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An Unusual Tracheal Hemangioma Successfully Treated with Propranolol

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Abstract A 2-month old, otherwise healthy infant male, presented with inspiratory stridor. A CT scan of the neck revealed an isolated decrease of the lumen in the middle third of the trachea. An MRI showed a markedly hyperintense lesion on T2-weighted images producing an obstruction of 80% of the airway lumen. A rigid bronchoscopy presented a submucosal port wine stain-like mass causing 90% obstruction of the airway at the level of the middle trachea and extending 1,5 cm down the airway. The patient was placed on oral propranolol at 2 mg/kg/day and showed a rapid response to the treatment, with regression of stridor and a significant reduction (less than 50%) of the mass in the images. A new bronchoscopy 3 months later revealed no airways obstruction.

Keywords: *bening tumour, hemangioma, propranolol*

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1. Introduction

Hemangiomas are the most common benign tumours in infancy with an estimated prevalence of 2%-3% in neonates and 10% under age one. These tumours usually occur in the head and neck (60%) and rarely in the laryngotracheal area (1.5% of all congenital laryngeal lesions). [1] The latter may be a life-threatening condition and multiple treatment modalities have been proposed including corticosteroids (systemic or topical [2], external irradiation, surgical excision, [3], laser vaporization, and interferon, all of which have potentially serious adverse effects.

In 2009 Denoyelle et al reported the first two patients with a subglottic hemangioma, successfully treated by propranolol [4]. Since that initial report, several authors have described improvement within 7 days. All the cases described corresponded to the most usual airway localization: the subglottic area.

We report an unusual case of hemangioma in the lower trachea, treatment with propranolol as the initial and only treatment.

2. Case Report

A 2-month old, otherwise healthy infant male, presented with gradual onset of inspiratory stridor and respiratory distress over a 2-week period. There were no apneic or cyanotic episodes but had feeding difficulties. There was no evidence of cutaneous hemangiomas at the physical examination. A CT scan confirmed the presence of a mass suggestive of an angioma (Figure 1). The MRI showed a markedly hyperintense lesion on T2-weighted images at the middle third of the trachea, 1.2 x 0.8 cm in diameter producing an obstruction of 80% of the airway lumen.

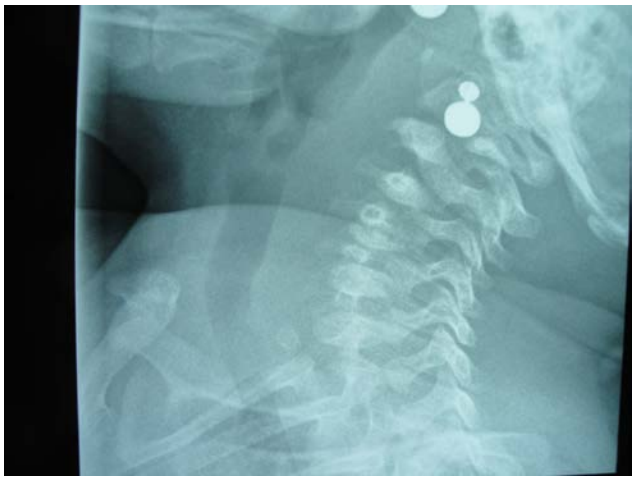

Figure 1. An x-ray film of the neck CT scan of the neck showing an isolated decrease of the lumen in the middle third of the trachea consistent with a tracheal tumor

The child was admitted to the hospital and underwent a rigid bronchoscopy that revealed a submucosal port wine stain-like mass causing 90% obstruction of the airway at the level of the middle trachea and extending 1.5 cm down the airway (Figure 2). The subglottic area was free.

The patient was placed on oral propranolol at 2 mg/kg/day divided three times per day. Previously, he had completed a cardiologic evaluation including an electrocardiogram and echocardiogram. The child showed a rapid response to treatment, with regression of stridor

and respiratory distress in 48 hours and a significant reduction (less than 50%) of the mass in the images.

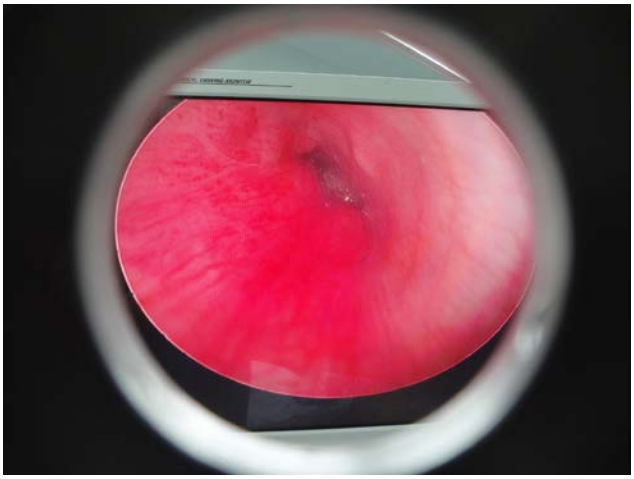

Figure 2. A rigid bronchoscopy showing a submucosal port wine stain-like mass causing 90% obstruction of the airway at the level of the middle trachea

3. Outcome

He was discharged home and a new bronchoscopy 3 months later revealed no airways obstruction (Figure 3). At 6 months, asymptomatic bradycardia (HR 60 x min) was noted and the dose of propranolol was decreased to 1mg/kg/d. During a 10 month follow-up no systemic side effects, such as alterations in sleep, lethargy, malaise, bronchospasm, nausea, or vomiting were observed. A new bronchoscopy at 10 months showed no airway obstruction.

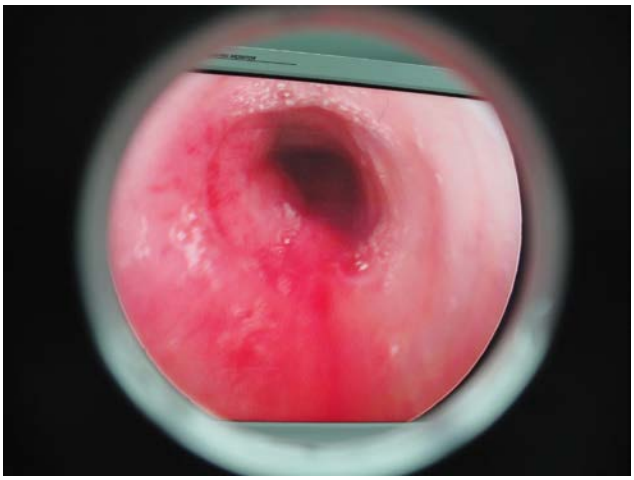

Figure 3. A new bronchoscopy 3 months later showing no airways' obstruction

4. Discussion

Hemangiomas are congenital vascular tumors that are usually found in the subglottis. Among pediatric patients with hemangiomas of the head and neck, 8.5% show cutaneous lesions with a beard distribution and 63% of them have some degree of symptomatic airway involvement [5]. The presence of cutaneous hemangiomas in a beard distribution should alert the evaluating physician to the potential association of upper airway or subglottic involvement.

Like other infantile hemangiomas (IHs), they are primarily constituted of endothelial cells accompanied by pericytes, fibroblasts, interstitial and mast cells. The general hypothesis was that subglottic hemangiomas (SGHs) were histologically and pathophysiologically identical to the more common cutaneous IHs. However, through the use immunohistochemistry, SGHs have recently been differentiated from IHs in that they are immunohistochemically negative for GLUT1 [3].

Plain neck films may suggest the diagnosis but contrast-enhanced CT/CT angiography (CTA) and MRI/MR angiography (MRA) are the most accurate at defining vascular lesions and their extent of involvement in the tracheobronchial tree. [7]. In our patient the MRI shows T2-weighted contrast (gadolinium) images with an isointense or hypointense soft-tissue mass and T1- weighted images with uniformly intense gadolinium enhancement which allow to detect even very small lesions.

The most common hemangioma in the airways is located in the subglottic area. In the 39 cases collected by Saeti et al [6] in a pediatric tertiary center (in 20 years), all the hemangiomas were subglottic as it was the case with the 14 cases reported by Leboulanger et al. [7] or the 19 cases reported by Badi et al [8]. Even when the location "in other areas of the airway" is vaguely mentioned, there are no case reports of specific case series of isolated involvement of the lower trachea without subglottic compromise. Only four adult cases with lower airway hemangiomas have been described [9].

The airway hemangiomas regress for several years until spontaneous resolution is reached over a 2- to 5-year period. [10]. Complete resolution is achieved by approximately 50% of children aged five and more than 70% by children aged seven. However, if left untreated, subglottic and tracheal hemangiomas can cause life threatening airway obstruction.

Several therapeutic options have been suggested to treat airway hemangiomas. Among the 39 patients reported by Saetti [6] (1986-2006), six patients only received systemic steroids, 11 had intralesional corticosteroid treatment after tracheal intubation and systemic corticosteroid administration and the largest group (n = 22) was treated with diode laser was used as primary therapy.

Bitar et al [11] reviewed all the cases of subglottic hemangioma reported in the English-language literature (1986-2002) and concluded that carbon dioxide laser surgery was the most widely used technique for treatment, followed by tracheotomy, systemic corticosteroids, intralesional steroids and open surgical excision. For many authors, diode laser (with a success rate of almost 95% and an incidence of minor complications of less than 10%) was the most appropriate treatment strategy. Finally, open surgical excision of hemangiomas has shown a high success rate (98%) but requires several days of stenting and is associated to a 10% complication rate, such as subglottic stenosis, bleeding, and wound infections.

Propranolol, an oral nonselective beta-blocker, has shown to induce regression of IH in a small series of neonates who showed rapid regression of disease when treated for cardiopulmonary conditions [12]. Patients began propranolol treatment (2-3 mg/kg/day) between 2 and 6 months of age, and treatment was continued for at

least 6 months. There was no reported re-growth at follow- up examination. After that initial report, Buckmiller et al [13] described the first case of subglottic hemangioma treated with propranolol. In 2012 this same group treated 32 patients with IH in different locations and reported that 50% of them as excellent responders and only 1.3% as nonresponders. Thirty per cent of the patients experienced minor side effects to propranolol, including somnolence (27.2%), gastroesophageal reflux (9.1%), respiratory syncytial virus exacerbation (4.5%), and rash (4.5%). More recently, Lebounlager et al [7] in a series of 14 cases, showed a noticeable and prompt reduction of the respiratory symptomatology but with recurrences in 2 of the 4 patients who stopped treatment. Based on these results, they emphasized the need for continuation of propranolol therapy at least until spontaneous regression of the IH, beyond 18 months of age [6]. A meta-analysis of propranolol for treatment of airway hemangiomas was published in 2012 [14]. It totalled sixty one, patients, of whom thirty five had exclusive airway lesions and only 14 patients received propranolol as the only therapy. The improvement of airway obstruction was clearly documented in 21 patients, with a 72% mean obstruction before intervention 20% afterwards ($p < 0.001$). Four children did not respond to propranolol (6.5%), and seven children suffered a hemangioma relapse after therapy discontinuation (11.5%).

A comprehensive review of the literature performed by Drolet et al [15] in 2011 yielded 177 articles about treatment of IH in different locations with popranolol. The majority of these publications included only a few patients and nearly all were retrospective reports. The most frequently reported complications were asymptomatic hypotension or hypotension, bronchospasm, hypoglycemia or hypoglycemic seizure, asymptomatic bradycardia, hyperkalemia, nightmares, somnolence, diarrhea, and gastroesophageal reflux. A multicenter, randomized, double-blind, phase 2-3 trial of propranolol in infants 1 to 5 months old with proliferating infantile hemangioma was recently published showing improvement in 88% of patients who received the drug. Re-treatment after discontinuation of treatment was necessary in 11.4% of patients. [16].

A consensus conference held in Chicago, Illinois, on December 9, 2011 [15] defined the recommendations for propranolol therapy including IH ocular compromise or airway obstruction (or risk of permanent disfigurement) as indications of treatment. Outpatient initiation of treatment may be considered only for infants older than 8 weeks of gestationally corrected age with adequate social support and without significant comorbid conditions [14].

After the publication of a randomized, placebo-controlled study by Léauté-Labrèze et al [16], the FDA approved an oral pediatric formulation of propranolol hydrochloride to treat proliferating IH requiring systemic therapy. The FDA-approved drug label for propranolol states that it is contraindicated in premature infants with corrected age < 5 weeks; infants weighing less than 2 kg; infants with asthma or history of bronchospasm, heart rate < 80 beats per minute, greater than first-degree heart block, or decompensated heart failure; blood pressure < 50/30 mm Hg; or pheochromocytoma.

The present case demonstrated that large tumors with a high degree of obstruction can be safely managed only with propranolol.

5. Conclusion

We have reported a life-threatening airway hemangioma of very unusual location which showed a successful response to propranolol therapy. This case suggests that propranolol can be used as monotherapy in the treatment of serious airway hemangiomas regardless of the location. Our case and the review of the literature of the last three years show that propranolol is a very suitable option due to its limited side-effects and rapid disease resolution. Further research should focus on the optimal treatment (doses and duration) and also the mechanism of potential resistance to propranolol.

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