INTRODUCTION

Normal voice requires laryngeal function to be coordinated, efficient, and physiologically stable. Any imbalances of this delicate system can affect phonation. Benign lesions of the vocal folds can cause imbalances in this system, which can result in varying degrees of dysphonia. Benign lesions represent a common problem that otolaryngologist encounter in clinic, but the exact prevalence of benign vocal cord lesions has been hard to determine.

PREVALENCE

Cohen et al in 2011 performed a large retrospective study to determine the prevalence and causes of dysphonia in the United States. This study compared the differences in etiologies provided by primary care physicians versus Otolaryngologist. The study looked at the United States claims database market scan from January 2004 - December 2008. There were approximately 55 million patients present in the database for this period of time. Of the 55 million, approximately 537,000 had an ICD-9 diagnosis of dysphonia, which makes an overall prevalence rate of approximately 1%. When comparing gender differences, 1.2% of females and 0.74% of males were given the diagnosis of dysphonia. Approximately 11% of patients with dysphonia had benign vocal pathology listed as a diagnosis.

ANATOMY

The laryngeal skeleton consists of nine cartilages. Three unpaired cartilages form the main structure: thyroid, cricoid and epiglottic cartilages. Three paired cartilages form the remainder of the framework: arytenoids, corniculates, and cuneiforms.

The arytenoids articulate with cricoid cartilage and form the cricoarytenoid joints. This is a multiaxial joint, which allows for sliding, rocking, and twisting motions. The cricoarytenoid joints form the primary moving structures of the intrinsic larynx. The arytenoids have a vocal process medially and a muscular process laterally which allows attachment of the vocal ligament and intrinsic musculature of the larynx. The actions of the intrinsic muscles on the arytenoids change the position and shape of the vocal cords.
The intrinsic muscles of the larynx are responsible for vocal fold motion. The posterior cricoarytenoid is the sole abductor of the vocal folds and is responsible for the glottic airway. There are 3 adductors of the vocal folds. The thyroarytenoid has two main muscle bellies, a lateral and medial belly. The contraction of the lateral portion shortens and adducts the vocal fold. Contraction of the medial portion shortens and thickens the vocal fold. The lateral cricoarytenoid is responsible for lengthening and adduction of the vocal cord. The interarytenoids are the only unpaired intrinsic muscles, which consists of the transverse and oblique muscles. These muscles are responsible for closure of the posterior glottis. The cricothyroid is the primary tensor of the vocal folds. It consists of two muscular bellies, a vertical and oblique oriented belly. Contraction of the cricothyroid results in vocal fold tightening and lengthening. The larynx receives its arterial blood supply primarily from the superior laryngeal artery and the inferior laryngeal artery. The superior laryngeal artery is a branch of the superior thyroid artery, which arises from the external carotid artery. The inferior laryngeal artery is a branch of the inferior thyroid artery, which arises from the thyrocervical trunk of the subclavian artery.

The larynx receives its nerve supply from two nerves: the superior laryngeal and recurrent laryngeal nerves. The superior laryngeal nerve arises from the inferior vagal ganglion and divides into two branches. The internal branch, which is the larger branch, supplies sensory innervation to the glottis and supraglottis. The external branch provides motor innervation to the cricothyroid muscle. The recurrent laryngeal nerve is another branch of the vagus nerve. The pathway of the nerve is different on the right versus left. On the left side the nerve loops around the aorta and ascends to enter the larynx near the cricothyroid joint. On the right, it loops around the subclavian and ascends to enter at the same point on the right. The Recurrent laryngeal nerve provides sensory innervation to the infraglottis and motor innervation to all intrinsic laryngeal muscles except the cricothyroid.

To understand vocal fold movement, it is important to understand the histology of the vocal folds. The most superficial layer is composed of nonkeratanized-stratified squamous epithelium. This differs from the rest of the larynx which is composed of respiratory epithelium. Deep to the epithelium is the lamina propria, which can be divided into 3 layers. The superficial layer is composed of a loose fibrous matrix with a gelatinous consistency important for the production of the mucosal wave. The intermediate portion is primarily composed of elastin, and the deep portion is composed of densely arranged collagen. The intermediate and deep layers form the vocal ligament. The deepest layer of the vocal fold is the vocalis muscle. The mucosa and vocal ligament extend over the vocal processes of the arytenoids creating a cartilaginous/aphonatory posterior one-third of the vocal cord and a membranous/phonatory anterior two-thirds of the vocal cord. This is an important anatomical feature in development of benign vocal cord lesions. Most benign nonneoplastic lesions affect the membranous vibratory portion.

**LARYNX**

The larynx serves several functions with the major functions being airway protection, respiration, and phonation. The first and most important function is airway protection; it acts as a barrier in preventing aspiration. It serves an essential function in respiration and acts as a gateway for airflow. The most complex and highly specialized function of the larynx is phonation.

The body cover theory helps to explain the wave like motion of the vocal cords required for normal speech. It describes a loose cover or mucosa moving freely over the stiffer body composed of the vocal ligament and vocalis muscle. There are several ways to view the vocal cords. Videostroboscopy is the gold standard for viewing laryngeal pathology because it produces a
magnified view of the larynx, and it simulates a slow motion view of the vocal cord mucosal vibratory patterns. Videostroboscopy allows for an in-depth look at the mucosal wave, which is important in visualizing asymmetry and abnormal closure patterns.

BENIGN VOCAL CORD LESIONS

Benign vocal cord lesions can be divided into two broad categories: non-neoplastic lesions and neoplastic lesions. Benign non-neoplastic lesions make up the majority of vocal fold lesions. Most of the lesions are associated with vibratory injury of the vocal cords but multiple factors can lead to the development of these lesions. The most common risk factors include extroverts with a talkative personality and occupations with high voice demands. Other factors that can potentiate vibratory injury include smoking, acid reflux, uncontrolled allergies, and infections.

VOCAL CORD NODULES

Vocal cord nodules are the most common benign lesions of the vocal folds. Nodules are most commonly seen in children and adult females. The most common presentation is hoarseness of variable duration and degree. Patients can also have varying degrees of breathiness and vocal breaks. Nodules are often seen in patients with vocal abuse or misuse, which include professional singers, teachers, and others in high voice demand jobs.

Vocal cord nodules appear as bilateral swellings located at the junction of the anterior and middle membranous portion of vocal folds. This is the point of the maximal shearing and collision forces between the cords. The nodules can vary in size, symmetry, contour, and color. Some variability does exist in the size of the nodule and the effects on voice; often, singers may have nodules with no vocal complaints. The development of nodules occurs in stages. Forceful or prolonged vibration at the membranous (vibratory) portion of the vocal cords lead to submucosal edema and vascular congestion followed by healing and remodeling of the superficial lamina propria. Long-term vocal abuse leads to hyalinization of the superficial lamina propria, which results in nodule formation. On videostroboscopy, vocal cord nodules create an hourglass closure with a relatively normal mucosal wave.

Treatment should be individualized based on voice demands. The primary treatment is voice therapy. Optimizing the laryngeal environment is a key to successful treatment. This includes eliminating phonotraumatic behaviors, setting guidelines for voice use, and optimizing hydration. Medical problems, which are associated with vocal cord irritation, should be treated appropriately. If conservative therapy does not improve symptoms surgery may be necessary. Other options that have been reported in literature for treatment of vocal nodules includes intralesional steroid therapy and Botox injections.

VOCAL CORD POLYP

Vocal polyps are primarily unilateral lesions, but can present bilaterally. Polyps can be broad based or pedunculated. The color of the lesions vary and can be red, white, or translucent lesions located at the junction of the anterior and middle third of the true vocal cord. As with vocal nodules, polyps are associated with vocal abuse and may be associated with anticoagulant use. There are two types of polyps: hemorrhagic and nonhemorrhagic. Hemorrhagic polyps often have an abrupt onset following extreme vocal effort. Nonhemorrhagic polyps are outpouchings of inflamed superficial lamina propria.
Polyp development is thought to be caused by shearing forces during vocal exertion, which results in capillary rupture and focal accumulation of blood or hematoma in the superficial lamina propria. This causes edema followed by infiltration of inflammatory cells, which ultimately results in the formation of a new matrix. Vocal cord polyps on videostrobe usually have intact mucosal waves sometimes with phase asymmetry due to impaired glottic closure.

The management of vocal polyps is different based on the size of the polyp. Small polyps will likely resolve with conservative management alone while larger polyps often require surgical intervention. Medically if possible patients should discontinue anticoagulants, and acid reflux should be controlled to prevent hyperemia and vessel dilations associated with reflux. Voice therapy is beneficial to patients with vocal polyps and sometimes is the only management necessary in resolving small polyps. Surgical removal is necessary when conservative therapies fail. Office based pulse dye lasers (585nm) have been shown effective in some studies for treating small hemorrhagic polyps.

**VOCAL CORD CYST**

Vocal cord cysts are usually unilateral but can be bilateral. They are sac like structures within the lamina propria, yellow or white in color, and have a distinct border. Vocal cord cysts are true cyst with an epithelial lining covering the cyst. There are two subtypes: epidermoid and mucus retention cyst. Histologically epidermoid cysts are covered by stratified squamous epithelium with a keratin content, and mucus retention cysts are covered by cylindrical epithelium with mucous content. Epidermoid cysts arise primarily from vocal abuse and mucous retention cysts can develop spontaneously.

The pathogenesis is different for the two types of cyst. Epidermoid cyst arise in one of two ways. They can develop when epithelial cells are buried congenitally in the subepithelial layer or from the healing of mucosa from voice abuse over buried epithelial cells. Mucous retention cyst form when mucous gland ducts become obstructed from conditions such as upper respiratory infections, voice overuse, and acid reflux. The videostrobe of a patient with a vocal cord cyst will have an asymmetrical mucosal wave at the site of the lesion. The side with the cyst will have a decreased wave and the wave on the unaffected side is often normal. Glottic closure depends on the size of the cyst and can vary.

The primary management option for cysts consist of surgical removal because vocal cysts do not resolve with conservative management alone. Supportive measures can help but will not resolve these lesions. Voice therapy plays a limited role in treatment of these lesions but it can be useful in the epidermoid variety, which are more likely to be due to vocal abuse.

**REACTIVE VOCAL CORD LESION**

Reactive vocal cord lesions can form in response to unilateral vocal cord lesions. Unilateral lesions create shearing forces on the contralateral cord resulting in a reactive callus with vocal cord hyperplasia. These lesions give unilateral lesions a bilateral appearance and are often times confused with vocal cord nodules. It is important to distinguish vocal cord nodules from unilateral lesions with a reactive callus due to the difference in prognosis and treatment strategies for these lesions. Reactive lesions on videostroboscopy can have an hourglass closure, but unlike vocal cord nodules wave asymmetry is often present. The primary management for reactive vocal cord lesions is to treat the primary lesion. Reactive lesions usually resolve with conservative management.

**REINKE’S EDEMA**

Polypoid corditis, reinke’s edema, or smoker’s polyps are terms that refer to bilateral diffuse polyposis. It is usually seen in patients with chronic irritant exposure and classically appears in middle
aged, talkative women with long-term histories of smoking. Patients present with a lower pitched voice than would be expected; women often present with complaints of a masculine voice. Polypoid corditis appears as outpouchings of the membranous vocal cord with an edematous water-balloon appearance. On videostroboscopy, polypoid corditis will present with a decreased mucosal wave and phase asymmetry due to ball-valving and asymmetrical edema.

The first step in management of a patient with polypoid corditis is smoking cessation. Voice therapy may help to introduce optimal vocal behavior and can sometimes reduce the size of the polyp resulting in improved vocal functioning. However, surgery is often necessary when the voice remains unacceptable to the patient.

**VOCAL CORD GRANULOMA**

Vocal cord granulomas occur primarily in men on the posterior one-third or cartilaginous/aphonatory portion of the vocal cord. Speech may sound normal in patients with vocal cord granulomas due to the location of these lesions. Granulomas occur in response to trauma and are often associated with reflux, chronic cough, throat clearing, and intubation. Granulomas can develop from forceful closure of the arytenoids or direct abrasion of the mucosa over the aryltenoid perichondrium. Granulomas often do not affect mucosal wave due to the location of the lesions in the cartilaginous portion of the vocal cord; however, large granulomas can affect glottic closure.

The primary management for patients with vocal granulomas is to treat the underlying cause of irritation. Voice therapy and anti-reflux medications are often the only treatment necessary. Granulomas will usually resolve over a 3-6 month period. Surgical removal may be considered but postoperative reoccurrence is common. Surgical removal is reserved for lesions that are enlarging, affecting the voice, or suspicious for malignancy.

**CAPILLARY ECTASIA**

Vocal cord varices or capillary ectasias are more common in female singers. The most common initial complaint is hoarseness after short periods of singing. These lesions appear as an abnormal dilation of capillaries that proceed anterior to posterior. Varices form as the result of vibratory microtrauma, which leads to capillary angiogenesis. Varices predispose the vocal folds to mucosal swelling, vocal fold hemorrhage, and hemorrhagic polyp formation.

Medical management of patients with varices is similar to the management of hemorrhagic polyps. Patients should discontinue anticoagulant use if possible and treat any underlying medical conditions that can affect vocal cord environment. Voice therapy is beneficial to patients presenting with these lesions. Surgery is an excellent option for patients who fail conservative management. CO2 lasers were used in the past, which sometimes led to scarring. KTP lasers are now being used due to its angiolytic properties and the potential to selectively ablate vessels without damaging surrounding tissue.

**INTRACORDAL SCARRING**

Intracordal scarring can result in aphony to relatively normal speaking voice and appears as a scarred stiff vocal cord. It can develop in response to repeated inflammation, vocal trauma, and vocal hemorrhage, which results in scarring of superficial lamina propria. Intracordal scarring can occur in patients with surgeries involving the lamina propria and when epithelial lesions require repeated procedures such as those for leukoplakia and recurrent papillomatosis. The lesions develop when the superficial lamina propria adheres to the underlying vocal ligament, disrupting the ability of the
mucosa to oscillate freely during speech. Videostrobe will show a markedly reduced or absent mucosal wave.

In management of intracordal scarring, treatment of general medical conditions like allergies and reflux should be optimized. Voice therapy is important and focuses on a “voice building approach.” The muscles involved in phonation are strengthened to compensate for the damaged mucosa and to soften the scar by “phonatory massage” which theoretically will allow the mucosa to oscillate more freely. These lesions can be treated surgically by incising and elevating the mucosa above the scar with early voice therapy but overall improvement in voice is variable. The best treatment option is prevention with precise surgical technique and early treatment of vocal trauma to avoid unwanted scarring.

LEUKOPLAKIA

Leukoplakia presents as a white hyperkeratotic plaque on the vocal cords, which represents a change in the epithelium, as normal glottic epithelium is non-keratinized. The incidence of vocal cord leukoplakia is 10.2 per 100,000 males and 2.1 per 100,000 females. The pathophysiology is unknown but likely related to chronic irritation of the vocal cords. These lesions can have varying degrees of dysplasia and can be broken down into 3 stages or categories: No dysplasia, mild to moderate dysplasia, and severe dysplasia. There is an 8-14% chance of malignant transformation in these lesions. On videostroboscopy, leukoplakia varies from having a normal to sluggish mucosal wave. It is important to understand that appearance does not always correlate with degree of dysplasia. A tissue diagnosis is necessary to rule out malignancy. These lesions can be removed by laser or excision.

PAPILLOMA

Vocal cord papillomas are the most common benign neoplasms making up approximately 84% of lesions. The prevalence rate among children is 4.3 per 100,000 and among adults is 1.8 per 100,000. Vocal cord papillomas are caused by HPV with type 6 and 11 strains being the most common. Type 11 has been associated with more aggressive disease. HPV type 16 and 18 have a higher risk of malignant transformation. A child has a 200 fold increased risk of acquiring vocal cord papillomas if the mother is infected with genital HPV at birth.

There are two types of vocal cord papilloma: juvenile and adult form. The juvenile onset form tends to be more aggressive with bulky, exuberant tissues resembling “clusters of grapes” present on the anterior portion of the true vocal cords. The adult onset form tends to be more localized, usually less aggressive, less exophytic with a velvety appearance, and little projection from the surface of the vocal cord. On videostroboscopy, there can be a mass effect with a decreased mucosal wave.

These lesions are primarily managed surgically. The CO2 laser has been the most widely accepted management option for papillomas; however due to the depth of penetration and the risk of scarring, CO2 lasers have been supplanted by pulsed dye and KTP lasers which are angiolytic. The microdebrider has been found useful in bulky lesions due to its ability to suction the affected tissue. There are many adjuvant treatments, which include interferon, Indole-3-carbinol, bevacizumab and Cidofovir. There is interest in the effects that the HPV vaccine will have on the incidence of recurrent respiratory papillomatosis; some believe it will decrease the incidence on the basis of herd immunity.

Cidofovir is a prodrug used since 1995 for intralesional vocal cord injection but has yet to be approved for this purpose. It is used as an adjunct to recurrent respiratory papillomatosis refractory to surgery alone. Cidofovir has only been approved for IV treatment of CMV retinitis in acquired
immunodeficiency patients. The reported side effects of intravenous usage of the drug consist of nephrotoxicity, hepatic dysfunction, and ocular toxicity. Concern has been raised about cidofovir increasing malignant potential. Studies have shown that 2-3% of patients with recurrent respiratory papillomatosis have malignant transformation, which is equivalent to patients with and without cidofovir exposure. In 2011, the Gilead general warning letter was released which warned that potential complications could result from off label usage including nephrotoxicity, neutropenia, oncogenicity, and fatality. In 2012, an international multicenter retrospective study was performed to evaluate the safety of cidofovir for intralesional laryngeal injections. 635 patients with recurrent respiratory papillomatosis were included in the study with 275 treated with cidofovir. Results showed no statistical differences in occurrence of neutropenia or renal dysfunction before or after cidofovir treatment. In addition, no statistical differences in upper airway and tracheal malignancies between the cidofovir group and non-cidofovir group were found.

Bevacizumab is another adjuvant treatment, which is under investigation for the treatment of recurrent respiratory papillomatosis. Bevacizumab is a monoclonal antibody, which inhibits VEGF and has antiangiogenic activity. It is hypothesized that this drug could have a synergistic affect with KTP lasers. In 2011, a prospective study of 20 adult patients with bilateral disease was performed. The patients in the trial were treated with KTP laser 4 times at 6 week intervals. At each procedure bevacizumab was injected into the vocal cord with greater volume of disease at presentation and the contralateral cord was injected with saline. The patients were reevaluated at each interval and 6 weeks after completion of the study. The study revealed no systemic or local complications. Three of twenty subjects had no noticeable disease in either cord following treatment; 16 subjects had less disease in the treated cord; and 1 subject had more disease in the treated cord. They concluded that injection of antiangiogenic medications shows potential to improve KTP treatment and may decrease the frequency of treatments.

CONCLUSION

Benign vocal cord lesions are common pathologies that will be seen in clinic. The management options of these lesions differ, and correctly diagnosing these lesions is important in treatment outcomes. Videostroboscopy is a crucial component in making the correct diagnosis and guiding treatment plans. Preservation of the normal anatomy is an important component to optimizing vocal outcomes.

REFERENCES


