Hemangiomas
Vascular Lesions of Newborn
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Disclosure

• I have no conflicts of interest

Case presentation

• Prenatal history: 33 week preterm born to a 30-year-old G3P1 mother via NSVD after an induction; Pregnancy complicated with IUGR and AEDV on antenatal ultrasound done at 32 weeks; Karyotype was normal
• Completed course of antenatal steroids
• Apgar scores 8 and 9 at 1 and 5 minutes
Course

• The neonate was initially NPO for 48 hours and feedings were increased to goal TF: 180 ml/kg/day with 24 kcal feeds by day 10
• on day 11, he was noted to have abdominal distension, altered nasogastric aspirates, and hematochezia

Course

• There was no lethargy, temperature instability, or apneas.
• Clinical examination revealed a distended abdomen with hepatomegaly (liver span: 7 cm). AXR showed dilated bowel loops with no pneumatosis intestinalis.
• The neonate was placed NPO, blood culture obtained and begun on intravenous antibiotics (Amp and Gent) for sepsis.
• By Day 17, there was no improvement in abdominal status, and features of cardiac failure in the form of pansystolic murmur, hepatomegaly, and cardiomegaly developed requiring mechanical ventilation.
• Repeat AXR showed pneumatosis intestinalis and piperacillin-tazobactam was started. Blood cultures remained negative.
• By this time, the neonate was also noted to have multiple cutaneous hemangiomas (5)
Labs

- White blood cell count: 9.3 with 45% neutrophils, 65% lymphocytes
- Hemoglobin: 13.7 g/dL (137.0 g/L)
- Platelet count: 65,103/mL (65,109/L)
- Sodium: 128 mEq/L (128 mmol/L)
- Calcium: 7.8 mg/dL (1.9 mmol/L)

Course

- An ultrasound of the abdomen on day 18 revealed multiple hypoechoic lesions in the liver with dilated intrahepatic vessels and no evidence of free air in the portal circulation

CT of the abdomen showing variable size hypodense nodules
Infantile hepatic hemangioendothelioma (IHH)

- the most common benign tumor of the liver in children, is seen almost exclusively (86%) in the first 6 months of life, with about one third of the cases presenting in the first month.
- Girls are more frequently affected (1.7:1)
- IHH is a type of capillary hemangioma, which consists of a network of capillary-sized and endothelium lined vessels.
- The typical triad of presentation is: multiple enlarging cutaneous hemangiomas, hepatomegaly, and congestive cardiac failure
- Anemia and especially thrombocytopenia may be seen, caused by trapping of platelets within the hemangioendothelioma with consumptive coagulopathy (Kasabach-Merritt syndrome).

Management

- In view of the clinical presentation with necrotizing enterocolitis, steroids were withheld, and the neonate was begun on oral propranolol at a dose of 1 mg/kg per day with the dosage increased to 2 mg/kg per day.
- Clinical improvement occurred, with resolution of congestive cardiac failure and necrotizing enterocolitis over the next 2 weeks.

VASCULAR LESIONS

- Vascular tumors, including benign, borderline, and malignant tumors
- Simple malformations, including capillary, lymphatic, venous, AV
- Combined vascular malformations
- Anomalies of major named vessels
- Vascular malformations associated with other anomalies, which include Sturge-Weber syndrome, Klippel-Trenaunay syndrome, macrocephaly-capillary malformation, Proteus syndrome, and congenital lipomatous overgrowth, epidermal nevi, spinal/skeletal anomalies/scoliosis (CLOVES) syndrome
Infantile Hemangiomas

- Infantile hemangiomas are benign tumors of vascular endothelium.
- More common among white non-Hispanic infants
- Familial transmission; F>M
- The incidence of hemangiomas is increased in preterm infants
- Prenatal associations include older maternal age, placenta previa, pre-eclampsia, and other placental anomalies.

Pathogenesis

- Phases of proliferation and involution (regression of vascular component with replacement by fibrofatty tissue)
- Hypoxia \( \rightarrow \) Proliferative phase homeostatic event
- GLUT1 and placenta-associated vascular antigens (Fc-gamma-receptor II, merosin, and Lewis Y antigen) are highly expressed in the endothelial cells of infantile hemangiomas during both the proliferative and involution phase
- Clonal proliferations of endothelial cells (vasculeogenesis)
- Imbalance of two VEGF receptor tyrosine kinases (VEGFR1 and VEGFR2)
- Increased quantities of bFGF and matrix metalloproteinases in the urine of patients with proliferating hemangiomas

Involution

- The spontaneous involution phase typically begins in the late part of the first year and continues over a variable number of years. Involution is characterized by histologic fibrosis of capillary lumina.
  - Increased numbers of mast cells and levels of tissue metalloproteinase (an inhibitor of new blood vessel formation) in involuting hemangiomas.
  - Upregulation of interferon-induced genes in involuting hemangiomas
  - Decreased quantities of bFGF in the urine of patients
Diagnosis and Evaluation

HISTORY

- Age at which the lesion was first noted and subsequent behavior of the lesion
- Presence of ulceration, pain, bleeding and/or evidence of secondary infection
- Whether any imaging studies, biopsies, or other prior evaluations
- Previous treatment and response
- Progressive resp failure; signs of high-output cardiac failure during early infancy in the presence of multiple (five or more) cutaneous hemangiomas (may indicate the presence of hepatic hemangiomas); Rapid growth + thrombocytopenia
- Any parental preconceptions?

In some newborns, a patch of telangiectasias with surrounding pallor is a premonitory cutaneous mark of infantile hemangiomas.

Superficial hemangiomas consist of a bright red papule, nodule, or plaque raised above clinically normal skin.

Deep hemangiomas are typically raised, flesh-colored nodules, which often have a bluish hue or an overlying telangiectatic patch.
Sharp-bordered and very raised hemangiomas, as depicted here, are associated with an increased risk of scarring.

Hemangiomas in visible sites of the lip are particularly prone to disfigurement.

Periorbital hemangiomas
The majority of hemangiomas that lead to visual complications affect the upper medial eyelid. However, a hemangioma of any size, morphology, or periorbital location may pose a threat to vision.

Distribution
• Localized lesions
• Segmental lesions
  – segment 1 involves the lateral forehead, anterior temporal scalp, and lateral frontal scalp,
  – segments 2 and 3 corresponded to the maxillary and mandibular
  – segment 4 involves the medial frontal scalp, nose, and philtrum.
Segmental hemangiomas are usually plaque-like and demonstrate a linear and/or geographic presence over a specific cutaneous territory. Infants with segmental hemangiomas should also be evaluated for PHACE syndrome.

The "beard" (Segment 3) distribution includes the preauricular skin, chin, anterior neck, and/or lower lip. Patients with segmental hemangiomas in this location are at increased risk of concomitant airway hemangioma with progressive resp failure in the first several months of life and should also be evaluated for PHACE syndrome.

PHACE syndrome
This full term infant was diagnosed with a non-critical coarctation of the aorta when she was two years old. On the third day of life she developed an extensive red mark on the left side of the face extending into the scalp. A brain MRA/MRI revealed multiple intracranial vascular abnormalities. These findings were typical of PHACE.

- Posterior fossa malformations:
- Hemangiomas
- Arterial anomalies
- Clefts, cleft lip, and cardiac defects
- Eye abnormalities.
Lumbosacral hemangioma

Hemangiomas located over the lumbosacral spine may be associated with spinal dysraphism or other underlying congenital anomalies. Segmental lesions are of greatest concern.

Acral Hemangiomas

COMPLICATIONS

- Most cutaneous hemangiomas are uncomplicated and require no intervention.
- Ulceration may lead to bleeding, infection, and, invariably, scarring.
- Bleeding is rarely profuse and can generally be stopped with application of direct pressure.

Treatment

- Treatment is individualized.
- Consultation with a pediatric dermatologist (proliferation phase)
- Hemangiomas are managed with clinical examinations and education of the family regarding the natural course; potential complications; treatment indications; and risks, benefits, and expectations of available treatment options
- Education
Goals of Treatment

- Prevention or reversal of life-threatening or function-threatening complications
- Prevention or minimization of disfigurement from residual skin changes
- Minimization of psychosocial distress for the patient and family
- Adequate treatment of ulceration to minimize scarring, bleeding, infection, and pain

Treatment of Uncomplicated hemangiomas

- Active nonintervention
- Topical beta blockers — timolol gel-forming solution 0.5%.
- Efficacy — In a 2015 systemic review and meta-analysis of 14 cohort studies and three randomized trials, the pooled response rate was approximately 80 percent for both topical propranolol and topical timolol
- Safety

Indications for systemic treatment

- Very large, rapidly growing cutaneous hemangiomas
- Lesions in the periorbital region
- Lesions in the airway, liver, or gastrointestinal tract
- Large, plaque-like (segmental) or nodular hemangiomas
- Any lesion of the face, especially when large or segmental; hemangiomas of the lip, nose (“Cyrano nose”), and auricle
- Large, nodular, superficial hemangiomas, especially those that exhibit a sharp, “cliff-like” border or pedunculated lesions (hemangiomas extending from a small base) have the greatest risk of scarring. These lesions are also at risk for leaving residual fibrofatty tissue that may require surgical revision.
Treatment of complicated hemangiomas

- Propranolol — a nonselective beta blocker, is the first-line agent for hemangiomas with the potential to impair function or cause permanent disfigurement, if there are no cardiac or neurovascular concerns.
- FDA approved in 2014
- Inhibits the growth and induces the regression of infantile hemangiomas. Potential mechanisms of action for propranolol may include vasoconstriction, decreased expression of VEGF and bFGF, and/or triggering of apoptosis.

Initiation of treatment

- Outpatient Hospitalization recommended in:
  - Infants ≤5 weeks of age
  - Preterm infants with corrected age ≥5 weeks
  - Infants of any age with inadequate social support
  - Infants of any age with comorbid conditions affecting the cardiovascular or respiratory system, including symptomatic airway hemangioma
  - Infants of any age with conditions affecting blood glucose maintenance

Adverse events

- Hypotension, bradycardia, hyperkalemia, bronchospasm, and hypoglycemia, are infrequent. Restless sleep, constipation or diarrhea, and cold extremities are more commonly reported.
- Propranolol should be discontinued during periods of illness or poor oral intake.
Other treatment options

- Systemic corticosteroids
- Vincristine
- Interferon alpha
- Surgical therapies

Congenital hemangiomas

- Congenital hemangiomas are rare, benign vascular tumors that are present and fully grown at birth
- Based upon their natural history, two major subtypes of CH have been recognized: rapidly involuting congenital hemangiomas (RICH) and noninvoluting congenital hemangiomas (NICH)
- In most cases, RICH involute completely by the age of 14 months, whereas NICH never regress but grow in proportion with the child and may require eventual excision.

An erythematous patch with fine and coarse telangiectasias is present. Note the perilesional blanching and small proliferative component.
RICH
A 6 x 8 cm partially compressible blue tumor with overlying red and purple papules and telangiectasias and surrounding pallor in a 10 month old boy. The lesion was present at birth and showed no signs of growth or regression.

NICH
• Noninvoluting congenital hemangiomas presenting as a flat bluish lesion with overlying telangiectasias resembling a vascular stain.

NICH
A 40 x 55 mm bluish patch on the right clavicular area with an overlying red telangiectatic vascular mass in a two-year-old boy. The child was born with a vascular nodule on the right clavicular area. Contrary to expectations, this asymptomatic lesion has continued to slowly increase in size proportion to the growth of the patient.
NICH

A 4 x 6 cm, partially compressible, bluish tumor with overlying red and purple papules and telangiectasia and surrounding pallor in a 10-month-old boy. The lesion was present at birth and showed no signs of growth or regression.

Case presentation

- 37 5/7 week female infant born to a 19-year-old, gravida 1, para 1 woman by cesarean section (for nonreactive fetal heart tracing).
- A 20-week ultrasonography revealed hydrocephalus, cysts within the cardiac ventricles, and pericardial effusion
- Apgar scores of 6 and 9 at 1 and 5 minutes
- Infant needed continuous positive airway pressure via T-piece device during resuscitation only

Course

- Birth weight of 3.54 kg (75–90th percentile), head circumference of 37 cm (>97th percentile), and length of 50 cm (50–75th percentile)
- Admission to the neonatal intensive care unit because of multiple port-wine stains on face, trunk, and extremities
- No family history of port-wine stains
Physical exam

- Infant transitioned to room air with normal oxygen saturations
- Extensive capillary telangiectasia and cutis marmorata on the trunk, back, legs, and arms
- A port-wine stain on the right forehead extending across the
- A 1-cm skin tag in the sacral region with a dimple noted
- No vesicles, rash, or petechiae
- Eyes had white sclerae and bilateral red reflexes, and no coloboma were seen; however, retinal evaluation revealed a choroidal hemangioma on her right macula
- Right leg was 1.5 cm longer than the left leg; there was a laterally displaced broad great toe, syndactyly of the second and third toes bilaterally, and broad toes; there were bilateral club feet
- The nostrils were patent, there was no flaring, and the right nasolabial fold was absent
Imaging

- The infant underwent imaging studies of the brain and heart, and skeletal survey radiography revealed the right femur, tibia, and fibula to be greater in length than those on the left, enlarged right facial bones, and a larger right cerebrum and ventricle compared with the left.
- Echocardiography did not confirm ventricular cystic structures or pericardial effusion
Megalencephaly Capillary Malformation

**Major criteria (at least 3)**
- Macrocephaly
- Capillary malformation(s)
- Overgrowth or asymmetry
- Neuroimaging abnormalities
  - Ventriculomegaly
  - Cavum septum pellucidum or cavum septum vergae
  - Frontal bossing
  - Cerebellar tonsillar herniation

**Minor criteria (at least 2)**
- Developmental delay
- Midline capillary malformation
- Neonatal hypotonia
- Syndactyly or polydactyly
- Connective tissue abnormalities
- Frontal bossing
- Hydrocephalus

VASCULAR MALFORMATIONS
- Anomalies of vessel morphogenesis. Endothelial turnover is normal.
  - Low flow (capillary, venous, lymphatic, or combination) and high flow (arterial, arteriovenous).
- Vascular malformations are always present at birth but often are clinically subtle and become more apparent over time as they slowly expand in proportion to the infant’s overall growth.
- Progressive ectasia

Nevus Simplex
**Port-wine stain**

- Port-wine stains or nevus flammeus are low-flow vascular malformations of dermal capillaries and postcapillary venules.
- Cutaneous port wine stain is the most common type of vascular malformation, occurring in 0.3 percent of newborn infants.
- Blanchable pink to red patches on skin and/or mucosa and may be located anywhere on the body, typically with a unilateral or segmental distribution that respects the midline.

**Sturge Weber syndrome**

- Sturge-Weber syndrome is a rare congenital, but not hereditary, a facial capillary malformation involving the V1 +/- V2 dermatome and an associated leptomeningeal vascular malformation.
- Glaucoma and neurologic abnormalities, including seizures, hemiparesis, intellectual disability (mental retardation), and behavior problems.
Klippel-Trenaunay syndrome

- an extensive port-wine stain with underlying venous and/or lymphatic malformations involving an extremity
- mutations in the gene for an angiogenic factor (VG5Q)
- May develop thrombophlebitis, DVT and pulmonary thromboembolism

Cutis marmorata telangiectatica congenita
Question

A full-term infant is born with a large, erythematous facial lesion in a beardlike distribution. A cleft in the sternum and a supraumbilical raphe are discovered on physical examination. Of the following, the diagnostic evaluation that RARELY uncovers an abnormality in this syndrome is:

1. echocardiography
2. magnetic resonance imaging of the brain
3. ophthalmology examination
4. renal ultrasonography
5. upper airway endoscopy

References

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