Neurofibromatosis of the larynx causing stridor and sleep apnea☆☆☆

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ABSTRACT

Background: Neurofibromatosis type 1 can rarely present in the larynx. Patients typically do not present with complete obstructive symptoms, but partial obstruction and stridor. We review our health centers’ case series of two patients, the first of whom presented with persistent sleep apnea post tonsillectomy and adenoidectomy, and the second who presented with noisy breathing. Additionally, we will review the literature on the management and treatment options for children with this rare clinical entity.

Methods: Retrospective case review.

Case report & results: A two-year old male underwent a sleep endoscopy following persistent evidence of obstructive sleep apnea on polysomnography after initial tonsillectomy and adenoidectomy. Family elicited concerns about noisy breathing at night and an accompanying video documented stridor while sleeping during the monitored polysomnography. Flexible fiberoptic laryngoscopy in the operating room revealed what appeared to be a cystic mass along the right aryepiglottic fold causing deviation of the laryngeal introitus towards the contralateral side. Subsequent direct laryngoscopy and excisional biopsy revealed pathology results consistent with a plexiform neurofibroma.

A six-month-old patient with stertor and stridor was found to have a laryngeal mass, subglottic stenosis, and progressive airway obstruction due to plexiform neurofibroma in the supraglottis, subglottis, and trachea.

We present a series of two patients incidentally diagnosed with neurofibromatosis type 1 by way of a laryngeal neurofibroma and review the literature on management options. Both patients were found to have accompanying café au lait spots. Both patients required tracheostomy for airway management, and one was successfully decannulated.

Conclusion: Laryngeal neurofibroma is a rare anomaly that can manifest with airway obstruction. Both patients presented here subsequently were noted to have café au lait spots on physical examination. The Otolaryngologist should be reminded of this anomaly when...
evaluation of a child with evidence of a submucosal laryngeal mass. We present our series including that of a patient whose diagnosis was prompted by persistent sleep apnea following adenotonsillectomy tonsillectomy and a patient with airway obstruction and subglottic stenosis due to a neurofibroma. The treatment of choice is complete excision of the neurofibroma while maintaining functionality of the larynx. This can lead to successful decannulation.

1. Introduction

Von Recklinghausen neurofibromatosis, NF1 has a reported incidence of 1 in 3300 live births and a prevalence of 1 in 4000 [1]. Patients can develop tumors of neural origin at any age and at any location. Laryngeal involvement, however, remains rare [2]. Patients should have 2 or more of the following findings to diagnose NF1:

1. Six or more café au lait spots:
   a. 1.5 cm or larger in postpubertal individuals
   b. 0.5 cm or larger in prepubertal individuals
2. Two more neurofibromas of any type or 1 or more plexiform neurofibroma
3. Axillary or groin freckling
4. Optic glioma
5. Two or more Lisch nodules (benign melanotic iris hamartomas)
6. A distinctive bony lesion:
   a. Dysplasia of the sphenoid bone
   b. Dysplasia or thinning of long bone cortex
7. A first degree relative with NF1

Neurofibromas consist of a proliferation of Schwann cells, fibroblasts and perineural cells [3]. In the advent of more aggressive management of children with persistent sleep apnea following tonsillectomy and adenoidectomy, we present two cases of a laryngeal neurofibroma diagnosed at our hospitals. One was found following sleep endoscopy after persistent sleep apnea after tonsillectomy and adenoidectomy, while the other presented in a more obstructive manner.

2. Case 1

A 2-year-old male presented to the Pediatric Otolaryngology clinic with symptoms consistent with sleep-disordered breathing. The patient underwent elective tonsillectomy and adenoidectomy in April of 2013 uneventfully. There were no noted abnormal laryngeal findings on laryngoscopy during intubation by the Anesthesia team. Following full recovery, the parents reported persistent symptoms of sleep disordered breathing and a decision was made by the Pediatric Pulmonologist to pursue a formal sleep study. Review of the sleep study video recording revealed evidence of stridor during supine sleep and an associated polysonomogram with an elevated AHI of 4.8. Both the Pediatric Pulmonologist and Otolaryngology physicians therefore recommended sleep endoscopy. Flexible fiberoptic laryngoscopy was performed revealing what appeared to be a cystic mass along the right aryepiglottic fold causing deviation of the laryngeal introitus towards the contralateral side. Given the patient’s lack of significant symptoms for obstruction, the decision was made for elective marsupialization of what was initially considered a saccular cyst. Interestingly, post operatively, the parents electively provided further information stating that the patient was also having dyspnea with exertion. The following week the patient returned to the operating room suite for excision and marsupialization of the cyst. Direct laryngoscopy was performed and initially aspiration with an 18-gauge needle was attempted which did not result in decompression (Fig. 1). Incisions were made with both cold steel and the OmniGuide® (OmniGuide Surgical, Cambridge, MA) carbon dioxide (CO2) laser without successful un-roofing of the suspected cyst. Ultimately it was determined to be a solid mass and a biopsy was taken using a cupped forceps. The patient was intubated and taken to the radiology suite for magnetic resonance imaging (MRI) (Fig. 2). MRI revealed a solid mass from the level of the vallecula that extended to the false cord on the right. The patient electively underwent a tracheostomy and formal excision via an open approach following pathology reports confirming a plexiform neurofibroma. (Fig. 3)

3. Case 2

A 6-month-old female was referred to the Otolaryngology Head & Neck Clinic for evaluation of noisy breathing since birth. The patient had no prior medical history evident and an
uncomplicated birth history was reported. The child was feeding well and gaining weight appropriately without evidence of any cyanotic episodes. Primary concerns elicited by the family included coughing and gagging, especially at night. A flexible fiberoptic laryngoscopy was performed revealing a right arytenoid mass that was submucosal in nature. The bulge extended into the post-cricoid region, but the patient maintained a patent airway. The patient was subsequently referred to the Pediatric Otolaryngologist who proceeded with repeat flexible laryngoscopy and CT imaging (Fig. 3). Microdirect laryngoscopy with endoscopic excisional biopsy was performed with pathology consistent with plexiform neurofibroma. Incidentally, postoperatively it was noted the patient had presence of multiple small cafe au lait spots on physical exam. The patient was observed closely in the Otolaryngology clinic and underwent repeat evaluations in the operating room as well as an initial MRI after diagnosis of neurofibromatosis type 1 (Fig. 4). Repeat airway evaluation subsequently revealed persistent swelling in the glossoepiglottic fold on the right and a Grade I subglottic stenosis. Following balloon dilation and a repeat biopsy of the tracheal wall revealing extension of tumor, the patient ultimately underwent a repeat MRI and subsequent elective tracheostomy within twelve months of the initial diagnosis. Clinical examination, imaging and repeat biopsy had now confirmed separate evidence of neurofibroma in the tongue and distal airway including partial obstruction of the left bronchus. The patient has remained tracheostomy tube dependent at this time given its unresectable status.

4. Discussion

Stridor in the neonate and infant population is most commonly secondary to laryngomalacia followed by unilateral vocal cord paresis [4]. Other entities including laryngeal tumors, although rare, can present in a similar fashion. Apart from the laryngeal neurofibroma presented in our series, reports of laryngeal hamartomas have been similarly reported [5]. Congenital cysts are typically located in the supraglottis and glottis proper. With increasing growth these lesions can cause complete obstruction of the airway, requiring tracheostomy [6]. Lesions that are less prominent may present in less prominent situations such as stridor during the day and may solely cause sleep apnea. Obstructive sleep apnea syndrome affects 1% to 4% of the pediatric population in the United States [7–12]. Although historically it has been stated that tonsillectomy and adenoidectomy routinely cured obstructive sleep apnea in children, recent studies have shown otherwise. Up to 75% of children undergoing tonsillectomy and adenoidectomy have some degree of residual sleep-disordered breathing after surgery [13]. The astute otolaryngologist should consider neurofibromas in addition to laryngomalacia in the examination of children with sleep apnea evident on polysomnogram and persistent sleep apnea after adenotonsillectomy. Flexible laryngoscopy in the clinic or sleep endoscopy should be employed in these more complicated situations. Fishman et al. have found that sleep endoscopy demonstrably guided therapy better than awake endoscopy [14].
Neurofibromas are typically associated with NF-1 and NF-2 or as solitary lesions noted sporadically [15]. Von Recklinghausen first reported on neurofibromatosis in 1882 and it is an autosomal dominant disorder [16]. The prevalence of NF-1 has been reported as 1 in 2500–3000 patients, while NF-2 is even rarer with an incidence of 1 in 40,000 live births [17]. Chevalier Jackson first reported the laryngeal neurofibroma in 1930 and it was not until 1940 that it was described in the pediatric population [18,19]. Chinn et al. recently reviewed the literature identifying 62 pediatric cases of laryngeal neurofibroma in the world literature presented as either case reports or case series [17]. The average age reported was 4.1 years, they most commonly were found on the aryepiglottic fold and stridor was present in 44% of the cases they reviewed. [17]

The mucous membranes of the upper part of the larynx are innervated by the internal branch of the superior laryngeal nerve [18,19]. Anastomosis occurs between the internal branch of the superior laryngeal nerve in the region of the aryepiglottic fold and therefore leads to the propensity for presentation at this anatomic subsite [20]. One of the two patients presented had a laryngeal neurofibroma along the aryepiglottic fold.

Direct visualization is the initial step to the diagnosis and management of laryngeal neurofibromatosis. Depending upon age, some patients may undergo flexible laryngoscopy in the outpatient clinical setting prior to definitive evaluation in the operating room. Once initial visualization is made, diagnostic imaging can be important in differentiating between various lesions and extent of the previously visualized entity. In both cases presented, magnetic resonance imaging (MRI) was completed under sedation given their age to further elucidate the involvement of adjacent structures. An MRI can provide superior soft tissue characterization and may delineate additional unsuspected tumors in patients with NF1 and NF2 [1]. T1 weighted images demonstrate iso- to hyperintense lesions while T2-weighted images may be hyperintense [21]. After imaging is obtained, definitive diagnosis via endoscopic biopsy is preferred. Given the benign nature of the disease entity, near total resection with preservation of laryngeal function was performed in our patients and is typically the treatment of choice. Endoscopic removal of a laryngeal neurofibroma was first reported by Bagwell in 1990 with the use of a CO2 laser [22]. The open approach was chosen in Case 1 to provide wider exposure and the ability to achieve a greater resection than what was anticipated endoscopically. The patient in Case 2 had advanced involvement and extent that removal was not deemed a beneficial intervention and tracheostomy was deemed appropriate. Airway management is crucial and both of our aforementioned patients underwent elective tracheostomy tube placement during their treatment process. It however has been established that regardless of technique the likelihood of recurrence is elevated because of the infiltrative nature of neurofibromatosis [23,24]. Because of the infiltrative growth pattern and poor margin control it is important to maintain close follow-up with patients so that less invasive procedures performed endoscopically can potentially be utilized. Our patients are followed closely every 4 to 6 months within the first year.

Historically, well-known causes of persistent sleep apnea in children have included adenoid regrowth, tongue-base prolapse, and laryngomalacia. Stridor is commonly derived from laryngomalacia, vocal cord paresis, subglottic stenosis and croup. Although rare, benign tumors of the larynx, specifically neurofibromas of the larynx may precipitate the diagnosis of neurofibromatosis type 1 or 2 and cause both of the aforementioned entities. With persistent sleep apnea, patients should undergo either a repeat laryngoscopy in the clinic if tolerable or a sleep endoscopy in the operating room. Although Mueller’s maneuver could be attempted in the pediatric population, the utility of it has been brought into question [25]. Ultimately both modalities have both positives and negatives with the extent of muscle relaxation in each state, although one should be employed in those patients with persistent sleep apnea.

REFERENCES


