Hemangiomas and Other Vascular Anomalies
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Pediatric Grand Rounds
March 29, 2013

Disclosure
- I have no relationships with commercial companies to disclose.
- I will be discussing off-label use of medications in children.
  - There are no FDA approved treatments for infantile hemangiomas.

Learning Objectives
- Differentiate between infantile hemangiomas and vascular malformations.
- Discuss available treatment options for infantile hemangiomas.
- Utilize comprehensive, multidisciplinary programs in the management of childhood vascular anomalies.

What’s in a name…..
Strawberry birthmark, capillary hemangioma, port wine stain, tufted angioma, lymphangioma, hemangioendothelioma, cavernous hemangioma, lymphangiohemangioma

“Hemangioma is a generic word that has been used to describe a wide variety of vascular lesions with different etiologies and natural history.” JB Mulliken, 1987

Vascular Anomalies
Hemangiomas
- Vascular Tumor
- Endothelial proliferation
  - High mitotic rate
- Natural History
  - Rapid growth
  - Plateau
  - Involution

Malformations
- Structural abnormalities
- Present at birth but may not be visible
- Grow symmetrically with patient
- Enlargement occurs due to changes in pressure and flow

ONE OF THESE IS NOT LIKE THE OTHERS………. 
INFANTILE HEMANGIOMAS

Infantile Hemangiomas

- Most common vascular tumor of infants
  - 4-5% of newborns affected
- Who
  - 5:1 Female to Male
  - Caucasian=Hispanic>Asian and African Americans
  - Pre-term
  - Multiple gestation
- Location
  - 70-80% occur in the head and neck

INFANTILE HEMANGIOMAS

Infantile Hemangiomas

- Type
  - Superficial or cutaneous only
  - Deep Dermal
  - Compound
  - Extracutaneous
    - Parotid gland
    - Liver
    - Airway
- 80% solitary skin lesion

Natural History

- Appears between 2 weeks and 4 months
- Grows rapidly for 6-12 months
  - Average 8 months of growth
- Rest or plateau from 8-14 months
- Spontaneous regression or involution
  - 1-10 years to involute
  - 50% involute by 5 years; 70% by 7 years
- Key Point – Grows fast, goes away slowly

“Hemangioma” of the Liver

Pediatric

- Focal
  - Usually rapidly involute
- Multifocal
  - Usually asymptomatic and associated with multiple skin lesions
- Diffuse
  - Hepatomegally
  - Hypothyroidism
  - Heart failure
- Kasabach-Merritt Syndrome uncommon

Adult

- Venous malformation
- Adult females over 40
- Incidental finding or during pregnancy
- May require no treatment
OTHER VASCULAR TUMORS

Congenital Hemangiomas

- Present at birth
  - Morphologically different than infantile hemangiomas
- Equally affects males and females
- Head, neck, and extremities
- Superficial
- Growth
  - Complete at birth or grows with child
- Involution
  - Rapidly involuting congenital hemangiomas (RICH)
  - Non-involuting (NICH)

Kaposiform Hemangioendothelioma (KHE) or Tufted Angiomas

- Rare
- Misdiagnosed as infantile hemangioma
  - Morphologically different
- Locally aggressive vascular tumor
  - Tense, red, shiny skin
  - Skin, soft tissue and bone of upper trunk and extremities
- Diagnosis
  - Classic MRI findings of infiltration
  - Biopsy may be necessary but not required
  - 75% present with Kasabach-Merritt Syndrome

PHACE Syndrome

- Posterior fossa abnormalities
  - Dandy Walker, cerebellar hypoplasia, pituitary aplasia
- Hemangioma
  - Face or neck > 5 cm
- Arterial lesions
  - Cerebral
- Cardiac abnormalities
  - Coarctation, aortic stenosis
- Eye
  - Cataracts, microphthalmos
- Hemangioma plus 1 major or 2 minor criteria

Complications

Kasabach-Merritt Syndrome

- Rapidly enlarging vascular tumor (KHE) with thrombocytopenia
- Consumptive coagulopathy
- Mortality 20-30%
- Most commonly associated with KHE, then tufted angiomas and congenital hemangiomas (not classic in infantile hemangiomas)

Diagnosis

- Clinical history
  - Physical examination
  - Lesion appearance
  - Biopsy rarely necessary

- Imaging
  - Sonogram to distinguish from vascular malformation
  - CT Scan or MRI
    - Lesions with atypical appearance or behavior
    - PHACE syndrome
    - Multiple lesions
      - 8 skin lesions associated with hepatic lesions

Local

- Ulceration
  - Bleeding
  - Pain
- Obstruction
  - Visual compromise
  - Oral lesions affect feeding
  - Airway lesions
    - Laryngobrachial
    - Tracheal

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Treatment

- Observation
- 12% require further treatment
  - Medical therapy
  - Surgery
  - Laser
- American Academy of Dermatology
  - “Infants with hemangioma that are obstructing vision or breathing, have ulcerated or bleed or have the potential for facial disfigurement require medical intervention.”

Medical Therapy

Corticosteroids
- Mainstay of treatment
- Oral or intra-lesional injection
- Decreases swelling and slows growth over 3-4 weeks
- Adverse effects:
  - Hypertension
  - Weight gain
  - Infection
  - Irritability
  - Hyperglycemia

Propranolol
- Newest treatment option
- Oral
  - 2-3 times per day dosing
  - Appears to promote earlier involution.
  - May see effects with first dose.
- Adverse effects:
  - Hypotension
  - Hypoglycemia
  - Arhythmia

Did you say Propranolol?

- Leaute-Labreze, 2008
  - French case series of 11 infants treated with propranolol
- Many case reports and case series published.
- No Phase I/II/III, prospective controlled studies yet.
- Relatively benign adverse effect profile
- Liquid formulation
- Routine use in pediatric cardiology
- Rapid wide-spread adoption of propranolol for infantile hemangiomas

San Antonio Experience

- Retrospective case series
- 22 patients
  - 45% (10/22) male
  - 64% (14/22) Hispanic
  - 32% (7/22) Periorbital
- Dosing 1.5mg/kg/day divided BID
- 55% (12/22) noted response by 4th dose
- Adverse Effects
  - 14% (3/22) diarrhea
  - 10% (2/22) insomnia
  - 0% wheezing
  - 0% symptomatic hypotension

Patient 1

Before

After
Patient 2
Before
After

Patient 3
Before
After

Initiation and Use of Propranolol for Infantile Hemangioma: Report of a Consensus Conference

Other Medical Therapy

Interferon Alpha
- Requires vascular access.
- Decreases new blood vessel growth.
- Adverse effects limit use to most severe cases:
  - Irritability
  - Neutropenia
  - Abnormal liver functions
  - 20% develop spastic diplegia

Vincristine
- Requires vascular access.
- Weekly injection.
- Recommended for non-responsive vision or life-threatening lesions
- Adverse effects:
  - Constipation
  - Hyponatremia
  - Jaw pain
  - Peripheral neuropathy
  - Neutropenia

Non-Medical Therapy

Surgery
- After involution:
  - Scar reconstruction
  - Fibrofatty tissue removal
- Early excision sometimes warranted.
  - Congenital hemangiomas that do not involute.

Laser
- Limited depth of penetration
  - Very superficial lesions benefit
- Telangiectasias that remain after involution
- Ulceration

VASCULAR MALFORMATIONS
Vascular Malformations

- Benign
- Always present at birth.
- DO NOT have 1-2 year growth cycle with long regression.
- May be isolated or associated with specific disorders.

Venular
- Angel Kisses and Stroke Bites
- Venous
- Lymphatic
- Arteriovenous
- Mixed

Capillary Malformations

- Capillary Malformations
  - “Port Wine Stain”
- Sturge Weber
  - Capillary malformation
  - Other neurologic abnormalities
- Klippel Trenaunay Syndrome
  - Capillary malformation
  - Bone overgrowth
  - Varicosities
  - Mixed vascular malformations
    - Capillary, venous and lymphatic anomalies

Venous Malformations (VM)

- Most appear in the skin
- Blue in color and soft
- Growth
  - Injury
  - Thrombus
  - Estrogen
  - OCP
  - Pregnancy
  - Puberty

Arteriovenous
- Firm mass, not easily compressible
  - High flow vs low flow
- Hereditary Hemorrhagic Telangiectasia (HHT) or Osler Weber Rendu
  - Genetic disorder associated with skin and mucosal telangiectasias and visceral AVM
  - http://hht.org/

Lymphatic Malformations (LM)

- Cystic hygromas, hemangiolympangioma or lymphangiomas.
- Grow with patient.
- Difficult to treat.
- Imaging may be needed to distinguish from venous malformations

Treatment

Medical
- Symptomatic
  - Pain Medications
  - Thrombus
  - Aspirin
  - Anti-coagulation
- These lesions are not proliferative; steroids and propranolol have little or no effect.

Compression
- Specially fitted compression stockings
  - Treat pain and swelling
- Challenges
  - Must be worn ALL day
  - Children grow and require multiple stockings over time
  - Adherence
    - Hot and sweaty in San Antonio Heat

Non-Medical Therapy

Surgery
- Most useful in small lesions.
- Complete resection is difficult.
- Lesion may return if not all affected vessels removed.

Sclerotherapy
- First choice in treatment of VM and some LM.
  - Effective in 75-90%
- Injection of a sclerosing or irritating agent into the lesion.
  - Improves symptoms
  - Decreases size
  - Does not eliminate lesion
Why do children with vascular anomalies need a hematologist?

- Management of anticoagulation.
- Treatment of Kasabach Merritt.
- Medical therapy with anti-neoplastic agents.
  - Some vascular anomalies are tumors!
- ASPHO National Meeting 2013
  - “Bah Humbug to the Disbelievers! Vascular Anomalies Are Disorders Needing the Care and Guidance of the Pediatric Hematologist/Oncologist”
  
  *Denise M. Adams MD (Moderator)*

Multi-disciplinary Clinics

- Plastic Surgeon
- Dermatologist
- Hematologist/Oncologist
- Ophthalmologist
- Interventional Radiologist
- Social Work
- Physical and Occupational Therapy

Conclusion

- The majority of infantile hemangiomas do not need treatment.
- Some vascular tumors can be aggressive and difficult to treat (KHE).
- Malformations are present at birth and do not grow and regress like hemangiomas.
- Children with complex vascular anomalies should be treated in comprehensive programs.

Questions

- NOVA – National Organization of Vascular Anomalies
  
  *http://www.novanes.org/*

References


Off-Label Use of Medications in Children

- 20% of FDA approved medication have a pediatric label.
  
  - Pediatric Research Equity Act (PREA) 1998
    
    *New drugs must have plan to include children or explain why not included.*
  
    
    *Drug companies get an extra 6 months of exclusive marketing if they also include children in their studies.*