

Case Report

The Role of Propranolol in the Treatment of Subglottic Hemangioma: Case Report and Review of the Literature

Elaine Odiase, Gopi Shah and Eric Berg*

Department of Otolaryngology-Head and Neck Surgery, University of Texas Southwestern Medical Center, USA

*Corresponding author: Eric Berg, Department of Otolaryngology-Head and Neck Surgery, University of Texas Southwestern Medical Center and Children's Health of Dallas, 2350 Stemmons Freeway, ENT F6.218, Dallas, TX 75207, USA, Tel: (214)456-0366; Fax: (214)456-7644; Email: Eric.Berg@UTSouthwestern.edu

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Case Report

A full-term 36 day old female was brought to the emergency room by her mother who reported 6 days of progressive stridor. Patient had been previously seen by the primary care physician who also noted the noisy breathing and elected close follow-up. In the interim the patient's mother noted that patient was choking more, having decreased oral intake, and decreased wet diapers. Mom also noted some purple discoloration to the lips when she observed her child having difficulty breathing. Mom denied other symptoms of upper respiratory illness or sweating during feeds, but did mention that the child's noisy breathing was most notable when crying or agitated and improved when placed prone or over mother's shoulder.

During Otolaryngology consultation, fiberoptic laryngoscopy was concerning for laryngomalacia. The subglottis was not clearly visualized. The patient was then admitted to the hospital for continued observation where symptoms progressed with desaturations, increased work of breathing with retractions, nasal flaring, and a "barking" cough despite IV steroids and multiple doses of racemic epinephrine. She was then transferred to the intensive care unit and operative laryngoscopy and bronchoscopy were performed for complete airway assessment. The subglottis was found to be 90% obstructed by a soft, vascular appearing submucosal lesion consistent with a hemangioma. With a single isolated lesion, further diagnostic imaging studies were not indicated and corticosteroids were injected intralesionally and propranolol therapy was initiated. Propranolol was titrated to a weight-based dosage of 2 mg/kg/day divided three times daily and continued to approximately 18 months of age. It was well tolerated without significant adverse events.

Questions

1. What is a subglottic hemangioma?
2. What are the dangers of subglottic hemangiomas?
3. How can subglottic hemangiomas present?
4. Who gets subglottic hemangioma?
5. Are there any treatments?

6. How was the use of propranolol to treatment subglottic hemangioma discovered?

7. Are there side effects or concerns of propranolol use?

Discussion

Hemangiomas are congenital vascular neoplasms generally diagnosed in infancy [1]. They typically present as cutaneous lesions, but can be found in the upper airway, the liver, and most areas of the body. Typically, they present a few weeks after birth and grow quickly during their proliferative phase for anywhere from 6-12 months. This is subsequently followed by spontaneous involution of the lesion around 12-18 months of age. Complete resolution is generally seen by age 3-7 years.

Although benign, hemangiomas occurring in the larynx can be far from safe. Subglottic hemangiomas can lead to signs of respiratory distress and even complete airway obstruction or even death [2]. The diagnosis is made and/or confirmed by microlaryngoscopy and bronchoscopy with the purple vascular lesion noted in the airway along the lateral or posterior aspects of the airway [3]. Diagnosis is generally based on clinical presentation and appearance alone. Imaging studies may be considered for lesions which have an unusual appearance or atypical clinical history. In cases of multiple cutaneous lesions, liver ultrasound may be considered to rule out undetected internal lesions.

These vascular lesions are seen in for 4 to 5 percent of the pediatric population. [1,4] Although hemangiomas account for the most common head and neck tumors found in children, subglottic hemangiomas are rare, accounting for only 1.5% of congenital laryngeal lesions [4,2].

50% of patients with subglottic hemangiomas also have cutaneous hemangiomas, more often in a "beard" distribution across the preauricular, perioral, and anterior cervical skin [2]. When large, plaque-like lesions are present in the head and neck, PHACES association (posterior fossa malformations, hemangiomas,



Figure 1: Subglottic Hemangioma-Pretreatment.



Figure 2: Subglottic Hemangioma-- Post-treatment.

arterial anomalies, cardiac defects, eye abnormalities, sternal cleft, and supraumbilical raphe) should be considered. If cerebrovascular malformations are found to be present, propranolol may be contraindicated due to the potential risk of cerebrovascular accident. Subglottic hemangiomas are seen in females twice more frequently than in their male counterparts. In addition, premature neonates and babies with low birth weights are more likely to suffer from these tumors [4].

The patients that are symptomatic typically present during the proliferative phase of the lesion with obstructive symptoms. In most cases stridor is the first symptom that makes families seek a medical professional. These patients are often challenging to assess and are at times misdiagnosed with croup and laryngomalacia which may present similarly [2,4]. Empiric treatment with steroids and racemic epinephrine, and at times reflux management, may lead to initial improvement. Steady progression of symptoms in spite of such intervention, especially in the absence of fever, runny nose, and other symptoms or upper respiratory infection should raise concern for an airway lesion such as subglottic hemangioma and prompt a formal airway assessment.

As the natural life span of hemangiomas generally includes spontaneous involution, intervention may not be needed. Lesions that cause significant functional or cosmetic consequences, or have complications such as bleeding or infection, generally require intervention. Lesions in the airway clearly present a significant risk of obstruction and rapidly progressive symptoms and even death are a possibility during the proliferative phase. These lesions are therefore much more likely to require treatment [1]. Historically, tracheostomy was performed while physicians watchfully waited for the hemangiomas to spontaneously involute. Tracheostomy is a definitive means of establishing a safe and secure airway but clearly has its own morbidity. Mucus plugging and accidental decannulation, especially in the pediatric population, is always a big risk. Delays in speech and language are also critical concerns in this crucial time of development.

Other surgical treatments include open resection, CO₂ or potassium titanyl phosphate (KTP) laser resection, and microdebridement. All have an increased complications risk of post-operative subglottic stenosis [5,6].

A variety of pharmacologic agents have been employed in the management of subglottic hemangiomas. Due to the prolonged proliferative phase of these lesions, long-term treatment is generally

indicated. Until recently the most widely utilized agents were corticosteroids [1]. Side effects of chronic systemic corticosteroids are growth retardation, peptic ulcers, avascular necrosis, metabolic abnormalities, high blood pressure, and other immune deficiencies in the age group [2,1]. Localized steroids seen with intralesional steroid lesions help reduce the systemic effects, but also have the drawback of requiring repeat injection with repeated exposure to general anesthesia. Other medical treatments include immunomodulatory drugs like interferon and vincristines which were traditionally reserved for severe life-threatening cases due to their significant side-effect profiles [1].

In 2008, the rapid regression of a series of cutaneous hemangiomas was reported in patients receiving propranolol for cardiac conditions [7]. Subsequent cases of propranolol treatment have consistently shown dramatic regression in both cutaneous and airway hemangiomas [4]. The role of propranolol was debated for a short time [3], but the results have been so impressive that propranolol was recently granted FDA approval and has essentially become the standard of care. While its exact mechanism of action is still being elucidated, proposed explanations for propranolol's dramatic effects include prompt vasoconstriction that is seen by color and texture changes of the hemangiomas themselves. In addition, decreased VEGF production and stimulation of apoptosis of endothelial cells are also thought to play a role [1].

While its side effect profile is also significantly lower than previously utilized pharmacologic agents, low blood pressure, hypoglycemia, bradycardia, bronchospasm, fatigue, and masking of poor cardiac function are potential complications of the medication [1,4]. Administration protocols vary between institutions and are still in evolution, but sometimes include baseline echocardiogram and electrocardiogram along with glucose and vital sign monitoring in addition to a thorough physical exam. Fortunately dosage is generally in the range of 2 mg/kg/day, low compared to dosages utilized for cardiac purposes, and significant side effects are proving rare in otherwise healthy patients.

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