Subglottic hemangioma

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Introduction

- Congenital vascular lesion
- Benign vascular malformation
- 1.5% of congenital laryngeal abnormality
- F:M ~ 2:1
- Rapid growth in the first month after birth
- Stabilize between 12~ 18 months
- Involute by 5 years old
- Nature history: unpredictable
Relation of cutaneous hemangioma and SGH
cervicofacial, mandibular, or "beard" distribution, preauricular skin, mandible, lower lip, chin, or anterior neck
Orlow et al.: ~63% association between cutaneous hemangiomas and symptomatic hemangioma in the upper airway or subglottis
Symptoms

- Recurrent croup
- Biphasic stridor, exacerbated with URI or crying
- Barking cough
- Hoarseness
- Cyanosis
- Hemoptysis
- Dysphagia
- Poor thrive
- 50% cutaneous hemangiomas

Absent~~!! Still can’t exclude SGH
## Congenital v.s. Adult laryngeal hemangioma

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<th>Summary of differences between infantile and adult laryngeal haemangiomas</th>
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Evaluation

- Endoscopic examination
  - Compressible submucosal lesion
  - Red to blue depending on the thickness and degree of vascularity
  - Biopsy is required only if findings on endoscopy are not diagnostic
  - Common location: left posterolateral
  - Circumferential, bilateral, or unilateral with or without posterior extension
Image study

- Neck plain film:
  - asymmetrical narrowing of the subglottic airway
  - Copper et al.: only 50% of subglottic hemangiomas presented asymmetrical narrowing

- MRI
  - for suspicion cervical or intrathoracic extension of hemangioma
  - solid tissue of intermediate intensity on T1-weighted
  - moderate hyperintensity on T2-weighted
  - flow voids(+) → shunting between feeding arteries and draining veins
Histology

- **Proliferation**
  - Increase fibroblast growth factor and vascular endothelial growth factor

- **Involution**
  - Endothelial apoptosis and the downregulation of angiogenesis
  - Accumulation of mast cells
  - Increase of the tissue inhibitor metalloproteinase
Fig. 3. (A) Hemangioma: proliferative phase. Closely packed, plump endothelial cells and pericytes with small vascular lumina are evident (H&E stain, original magnification ×400). (B) Hemangioma: involuting phase. Less closely packed, plump endothelial cells and pericytes with thick vascular basement membrane are evident. The channels are separated by delicate connective tissue (H&E stain, original magnification ×400).
Immunohistology

- North et al. 2000:
  - erythrocyte-type glucose transporter protein (GLUT-1), is highly expressed by infantile hemangioma at all stages
  - high specificity, not observed in other vascular tumors or vascular malformations
  - 10-fold higher in children of women who undergo chorionic villus sampling
Purvis et al., 2006:
No subglottic haemangiomas demonstrated diffuse positive GLUT1 staining as in cutaneous infantile haemangiomas
Treatment
Conservative treatment

- Need to close monitoring
  - Rahber et al.:
    - 13 patients who were monitored conservatively without any complication
    - Most common site: unilateral and left side, no circumferential lesion
    - All were less than 30% subglottic narrowing without any significant respiratory or feeding difficulty within 21 months following time
Radiation therapy

- New and Clark, 1919
  - external-beam radiation for the treatment of subglottic hemangioma
- Ferguson and Flake, 1961
  - advocated the use of tracheotomy with radiation therapy for the management of subglottic hemangioma

Risk:
- damage to the normal airway mucosa
- secondary malignancy, ex: thyroid cancer, sarcoma
Cryotherapy

- Schechter and Bill, 1972, use with steroid
- Disadvantage
  - Depth of tissue destruction is unpredictable
  - Result in subglottic stenosis
Tracheotomy

- Suehs and Herbur, 1940, waiting for spontaneous resolution
- Not influence the natural history of the hemangioma
- Average in place for approximately 2 years
- Indication: hamangioma in the area of glottis and supraglottic
  - multiple lesions of subglottis and trachea
  - contraindication to another treatment
Corticosteroid

- Cohen, 1973, systemic steroid use
- Mechanism:
  - Increase the sensitivity of the hemangioma to physiological vasoconstriction
  - Blockage of estradiol-17b receptors in the hemangioma
- Rahler et al, 2006:
  - < 50% subglottic narrowing and do not have circumferential involvement respond well to systemic corticosteroid treatment
Method

- Prednisolone 2 to 3 mg/kg per day
- Response within several days to 1 week
- If not resolution of symptoms in 2 to 3 weeks → tapered quickly and stopped, and other treatment modalities should be considered
- No data support higher dose or prolonged treatment improves response rate

Response rate:

- Enjolras et al.: 30% accelerated regression, 30% no response, 40% equivocal response
Side effect of corticosteroid

- Cushingoid features
- Infection
- Growth restriction
- Peptic ulcer
- Decreasing the maintenance dose, alternate-day treatment, and intralesional corticosteroid injection could diminish some of these risks.
Intralesional steroid injection

First by Meeuwis et al, 1990
- Repeated endoscopic injection
- Prolong intubation time

Hoeve, 1997
- ~ 60 mg methylprednisolone, q4week
- Mean 3 injection
- Average intubation period: 37 days
- Medium size without extralaryngeal extension
Laser ablation

- CO2 laser
- Nd: YAG laser
- KTP laser
CO2 laser

- First by Simpson, 1979
- 1980, Healy et al.: the successful management of 11 patients with one or two CO2 laser applications
- Walker et al. 1999: requiring oral steroids and Interferon alfa-2a

Setting
- Laser at pulse mode 2-5 W
- Avoid circumferential mucosa injury

Sie et al., 10 years of experience: 20% rate of posttreatment subglottic stenosis
Nd:YAG(1064nm) laser and KTP(532nm) laser
- Absorbed by hemoglobin
- Applicable to the treatment of hemangioma and other vascular tumors
- Deep penetration, less mucosa damage → decreased risk of subglottic scar and stenosis
- Setting: Nd:YAG, 10–15 W; KTP laser, 5–7 W in a single-pulse or repeated-pulse mode at 0.5 s.
- may cause thermal damage to the cricoid and tracheal cartilage
Madgy et al. 2001, 6 cases of SGH managed with the KTP laser.

- 4/6 required two treatments, the rest required only one
- All patients received steroids after surgery
- Achieve 60 to 70% airway patency
- Three of the patients (50%) progressed with mild subglottic stenosis, but all were asymptomatic
Interferon alfa-2a/2b

- **Mechanism:**
  - block angiogenic stimulus (ex. FGF)
  - inhibit endothelium proliferation and migration

- **Dosage**
  - 2~3 million U/m2, subcutaneous, qd for 6~12 months
  - The response is slower than steroids, Walker *et al.*

- No evidence of synergistic effect with steroid

- Indication: deep component involving the mediastinum or large hemangiomas
Garmendia et al. 2001. 39 cases of treat with IFN alfa-2b (newborn to 14 years old):

- 71.1% indicated clinical regression
- None had progression
- better response among children age 1 to 5 years
Side effects with the use of IFN -2a and -2b
- fever, myalgia,
- thrombocytopenia, anemia
- anorexia,
- inflammation in the injection site
- exacerbation of autoimmune disorders
- Neurotoxicity
  - changes in deep tendon reflexes
  - Seizures
  - personality changes
  - spastic diplegia.
Barlow et al.:
- spastic diplegia(+) in 20% of 26 children less than 2 y/o which hemangiomas that did not respond to previous steroid treatment
- This suggests that this treatment modality is inappropriate for infants and young children
Surgical intervention

- Evan et al. 1974:
  - Excision of hemangiomas followed by laryngotracheoplasty
  - All 3 patients required a tracheotomy and postoperative stenting

- Single stage LTR, Wiatrak, 1996:
  - Open surgical resection to be performed under temporal tracheostomy
  - Short-term nasotracheally endotracheal intubation for 1 week
Shyan, 2006: open excision of subglottic hemangiomas to Avoid Tracheostomy
- 22 patients (male 11 female 11)
- 20/22 received SS-LTR
- 20/22 received anterior cartilage graft
- Post op intubation time: 5 days
- 3/21 post op granuloma, 1/21 residual stenosis

Indications, Rahbar, 2004 :
- large, obstructing, or bilateral hemangiomas
- in the proliferating phase
- extralaryngeal extension

Complications
- Subglottic stenosis
- Recurrent laryngeal nerve injury
Endoscopic microdebrider

- Need a smaller 2.9 mm. blade was developed
- Benefits
  - eliminate the obstructive portion of the lesion
  - Preservation of the perichondrium and cartilage intact
  - minimizing secondary thermal mucosal damage
  - Less postoperative edema and airway obstruction
- Michael et al, 2008, 2 case of subglottic hemangioma
  - Pre/post op intralesional methylprednisolone injection was done
  - Patient discharge 48 hours later and asymptomatic for 8 weeks
Vincristine

- Payarols, 1995: combine use with steroid
- Mechanism
  - Inhibit mitotic spindle microtubule by binding tubulin
- Indication
  - Functional and life threatening hemangioma
  - Contraindication to steroid
- D.J. Purvis et al, Absent/reduced glucose transporter-1 protein expression in infantile subglottic haemangiomas, British Journal of Dermatology 2006 155, pp1041–1044
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