The Clinicopathologic Spectrum of Benign Mass Lesions of the Vocal Fold due to Vocal Abuse

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Abstract

Benign masses of the vocal fold related to phonotrauma are clinically classified into polyps, nodules, Reinke’s edema, and cysts. Despite the apparent distinctiveness of the clinical nomenclature, low inter- and intraobserver diagnostic agreement has been reported. Excepting cysts, which are epithelial lined, histologic examination of the remaining lesions has shown a variety of overlapping features insufficiently specific for the clinical diagnoses. This study reviews the clinicopathologic characteristics among these benign lesions of the vocal fold. A total of 78 nonneoplastic lesions of the vocal fold were reviewed by 2 pathologists for the presence of epithelial hyperplasia, basement membrane thickening, edema, vascular proliferation, and extracellular “amyloid-like” fibrin. In 46 cases with prebiopsy stroboscopic images, 2 otolaryngologists classified each lesion as polyp, nodule, Reinke’s edema, cyst, or other. They agreed in 43% (n = 20, 13 polyps, 5 nodules, 1 Reinke’s edema, 1 other) and disagreed in 57% (n = 26). There was no histologic feature that reliably distinguished among the lesions. In addition, reactive stromal cell atypia was present in 14 cases. Cysts were distinctive, as all were epithelial lined. The clinicopathologic classification of benign laryngeal lesions is neither clinically reproducible nor histologically unique. Treatment will continue to be individualized based on clinical judgment.

Keywords
vocal nodule, vocal polyp, Reinke’s edema, benign laryngeal lesion, singer’s node

Introduction

Benign tumefactive lesions of the vocal fold are common, usually related to vocal abuse, gastroesophageal reflux, and/or smoking. The standard clinical classification includes 4 entities: (a) polyps—unilateral, sessile, or pedunculated lesions of the anterior third of the vocal fold; (b) nodules—bilateral, symmetric swellings of the anterior to middle vocal fold; (c) Reinke’s edema—unilateral or bilateral swelling of the entire focal fold; and (d) cysts—discrete unilateral swellings clinically similar to the foregoing 3 lesions (see Figure 1, Plates A-D). Excluding cysts, the histologic examination of these benign vocalopathic lesions has shown the similar and variable presence of epithelial hyperplasia, basement membrane thickening, edema, vascular proliferation or ectasia, and extracellular fibrin (“amyloid-like” material).¹,² There are no universally agreed histologic criteria for any lesion and no singular feature or combination of features has yet been able to distinguish among them. Cysts are histologically distinct, being lined by typical respiratory epithelium (mucus-retention cysts), stratified squamous epithelium (squamous inclusion cysts), or specialized salivary gland epithelium such as oncocyttes. None of the above 4 categories are typically ulcerated and are thus clinically distinguished from contact ulcers, which are also complications of gastroesophageal reflux.

The clinical evaluation of these benign laryngeal lesions employs a combination of history, physical examination, and videostroboscopy, all of which aid in evaluation of the anatomy and vibratory characteristics of the glottis. Despite the specific clinical nomenclature, the clinical literature reports low inter- and intraobserver diagnostic agreement³,⁴

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Figure 1. Plates A-D, Laryngoscopic images of (A) polyp, (B) nodules, (C) Reinke’s edema, and (D) cyst. Plates E-H, Representative photomicrographs demonstrating (E) epithelial hyperplasia and basement membrane thickening, (F) vascular ectasia, stromal edema, and perivascular fibrin/amyloid-like deposit, (G) stromal fibrin/amyloid-like nodule, and (H) simple cyst with high-power inset. Plates I-K, Isolated stromal cell atypia in 3 cases.
perhaps an additional reflection of the absence of diagnostic histopathologic criteria. Diagnostic concerns notwithstanding, treatment issues remain. The treatment of these lesions varies. Nodules are initially treated conservatively with voice therapy, whereas polyps, Reinke’s edema, and cysts are often excised surgically. Previous studies, which have appeared in the clinical literature only, have unsuccessfully attempted to correlate the clinical and pathologic features of benign mass lesions linked to vocal abuse. The histologic distinctiveness of cysts notwithstanding, as a practical matter, surgical pathologists have recognized the nonspecific histologic features of the remaining lesions and often report their findings descriptively. Using a relatively large series of histologically evaluated cases, this study explores the clinicopathologic correlation, or lack thereof, among the benign noncyst mass lesions of the vocal fold.

Materials and Methods

With institutional review board approval, a retrospective search of the clinical records from the Voice Center in Otolaryngology–Head and Neck Surgery (OHNS) at the University of Chicago was matched with a search of the surgical pathology database in the Department of Pathology. A total of 78 nonneoplastic, nonulcerated lesions of the vocal fold (searched as mass, lesion, polyp, nodule, or cyst) between the years 1997 and 2009 were identified. The actual pathologic sign-out diagnoses for all 78 lesions (as rendered by a typical sign-out rotation of several general surgical pathologists) were largely descriptive or qualified as “consistent with” whatever clinical diagnosis appeared on the pathology requisition. These narrative diagnoses were not used in the final analysis. Clinical records and corresponding stroboscopic images were available for 46 cases and were reviewed by 2 OHNS otolaryngologists (ENTs). The 2 ENTs (having examined the clinical and stroboscopic data) classified each lesion as polyp, nodule, Reinke’s edema, cyst, or other (unclassified).

All hematoxylin and eosin–stained slides from all 78 cases were reviewed by 2 pathologists for the presence of the following 5 histologic features: epithelial hyperplasia, basement membrane thickening, edema, vascular proliferation/ectasia, and extracellular “amyloid-like” fibrin. These features were tabulated as present or absent, although dominant patterns of expression were resolved by consensus. Cysts were identified as epithelial-lined structures and were excluded from the final clinicopathologic analysis.

Results

Among the 46 cases reviewed clinically, agreement between the ENTs was 43% (n = 20, 13 polyps, 5 nodules, 1 Reinke’s edema, 1 other). Histologically, the one case identified as “other” consisted of granulation tissue. Table 1 shows the distribution of histopathologic features among the clinically rendered diagnoses. Histologically, epithelial hyperplasia was present in 39% of polyps, 40% of nodules, and 46% of cases not-agreed-on. Basement membrane thickening was present in 31% of polyps, 40% of nodules, and 54% of cases not-agreed-on. Edema was present in 69% of polyps, 20% of nodules, and 69% of cases not-agreed-on. Vascular proliferation was present in 62% of polyps, 0% of nodules, and 27% of cases not-agreed-on. Extracellular “amyloid-like” fibrin was present in 69% of polyps, 20% of nodules, and 50% of cases not-agreed-on. Parenthetically, of the 6 cysts identified by the pathologists, 4 were classified as cysts by either of the 2 ENTs. Histologically, all cysts were epithelial lined (see Figure 1, Plates E-H).

Among the remaining 32 cases with a clinical diagnosis but without detailed stroboscopic data, histologic examination demonstrated a similar range of epithelial hyperplasia, basement membrane thickening, edema, vascular proliferation/ectasia, and fibrin/amyloid-like material as noted above. There were 3 papillomas and 1 suture granuloma. No suspicion of malignancy was identified in any case. Stromal cell atypia was present in a total of 14 of the 78 cases (see Figure 1, Plates I-K).

Discussion

Excepting epithelial lined–cysts, benign masses of the vocal fold resulting in hoarseness are relatively common in individuals whose personal or professional life puts them at risk for phonotrauma, such as singers or teachers.
removal follows an integrated clinical and videostroboscopic evaluation in patients who are unresponsive to behavioral intervention. The existence of different clinical entities with common pathologic alterations could raise a question about the relevance of the clinical diagnoses, especially if the treatments are similar. Previous studies have attempted to show morphologic distinctiveness of each lesion, but without success. The results of these studies, none appearing in the pathology literature, parallel the observations reported here. Loire et al reported that polyps are characterized by fibrinous material, nodules have epithelial hyperplasia and basement membrane thickening and Reinke’s edema demonstrates submucosal edema and vascular proliferation. On the other hand, Dikkers and Nikkels found that epithelial hyperplasia, basement membrane thickening, and submucosal edema “had no discriminative value” in differentiating these lesions, but they did find a predominance of extracellular fibrin in polyps. Wallis et al also concluded that the overlapping features of edema, inflammation and fibrin preclude definitive diagnosis of polyp or nodule, although ectatic vascular proliferation is more common in polyps. Staining for elastin (with Verhoeff-van Gieson), collagen (with Masson trichrome), and hyaluronic acid (with Alcian blue) showed overlapping histologic features that were not significantly different among the lesions. Just as histologic features may overlap, common stroboscopic characteristics may also lead to varied interpretations of cysts and nodules, as reported by Woo et al.

Authors of a recent report were unable to demonstrate agreement between clinical and histologic diagnoses. Therefore, they recommended use of a unifying histopathologic term for clinically defined polyps, nodules, and Reinke’s edema. The findings in the present study support this recommendation. Of 46 cases classified by 2 ENTs, they agreed in 43% (mostly polyps and nodules) and disagreed in 57% of cases. As evidenced by high interobserver variability, an accurate clinical/stroboscopic diagnosis is difficult to achieve. Not only was there poor interobserver agreement, but there were no clear histologic differences between polyps and nodules. In the cases agreed on by the 2 ENTs, varying percentages of epithelial hyperplasia, basement membrane thickening, edema, vascular ectasia, and extracellular “amyloid-like” fibrin were found. Vascular proliferation and extracellular fibrin were present slightly more frequently in polyps than nodules.

One potential histologic diagnostic dilemma is stromal cell atypia. One author reported “unusual fibroblasts” in laryngeal polyps, and 14 of our cases demonstrated isolated stromal cell atypia. These atypical fusiform stromal cells, possibly fibroblasts, have been described in nasal polyps, without any progression to malignancy. The presence of these cells in nasal polyps and the present group of benign laryngeal lesions likely represents a reactive change not an indicator of underlying neoplasia.

Although treatment may be individualized per clinical judgment, the present study has demonstrated that the classification of a benign laryngeal lesion related to vocal abuse, for example, polyp, nodule, or Reinke’s edema is neither clinically reproducible nor histologically unique. Only true cysts, having an epithelial lining, are histologically distinct and should perhaps be subclassified by the nature of the epithelial lining. In the past, a common generic term for vocal abuse lesions has been “singer’s node.” Although this term may not be satisfactory to all who treat these patients, the histologic similarities among these tumefactive vocal-pathic lesions suggests the need for a common diagnostic pathologic term.

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