Subglottic Hemangioma

Objectives

Objective 1: Define subglottic hemangioma and provide 3 presenting symptoms. 
- Define hemangioma
- Discuss subglottic hemangioma including epidemiology, clinical presentation and diagnosis

Objective 2: Discuss treatment options to consider in the care of the child with subglottic hemangioma.
- Airway management
- Medical treatment
- Surgical considerations

Objective 3: Identify psychosocial considerations affecting the family of a child with subglottic hemangioma
- Complexity of care
- Body image
- Life threatening nature of disease
- Impact of care, cost, time, follow-up
- Case presentations

Objective 4: Participate in an interactive discussion on subglottic hemangioma.
- Question and answer period

Infantile Hemangiomas

- Benign vascular tumors composed of endothelial cells involving the skin and subcutaneous tissues
  - Superficial hemangiomas remain bright red
  - Deep hemangiomas become palpable blue nodules
- Most common tumor of childhood
  - Incidence 1-2% of infants
  - Seen in all racial groups
  - More common in Caucasians
  - Occur more frequently in low birth weight and premature infants
  - 2:1 female predominance
- Pathogenesis is not understood
  - Growth factors and hormonal and mechanical influences have been postulated to affect the abnormal proliferation of endothelial cells
  - No genetic alteration has been implicated

Histology

- Glucose transporter 1 (GLUT-1) stain is very sensitive and specific for histologic confirmation of infantile hemangiomas
- Both proliferating and involuting subglottic hemangiomas uniformly stain positively for GLUT-1
- Other cutaneous vascular neoplasms, malformations, and normal cutaneous vasculature do not make this stain.

Infantile Hemangioma Growth Phases

- 20% are not visible at birth
- Most become apparent in first 2 months of life
- Proliferative phase- usually lasts 6-9 months (individualized)
- Involution phase- may last up to 10 years
  - 50% resolution at age 5, 70% at age 7, 90% at age 9

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Complications
Infantile Hemangiomas

- Common complications
  - Ulceration and secondary bacterial infection
- Major complications
  - Airway obstruction
  - Thrombocytopenia due to platelet trapping within the lesion
  - Kasabach-Merritt syndrome
  - Visual obstruction
  - with resulting amblyopia
  - Cardiac decompensation
  - high output failure

Airway Hemangioma

- Subglottic hemangioma is a rare, potentially life threatening tumor of infancy which poses serious treatment challenges
  - mortality rate of close to 50% when left untreated (Ferguson, 1961)
- Epidemiology
  - 1.5% of all congenital anomalies of the airway
  - Females affected twice as much as males
  - Self limiting course
- Pink or purple submucosal subgottic lesion which is smooth, asymmetrical and compressible

PHACE SYNDROME

- PHACE syndrome
  - posterior fossa abnormalities
  - Hemangiomas
  - arterial abnormalities
  - Cardiac
  - eye anomalies
  - alias clothing
  - Highest incidence in patients with cutaneous hemangiomas (especially bilateral mandibular regions) and concurrent airway hemangiomas
  - 47% (3/17) incidence of PHACE syndrome in patients with large facial hemangiomas and documented airway hemangiomas (Haggstom, )

Sometimes you see them… ……..Sometimes you don’t

- Hemangiomas of the airway are often lumped under the label subglottic hemangioma
- Beard like distribution has high incidence of airway involvement (50%)
- 50% of patients with subglottic hemangioma have a concomitant cutaneous lesion
- 1-2% of patients with cutaneous lesions have airway hemangioma

Clinical Presentation of Subglottic Hemangioma

- Usually asymptomatic at birth
- Progressive respiratory distress as the lesion grows
  - 6-8 mos
- Biphasic stridor, barking cough, normal or harse cry, and failure to thrive
- Croup- patients with “recurrent croup” are prime candidates for further evaluation for SGLH, especially when their episodes of respiratory distress are worsening and are not associated with fever or rhinorhea

Level of Obstruction with symptoms

<table>
<thead>
<tr>
<th>Level of Obstruction</th>
<th>Respiratory Noise</th>
<th>Work of Breathing</th>
<th>Voice/Cry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal Obstruction</td>
<td>High pitched</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Subglottic Obstruction</td>
<td>Low pitched, stridor</td>
<td>Prolonged inspiration</td>
<td>Weak to Hoarse</td>
</tr>
<tr>
<td>Tracheal Obstruction</td>
<td>Expiratory wheeze</td>
<td>Prolonged expiration</td>
<td>Weak to Aphonic</td>
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Special Notes

- Sound produced by turbulent airflow through the airways
- Degree of stridor not a reliable indicator of severity
- Variable based on activity

Other Factors

- Cough
- Cyanosis
- Presence of feeding issues
- Positional effect on symptoms
Diagnosis

- History and physical exam
- Flexible laryngoscopy
  - Allows visualization of nasal cavity, pharynx and larynx
  - Lesions below the glottis are not well visualized
- Direct Laryngoscopy & Bronchoscopy
  - Gold standard for all complex airway lesions
- Diagnostic Imaging
  - Chest film / Lateral Neck films
  - CT scan/MRI

(Tamburic and Perkins, 2010)

Treatment Options
Subglottic Hemangioma

- If untreated, life threatening
  - Ferguson (1961) reported 50% mortality rate
- Medical treatment
  - Propranolol (Leaute-Labreze, 2008)
    - Highly efficacious and relatively safe
  - Systemic steroids
  - Intraleisional steroids
  - Chemotherapeutic agents (vincristine, interferon)
- Surgical treatment
  - Laser endoscopic resection
  - Open submucosal resection
  - Tracheostomy

Propranolol

- Propranolol is a non-selective beta-blocker that causes capillary vasoconstriction, decreased expression of vascular endothelial growth factors, and apoptosis of capillary endothelial cells
- Most patients will respond within one to two weeks
- Typical dose consists of 2-3 mg/kg/day divided into three doses
- Side effects: lethargy, hypoglycemia, hypotension, bronchospasm
- Close follow-up is essential
- Monitor for adverse effects
- Monitor efficacy
- Titrate doses as the child’s weight increases
- Typically treat for 12 months to cover the natural period of proliferation, then taper dose over 4 weeks
- Yale’s protocol—Typically cardiac work up and hospitalization for initiation; dose gradually increased to therapeutic levels over several days

Excellent efficacy and Safety Profile

- Huge advantages over traditional treatment options
  - Non-invasive
  - Rapid onset
  - Avoidance of tracheostomy
  - Avoidance of prolonged steroid therapy
  - Avoidance of manipulation of subglottic tissues
  - Avoidance of prolonged periods of intubation
  - Low complication rate
  - Inexpensive
Systemic corticosteroids

- Initial treatment of choice prior to propranolol
- Estimated 25% of lesions responded
- Serious adverse effects (12 to 18%)
  - Growth retardation
  - Cushing’s syndrome
  - Hypertension
  - Gastrointestinal ulcers
  - Hirsutism
  - Immunosuppression
  - Cardiomyopathy

Intra-lesional injection of steroids

- Decreased systemic steroids
- Usually requires repeated procedures and post procedure intubation
  - 82% effectiveness in one study but required a mean of 6 procedures and 37 days of intubation to achieve success
- Better for focal lesions

Chemotherapy

- Used in 1% of patients
- Primarily used in life threatening cases when patient is unresponsive to other treatments
- Interferon infusions (IFN-α2a and IFN-α2b)
  - Associated with various side effects including
    - Spastic diplegia (5-20%), higher incidence in children <12m
    - Malignant necrotising, and liver enzyme elevations
- Vincristine—acts by interfering with the mitotic spindle
  - One small study demonstrated a response to vincristine in seven out of nine patients, including five with laryngeal or tracheal lesions
  - Scattered reports of single cases of IFN in various locations showing response

Laser Therapy

- Viable option for small unilateral lesions
  - Success rate as high as 89%
  - Allows focal tissue ablation despite a restricted working space within the airway
  - Variety of lasers including CO2, neodymium: yttrium-aluminum-garnet (Nd:YAG), Nd:YAG via a potassium titanyl phosphate crystal (KTP), diode laser
  - Typically need via an endoscopic approach
- Significant complications
  - Increased risk of subglottic stenosis (25%), particularly in patients with bilateral or circumferential lesions and in patients requiring multiple treatments
  - Multiple treatment sessions
  - Risks of burns, airway fires and complications of the endoscopic approach

Open Surgical Excision

- May be the best surgical option for patients with large, bilateral or circumferential lesions
  - Reported 94% success rate
  - May require lengthy intubation, ICU stay or tracheotomy
  - May avoid tracheostomy
  - If patient does have a tracheostomy, it may allow for quicker decannulation
- Complications: subglottic stenosis, anterior glottic webs and granulomas

Tracheostomy

- May be used to bypass the airway until the hemangioma shrinks
Case Study 1: Meet Ava

- 1-month-old baby girl presenting with 1 day history of increased upper airway noise and a history of facial hemangiomas
- Referred urgently by Pediatric dermatology
- PMH- FT infant born by C-section, facial hemangiomas, no meds, NKDA
- Family Hx- non contributory
- Review of Systems- negative except for facial hemangima

Fiberoptic laryngoscopy

- Nasal cavity: patent, vascular patches noted on the nasal surface of the soft palate in the right posterior region at the level of the choana
- Hypopharynx: tissue (bluish hue) along the false and true vocal folds, causing very minimal obstruction, but concerning for the appearance may be that of a deeper hemangioma, normal VC mobility, normal subglottic air shadow

Airway protection

- Emergent tracheostomy performed
- Transfer to pediatric unit on room air
- Focus on family education
- Oral steroids
- Started on 5mg/kg/day bid and weaned based on response of hemangioma
- Followed by multiple services
- - Otolaryngology, dermatology, social work, PT/OT, psychology, diet, physical, child life
- PHACE syndrome work-up

PHACE SYNDROME

- PHACE syndrome
  - posterior fossa abnormalities
  - Hemangiomas
  - arterial abnormalities
  - Cardio
  - eye anomalies
  - normal chromo
- Ava’s workup was normal
  - Cardiac evaluation
    - WNL small PFO
  - Diagnostic imaging
    - MRI of brain- WNL
    - Normal ophthalmologic exam

Issues while in the Hospital

- Ulcerations and breakdown of her lip and chin
  - multiple laser surgeries
  - Trach switched to Flextend
  - Wound management
- Insurance Issues
  - Medically ready for d/c in early July
- Feeding issues
  - began in July

Feeding Difficulties

- Poor weight gain
  - oral intake down to 65kcal/kg
- BMI formula
  - calories increased to 27kcal
- GERD identified on UGI
  - prevacid and pepcid prn simethicone and maalox
- US upper quadrant
  - no hemangioma noted
- Esophagram and Endoscopy
  - no hemangiomas/compression noted
- NG feeds
- Enteral gastrostomy tube
- Persistent oral aversion and poor oral intake for months to come
Home on August 16, 2007

- Bronchoscopy prior to discharge home (8/14/07)
  - showed significant airway obstruction from circumferential hemangioma
- Home services
  - Nursing with focus on airway/feeding, trachea, skin assessment
- Close follow-up with PCP, otolaryngology, dermatology
- Medications
  - Orapred 9mg bid
  - Prevacid 15mg bid, Pepcid
- Everyone did really well at home
- Steroids d/ced in November due to progressing involution of facial hemangioma and concern for long term steroid use

January 2008 - Cardiomyopathy

- January, 2008 - hospitalized due to cardiac wall thickening
- Cardiology consult: Started on atenolol and doing well
- Case reports of steroid-induced obstructive cardiomyopathy
  - Case report in child with subglottic stenosis (Balys et al., 2005)
  - Multiple reports in premature infants (Shuster et al., 1991; Finer et al., 2000)
- Signs and Symptoms
  - Tachycardia, new cardiac murmur, increased oxygen requirements, decreased UO, decreased peripheral perfusion

2008

- On exam, significant reduction in her facial hemangioma
- Titrating PMV, CMS to periods of time
- Bronchoscopy in early March showed continued significant obstruction
- PCP and subspecialists happy with progress
- Oral feeding trials in process
- Couple minor infections responded well to tx
- Ear hemangioma
  - April visit - first noted hemangioma in the outer and middle ear
  - Also treated for OM on several occasions by PMD
  - Also increased steroids for several months due to PMD
  - Initial case report unexpectedly revealed propranolol efficacy after a child with cardiomyopathy and massive hemangioma was started on propranolol

Ava is now doing well on propranolol

- Focus on establishing oral feedings
  - Very aggressive oral therapy
- 3/17/09 - bronchoscopy
  - Shows rim of hemangioma
  - Excision of large suprastomal granuloma
- 5/5/09 - office visit
  - Doing fantastic, continued involution of facial hemangioma, now using PMV in the middle ear, taking all nutrition by mouth!!!
- 6/9/09 - bronchoscopy looked great
  - Admitted to the hospital for decannulation

2009

- Ava is now doing well on propranolol
- Focus on establishing oral feedings
  - Very aggressive oral therapy
- 3/17/09 - bronchoscopy
  - Showed rim of hemangioma
  - Excision of large suprastomal granuloma
- 5/5/09 - office visit
  - Doing fantastic, continued involution of facial hemangioma, now using PMV all the time, taking all nutrition by month!!!
- 6/9/09 - bronchoscopy looked great
  - Admitted to the hospital for decannulation
- 3/10 - Bronchoscopy and closure of TCF
Closure of Tracheocutaneous Fistula

• March 30, 2010
• Bronchoscopy and closure of TCF

Case Study 2- Kayla

• 2mo ex-35 week twin presented with several weeks of unremitting stridor, substernal retractions and feeding difficulties
• Hospital admission
  – Initial diagnosis of croup
  – Oral steroids and racemic epi
• No improvement in symptoms
• Referral to ENT
  – DL and B

Left subglottic hemangioma at initial diagnosis

Initial bronchoscopy showed 95% obstructing subglottic hemangioma.

Postop

• PICU admission
• Cardiology consultation
• EKG obtained (normal)
• Propanolol- increasing to 2mg/kg/day divided into q6 hour dosing
• Symptoms including stridor, retractions and feeding difficulties resolved completely within 48 hours
• DC home on oral propanolol 2mg/kg/day q6 hrs

2 weeks after initiation of oral propanolol

• Repeat bronchoscopy
• Following 2 months
  – weight increased from 3rd %ile to 10th %ile
  – No stridor or retractions
• Propanolol dose weight adjusted q 4 wks

Approximately 50% obstructive

At 5 months of age
(3m after Propanolol)

• Gradual return of stridor, retractions and feeding difficulties

Approximately 80% obstructive
Hmmm….what is going on?

- Hospital admission
- Propanolol dose increased to 3mg/kg/day q6 hours
- Symptoms persisted
  - intermittent oxygen desaturations to the low 80s
- Surgical excision
  - open resection of the subglottic hemangioma and laryngotracheal augmentation with thyroid ala cartilage graft
- Intubated in the PICU for 24 hours

Post-op Open Excision

24 hours after open excision with laryngotracheal augmentation using thyroid ala cartilage graft

Take Home Messages

- Clinical suspicion for a subglottic hemangioma in an infant with stridor
  - High in cases where there is a synchronous cutaneous lesion
  - In infants without cutaneous involvement, diagnosis may be delayed and more challenging, given the possibility of an infectious etiology
- Although propanolol is highly effective in most patients, a healthy dose of caution is necessary
  - Close follow-up
  - Family teaching and counseling

Case Study 3- Dallas

- 6m old presents with noisy breathing and snoring
- Present since birth
- Hemangioma on the right arm
- Propranolol medication started three weeks ago
- Stridor with agitation
- Excellent growth
- No respiratory distress

Fiberoptic Laryngoscopy