- **LLA/HEENT:** (see photo)
- **C/S:** W/Q OU
- **AC:** F/S OU
- **I/P:** R+R OU
- **L:** Cl OU

- **DFE:**
- **Vit:** Cl OU
- **C/D:** 0.2 s/p OU
- **Mac:** flat OU
- **V/P:** WNL

- **CRx:**
- **OD:** +5.00-2.00x90
- **OS:** +3.00
History and Examination
Your Differential Diagnosis?
Differential Diagnosis

- PHACES syndrome
- Infantile Capillary hemangioma
- Diffuse neonatal hemangiomatosis
- Vascular malformation
- Kasabach-Merritt Syndrome
- Sturge-Weber Syndrome
- Von Hippel-Lindau Syndrome
Your Next Steps?
Labs/Imaging

- CBC: 5.9>13.5/43.9<236
- MRI brain/orbits with contrast
- MRA brain/neck
MRI Face/Orbits/Brain w/Con
MRI Face/Orbits/Brain w/Con
MRI Face/Orbits/Brain w/Con

TR: 596
TE: 15
AC: 2

Image no: 14
Pos: HFS
FoV: 179.999994277954 mm
Series: 301
Image 9 of 22
10/2/2013, 2:26:40 PM
MRA Head
PHACES Syndrome

- Posterior fossa malformations
- Hemangiomas
- Arterial anomalies
- Cardiac defects and coarctation of the aorta
- Eye abnormalities
- Sternal abnormalities or Ventricular Septal Defects
Ocular and Systemic Manifestations of PHACES (Posterior Fossa Malformations, Hemangiomas, Arterial Anomalies, Cardiac Defects and Coarctation of the Aorta, Eye Abnormalities, and Sternal Abnormalities or Ventral Developmental Defects) Syndrome

Alaina Kronenberg, MD,a Francine Blei, MD,b,c Emily Ceisler, MD,d Mark Steele, MD,d Louis Furlan, MD,d and Sylvia Kodsi, MDa


TABLE 1. Ophthalmic abnormalities in PHACES

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Side involved</strong></td>
<td>OU</td>
<td>OS</td>
<td>OS</td>
<td>OD</td>
<td>OS</td>
<td>OD</td>
</tr>
<tr>
<td><strong>Vision at last visit</strong></td>
<td>20/25 OD LP OS</td>
<td>20/30 OU</td>
<td>OD prefer</td>
<td>Will not fix</td>
<td>CSM OU</td>
<td>CSM OU</td>
</tr>
<tr>
<td><strong>Ptosis</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Proptosis</strong></td>
<td>Bilateral</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Amblyopia</strong></td>
<td>Right eye occlusion</td>
<td>Yes, occlusion and strabismic</td>
<td>Yes, occlusion</td>
<td>Yes, occlusion</td>
<td>Yes, occlusion</td>
<td>Yes, occlusion</td>
</tr>
<tr>
<td><strong>Strabismus</strong></td>
<td>Sensory left hypertropia and exotropia</td>
<td>Early-onset esotropia</td>
<td>Early-onset esotropia</td>
<td>Sensory left exotropia</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Anterior Segment anomalies</strong></td>
<td>Anterior polar cataract OD</td>
<td>No</td>
<td>Loss of lashes, trichiasis</td>
<td>Trichiasis</td>
<td>Heterochromia</td>
<td>No</td>
</tr>
<tr>
<td><strong>Posterior segment anomalies</strong></td>
<td>Optic atrophy OS</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

OD, right eye; OS, left eye; OU, both eyes; CSM, central, steady and maintained.
Kasabach-Merritt Syndrome

- Hemangioma with thrombocytopenia
- Vascular tumor present at birth
- Can trap platelets when growing rapidly; also uses up clotting factors → bleeding/DIC
- Usual location is trunk, upper and lower extremities, retroperitoneum, cervical/facial areas
- Treated with surgery, embolization, external compression bandages, corticosteroids, alpha interferon
Kasabach-Merritt Syndrome

http://trombositopenia.pbworks.com/w/page/22488618/Kasabach-Merritt%20Syndrome
Sturge-Weber Syndrome

- Occurs sporadically; mutation in GNAQ gene
- Port-Wine stain
- Glaucoma
- Seizures
- Mental retardation
- Ipsilateral leptomeningeal angioma

http://www.aapos.org
Infantile Hemangiomas: Epidemiology

- 2-3x more common in females
- Most common in Non-Hispanic whites
- Increased in preterm infants
- Multiple gestation pregnancies associated with multiple hemangiomas
- Older maternal age, placenta previa, pre-eclampsia are other risk factors
Hemangiomas: Pathophysiology

- Composed of plump, proliferating endothelial cells
- Clonal proliferations of endothelial cells resulting from vasculogenesis, not angiogenesis
- Increased FGF, VEGF R expression, PCNA, MMPs
- Rapid proliferation in first year of life, then gradual replacement by fibrofatty tissue
- GLUT1 highly expressed in endothelial cells of hemangiomas during proliferative and involutional phases
Hemangiomas vs Vascular Malformations

- Hemangiomas
  - appear in first few weeks of life
  - spontaneously regress

- Vascular malformations
  - always present at birth
  - persist unchanged through adolescence and adulthood

<table>
<thead>
<tr>
<th>Stage</th>
<th>Morphologic Subtype</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nascent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early proliferative</td>
<td>Localized</td>
<td>Superficial</td>
</tr>
<tr>
<td>Late proliferative</td>
<td>Segmental</td>
<td>Deep</td>
</tr>
<tr>
<td>Plateau</td>
<td>Indeterminate</td>
<td>Mixed</td>
</tr>
<tr>
<td>Involuting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abortive</td>
<td></td>
<td>Medical Knowledge</td>
</tr>
</tbody>
</table>
Natural History of Hemangiomas

- Proliferation Phase (0-1 yrs)
- Involuting Phase (1-5 yrs)
- Involuted phase (>5 yrs)

Histopathology

- Aggregates of closely-packed, thin-walled capillaries with endothelial lining
- Blood-filled vessels separated by scant connective tissue
- Glut1: a marker highly specific for hemangiomas
Indications for Treatment

- Life-threatening conditions (heart failure, respiratory distress)
- Functional risks (amblyopia, swallowing disorders)
- Painful, ulcerated hemangiomas
- Aesthetic considerations
Growth Characteristics of Infantile Hemangiomas: Implications for Management

Chang et al. Pediatrics 2008 122:2, Table 1

<table>
<thead>
<tr>
<th>Anatomic Location/Morphology</th>
<th>Associated Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial, large segmental</td>
<td>PHACES syndrome (posterior fossa malformations, hemangiomas, arterial anomalies, cardiac defects, eye abnormalities, sternal clefting)</td>
</tr>
<tr>
<td>Nasal tip, ear, large facial (especially with prominent dermal component)</td>
<td>Permanent scarring, disfigurement</td>
</tr>
<tr>
<td>Periorbital and retrobulbar</td>
<td>Ocular axis occlusion, astigmatism, amblyopia, tear-duct occlusion</td>
</tr>
<tr>
<td>Segmental “beard area,” central neck</td>
<td>Airway hemangioma</td>
</tr>
<tr>
<td>Perioral</td>
<td>Ulceration, disfigurement, feeding difficulties</td>
</tr>
<tr>
<td>Segmental overlying lumbosacral spine</td>
<td>Tethered spinal cord, genitourinary anomalies</td>
</tr>
<tr>
<td>Perineal, axilla, neck, perioral</td>
<td>Ulceration</td>
</tr>
<tr>
<td>Multiple hemangiomas</td>
<td>Visceral involvement (especially liver, gastrointestinal tract)</td>
</tr>
</tbody>
</table>
Patient Management

- Decision to initiate propranolol and titrate to maximum tolerated dose (goal 2 mg/kg/day)
- Initial Pediatric cardiology consult for EKG/Echo
- Follow-up with dermatology and pediatrics
- Educated mother regarding condition and its effects on the eye
Steroid Therapy

- May function by direct inhibition of production of angiogenic factors (VEGF-A, IL-6, MMP)
- Usual systemic dose: 3-6 mg/kg/day for 1-2 months, depending on lesion size
- Most common complication: cushingoid facies; however other complications of steroid use possible
Steroid Therapy

- No longer first line for infantile hemangiomomas
- Local intralesional steroids for small localized lesions: triamcinolone 3mg/kg (overall 85% response rate in a retrospective review)
- Topical corticosteroids: clobetasol cream- best for small superficial hemangiomomas at risk for ulceration
Interferon Therapy

- Inhibits angiogenesis; used for aggressive hemangiomas not responsive to steroids
- Dose: 3 million U/m2/day for weeks-months
- AE: fever, irritability, neutropenia, LFT abnormalities; severe neurotoxicity including spastic diplegia (3.6% of 441 patients in one study)
QUESTION

- An 2 ½ yr old female with a history of confirmed orbital cavernous hemangioma via neuroimaging presents to your practice with sudden and severe LUL swelling, intense pain and exophthalmos OS. The left pupil has an afferent pupillary defect and imaging suggests intraorbital hemorrhage. What is/are your next step(s)?
Orbital cavernous hemangioma in an infant with intracranial lesions: a case report

Eleni Evagelidou¹, Elena Tsanou²*, Ioannis Asproudis³, Spiridon Gorezis⁴, Miltiadis Aspiotis¹, Dimitrios Peschos² and Antigoni Siamopoulou¹

Cases Journal 2009, 2:6912

- Removal of cavernous hemangioma via anterior orbitotomy
- Second procedure required due to persistence of growth
- End result: Atrophy of left optic nerve
Surgical Therapy

- Indications: involuted lesions with residual scars or loose skin, small localized periorbital hemangiomias, slowly involuting lesions of cosmetic significance; when risks of medical therapy > surgical therapy
Embolotherapy

- Indicated when risk of spontaneous hemorrhage is high or causing functional anomaly due to size
- Also useful prior to surgical resection
- Goal is to block a large percentage of tumor vessels.
- Embolic materials: Polyvinyl alcohol particles or microspheres
Embolotherapy
Propranolol Therapy

- First-line treatment for rapidly advancing, high-risk infantile hemangiomas
- Titrate to a target dose of 2 mg/kg/day
- Mechanism(s): vasoconstriction, modulation of pro-survival signal transduction pathways, endothelial cell apoptosis
- Topical beta blockers for small superficial hemangiomas - long term data missing
- Contraindications include bradycardia, hypoglycemia, bronchial asthma
Topical Beta blocker Therapy

- For superficial hemangiomas of minor cosmetic concern
- Timolol 0.5% topical gel
- May help prevent rebound growth in children being tapered off oral propranolol
Key Points

- Periorbital hemangiomas have the potential to cause amblyopia and significant ocular morbidity.
- A multidisciplinary workup for systemic syndromes should be initiated for large facial hemangiomas.
- Treatment for hemangiomas should be based on age, size of the lesion, functional risk and damage to nearby structures, and cosmetic considerations.
Patient Update

- Patient continues treatment with propranolol; followed by ophthalmology, dermatology, and pediatrics
Reflective Practice

This case allowed me to care for a pediatric patient with a potentially sight-threatening variation of fairly common condition. I learned about the variety of patient presentations and treatment options available to manage this condition.
Core Competencies

Patient Care: The case involved thorough patient care and careful attention to the patient’s past medical history. The patient received timely and appropriate medical management and follow up care in the eye clinic in addition to dermatology and pediatric medicine.

Medical Knowledge: This presentation allowed me to review the presentation, differential diagnosis, proper evaluation/work up and treatment options for infantile hemangiomas.

Practice-Based Learning and Improvement: This presentation included a literature search of current treatment modalities for infantile hemangiomas.

Interpersonal and Communication Skills: The patient and family were treated with respect and every effort was made to communicate with the family in a logical, understandable manner.

Professionalism: The patient’s workup and treatment was initiated in a timely manner. She was informed of her diagnosis and explained the reasoning behind our workup.

Systems-Based Practice: The patient was managed by the oculoplastics and pediatric ophthalmology services, in addition to dermatology and pediatrics.
Selected References


- Metry DW, Levy ML, Corona R. Epidemiology; pathogenesis; clinical features; and complications of infantile hemangiomas. UpToDate.
Thank You

- Patient and mother
- Dr. Elmalem