



Allergic laryngitis: unraveling the myths

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Purpose of review

This article provides a thorough review of the literature highlighting the articles that have advanced our knowledge about the sensitivity of the larynx to allergens in the air or ones consumed. This area of inquiry requires continued interest and investigation. As the field of clinical laryngology changes, and more information is discovered about the possible causal association between allergy and vocal pathologies, practicing otolaryngologists, allergists, and other medical professionals may discover more comprehensive methods to evaluate and treat their allergic patients, particularly those who present with complaints of dysphonia, dysphagia, laryngopharyngeal reflux (LPR), and/or dyspnea.

Recent findings

There continues to be epidemiological studies designed to describe the relationship of allergy to vocal symptoms and signs. Both population and smaller studies have recently attempted to link these two conditions. Unfortunately, the patient with chronic laryngeal complaints is often tagged by default with the diagnosis of LPR and treated with proton pump inhibitors, which are not always beneficial. The endoscopic assessment may not be as reliable to make the diagnosis of LPR as the examination is subjective and the inter-rater reliability is low. It has been demonstrated by direct laryngeal provocation studies that sticky-viscous endo-laryngeal mucous is the only reliable finding consistently associated with allergy potential allergic tissue reactivity.

Summary

The interrelationship of allergic sensitivity and chronic laryngitis in certain individuals is becoming clearer because our knowledge of inquiry has increased and the available routine technology to diagnose these conditions has remarkably improved. Notwithstanding these advancements, much more research is needed on this subject to reduce the frequency of mis-diagnoses and mis-management of allergic patients.

Keywords

allergic laryngitis, allergic rhinitis, allergy, atopy, dysphonia, hoarseness, voice changes

INTRODUCTION

Producing a comprehensive report on the vulnerability of the larynx to various inhaled or ingested allergens is very challenging, mostly because there is a paucity of clinical and bench research on the subject of allergic laryngitis. In fact, there is little consensus in the scientific literature relative to whether or not this condition is a true clinical entity. One would be hard pressed to assemble a panel of experts on laryngeal pathologies who are in agreement not only about the validity of this diagnostic terminology but also the predictable anatomical and functional abnormalities associated with presumed allergic laryngitis. Adding more uncertainty to this discussion is the frequent general causal associations between (a)llergy text should match the other conditions allergy involving the unified airway, (a)cid reflux disease, and (a)sthma. This triple A coexistence in many patients often serves as a roadblock to definitive differential

diagnosis in any given patient, placing the examiner at risk for mis-diagnosis and mis-management because of many overlapping and potentially inter-related clinical signs and symptoms of these three conditions [1–3]. At the outset we respectfully ask readers for their indulgence relative to their initial acceptance of the term ‘allergic laryngitis’ so that we can proceed with a detailed analysis of the complex and controversial literature base on this subject matter with hopes for offering readers greater clarity by the close of this review.

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KEY POINTS

- Laryngoscopic findings for reflux are subjective and have a low inter-rater reliability.
- Thick, viscous mucous secretion in the endolarynx is the most notable finding in allergic patients with voice difficulties.
- A comprehensive allergy workup is helpful in the workup for patients with chronic vocal complaints.

The diagnosis of allergic laryngitis is elusive. It is often a diagnosis of exclusion after all other possible clinical situations have been considered and ruled out. The purpose of this review is to highlight recent articles relating to laryngeal allergy and to discuss clinical implications to consider when and how to treat patients with presumed allergy-related vocal complaints. It is our hope that this information will stimulate clinical researchers to undertake additional investigations into this area of inquiry.

BACKGROUND

The diagnosis of laryngeal allergy was initially introduced in 1971 [4]. For the past four decades several clinical researchers have studied laryngeal mucosa reactivity to various antigen exposures, both directly via provocation methodologies in individuals with newly discovered allergic sensitivities and indirectly in individuals with long histories of allergy [5–9,10^{***}]. These investigations promoted discussion about the convergence of viscous, sticky-thick mucus secretions both from the lungs and nasal cavity at the level of the laryngeal inlet; the exacerbating effects of co-occurring endolaryngeal mucous secretions were also occasionally noteworthy. Numerous concurrent sequelae were consistently observed in experimental individuals, including immediate throat clearing behaviors, globus sensation, vigorous coughing responses, and reactive secondary vocal fold edema and hyperemia. These negative ‘allergic’ reactions resulted in prompt, transient, and chronic voice difficulties, characterized by variable complaints of hoarse-raspy-asthenic voice quality disturbances and coexisting limitations in pitch range and vocal volume controls [11,12].

The yearly prevalence of vocal disorders is 6–8% [13,14], and the lifetime prevalence of dysphonia is almost 30%. As acute and chronic laryngitis is a frequent cause of vocal complaints, establishing a correct diagnosis is important in this patient population. The diagnosis of allergic laryngitis is difficult

in the shadow of other causes of chronic inflammation, such as laryngopharyngeal reflux (LPR), as mentioned previously. Current diagnostic methods for LPR are associated with low inter-rater reliability and poor specificity to distinguish between these two conditions [15]. Summarily, most of these clinical researchers have reported that the prevailing examination findings in patients with suspected allergic laryngitis and associated voice difficulties are thick-viscous endolaryngeal secretions and transient or chronic reactive vocal fold edema and hyperemia.

ETIOLOGY UNIFIED AIRWAY CONCEPT

Immunoglobulin E (IgE)-mediated allergic responses have been well documented to play a large role in nasal and pulmonary diseases. There is a common epithelium and shared mediator responses of the upper and lower airways. This ‘unified airway’ concept has also been described to result in adverse laryngeal, nasal cavity, bronchi, and the middle ear effects [15–18]. Pathological changes in any one of these organ linkage components have been shown to induce a variably widespread inflammatory response in both the upper and the lower airway segments [19–23]. There is a strong epidemiological link between allergic rhinitis and the development of asthma [22–24]. In fact, treatment of allergic rhinitis has been shown helpful in controlling asthma and preventing its progression [25,26], and early immunotherapy can reduce the development and worsening of asthma signs and symptoms [27].

CLINICAL PRESENTATION AND DIAGNOSIS

Allergic laryngitis can present as a conglomeration of laryngopharyngeal symptoms, which can be acute or chronic; this condition rarely presents as a single complaint entity. Most patients present with variably exacerbating and chronic symptoms, as previously described: cough, throat clearing, sensations of a foreign body and excessive mucous in the throat, and postnasal drainage. Because of the overlapping presenting symptoms observed in patients with histories of documented LPR and in those individuals with suspected allergic laryngitis, examiners are strongly challenged when charged with reaching a definitive diagnosis and treatment recommendations for any given patient with either or both of these potentially underlying conditions. Although there is little debate that 24-h pH monitoring is the definitive, gold standard method to identify the presence of an unusual degree of reflux activity in the symptomatic patient, this

measurement tool is not commonly utilized by most practitioners to verify this clinical suspicion; largely due to the availability (or lack thereof), expense, and invasive-discomfort characteristics of such technology [28]. Most recently dual pH probes with multi-channel intraluminal impedance testing have been utilized to provide objective evidence of pharyngeal reflux exposure in patients with suspected LPR [29]. This test was positive in 47% (51 patients) of the 109 patients tested; 39% (43 patients) of the tests were negative, 15% (14 patients) of the tests were equivocal. Early objective testing allowed for identification of those who would not benefit from proton pump inhibitors and who were instead good candidates for Nissen fundoplication when appropriate [30–32].

The reflux symptom index (RSI) is a validated questionnaire developed to help predict the clinical diagnosis of LPR [33]. An affiliated diagnostic laryngoscopic evaluation tool (reflux finding score – RFS) was also developed to help predict the presence of LPR [34]. Unfortunately, due to the subjective nature of the associated scoring systems of these examination batteries, the low specificity of each test, and the inherent challenges to achieving good levels of inter-rater reliability, these laryngeal examination testing forms are not used routinely by physicians in most clinical settings [35,36]. Rather, perhaps the most prevalent usage and adoption has been for academic-research purposes.

EVIDENCE OF ALLERGIC LARYNGITIS

There are several studies showing a link between allergic disease and vocal symptoms. In one such investigation a population of 49 students with allergic rhinitis symptoms on immunotherapy for 3 years was compared with 54 control patients with no known allergic disease [37]. Results showed that patients with allergic rhinitis had an increased number of vocal complaints compared with their normal counterparts. These complaints improved with increasing duration of immunotherapy treatment. Another investigation focused on allergic and non-allergic patients during birch season [38]. Results demonstrated that the former subgroup exhibited significantly higher voice handicap index (VHI) scores [39] than the nonallergic individuals. Similar findings were reported by others [5]. Patients with allergic and nonallergic rhinitis were shown to exhibit higher odds ratios of dysphonia than individuals without signs of rhinitis [40], and those individuals in this investigation with the poorest rhinoconjunctivitis-related quality-of-life scores had the lowest voice-related quality-of-life scores and highest RSI scores. Perhaps even more

interesting were the results demonstrating that individuals with both allergic rhinitis and nonallergic rhinitis had higher incidences of dysphonia than nonallergic study counterparts, likely owing to the aforementioned chronic, reactive throat clearing and coughing behaviors in the former subgroup. More recently, other clinical researchers reported higher VHI scores in individuals with allergies versus age-matched nonallergic controls [41]. These findings were augmented by various acoustic, clinical voice, and laryngeal videostroboscopic test results, all of which corroborated the perceptual abnormalities in voice exhibited by the individuals with allergy histories.

Even more recently other researchers examined a large cohort of individuals using in vitro allergy testing for primary symptoms of rhinitis, laryngitis, otitis media, and sinusitis in patients not previously diagnosed definitively as having an allergic disorder [42]. Results revealed that more than half of the individuals with laryngeal-related complaints, such as histories of intermittent dysphonia, had positive test results to at least one inhalant allergen. The odds ratio of having a positive test for allergies was statistically similar among patients evaluated for rhinitis and chronic sinusitis. Of note, dust mite antigen sensitivity was by far the most common finding. Dust mite allergic individuals were also extensively evaluated for associated vocal pathologies and laryngeal provocation reactions by many other researchers, as mentioned earlier [5–8]. As noted previously, LPR may be overdiagnosed or misdiagnosed when allergic laryngitis is present. Due to significant overlap in symptoms, LPR diagnoses based on the physical findings are often unreliable due to inherently poor inter-rater reliability of the RFS [43]. Conversely, these researchers reported strong inter-rater agreement relative to the presence of thick endolaryngeal mucous and associated reactive vocal fold edema, erythema, and hyperemia in individuals with known allergies.

Several clinical researchers have reported a large percentage of positive atopic findings in those patients who suffer with chronic reflux and dysphonia signs and symptoms [2,43]. These researchers cautioned laryngologists to be careful to differentiate laryngitis owing to LPR, allergic secondary reactions, or both. Allergy specific subsets of the VHI were created and utilized as part of the data collection research methodology. Summarily, results revealed that patients with high VHI scores had similarly pronounced prevalent air-borne antigen sensitivities and high historical incidences of undiagnosed allergy; that allergic laryngitis should not be ruled out as causally related to various abnormal vocal signs and symptoms, especially in patients

with positive allergy testing results. These findings also led to suggestions for effective type-specific management strategies for such vulnerable patients.

The lifetime prevalence of dysphonia is 30%, with approximately 7% of the population experiencing voice problems at some point in their lives [13,14,44,45]. These data were largely based on telephone interviews and self-questionnaires rather than actual voice laboratory laryngeal examinations. A national survey of nearly 20 000 participants to collect general medical health histories and formal examination results from a random database was conducted [46]. All individuals underwent rigid endoscopic examinations performed by residents and reviewed later by their attending faculty advisors. The study is unique because patients who were asymptomatic were screened for laryngeal findings. Recorded abnormal laryngeal findings included the following percentages: laryngitis in 3.5%, vocal nodules in 1.5%, vocal polyps in 4.0%, and Reinke's edema in 3.5%. The prevalence of these results was greater in men, and various respiratory conditions were associated with increased incidences of reported voice difficulties. History of allergic rhinitis were positively correlated with vocal nodules, laryngitis), and epiglottic cysts; chronic throat clearing behaviors reported by those with histories of allergic rhinitis were considered to be causally related to these vocal pathologies.

In a very recently published study, several clinical researchers investigated the effects of iron soot and house dust mite allergen (HDMA) on the larynx and the trachea of guinea pigs [10¹¹]. These animals were separated into four 6-week groups, exposed either to HDMA, soot, or both. The mean eosinophil profile was the primary outcome measure in glottic, subglottic, and tracheal epithelium and submucosa, examined in the sacrificed animals. Significant eosinophilia was noted with the soot and HDMA combination. These findings supported previous research relative to notable adverse effects of inhaled irritants in several segments of the unified airway, resulting specifically in characteristic laryngeal inflammation. A recently published tutorial on laryngeal inflammation offers a comprehensive review of the literature on acute and chronic forms of this condition [47¹²]. Within the context of this review, allergic laryngitis is discussed and integrated into a clinical algorithm for differential diagnosis and treatment considerations.

Another model investigation of direct stimulation of the larynx was designed to study potential vocal functional disturbances, following a double-blind crossover methodology of data collection [48]. Phonatory threshold pressures were measured in five patients after antigen stimulation. Increased

antigen concentrations caused significant increases in mean phonatory pressures. These results were consistent with previously reported conclusions that in asthma-free patients antigen stimulation can cause objective laryngeal abnormalities [5–8].

CONCLUSION

For the past 50 years, clinicians and researchers alike, in various fields of study, have become increasingly interested in the possible causal association between allergies and vocal pathologies. The information presented in this review of the relevant literature base on these individuals has highlighted the previous direction of such clinical and scientific inquiries and the need for further study to demonstrate unequivocally that such pathophysiologic relationships truly exist. It has been reported that a subset of atopic individuals often present with complaints of intermittent or chronic dysphonia, the causes of which may be multifactorial and potentially inter-related. A recurring and notable finding reported by numerous researchers is the presence of thickened, viscous, and sticky endolaryngeal secretions in patients with allergies and voice difficulties; transient vocal fold edema and erythema may coexist in many individuals. When these differential features are identified on laryngoscopy they should strongly alert the examiner that allergic response a tissue irritability may be at least partially responsible the phonation subsystem signs and symptoms. In each case, a comprehensive allergy workup may help substantiate the differential diagnosis and an appropriate treatment algorithm that recognizes all possible contributing pathological variables, including allergy, LPR, asthma, voice abuse behaviors, and so on. As is frequently the case in areas of limited scientific investigation, much more prospective clinical and bench research is needed to delineate the actual role of allergy in different populations with vocal pathologies. The results of such anticipated study may yield very practical diagnostic and treatment solutions for clinicians whose practices include patients with laryngitis of unclear origin.

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Conflicts of interest

The authors declare no conflicts of interest.

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- of outstanding interest

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