Predictive Value of Globus Pharyngeus in Patients With Functional Dysphonia Versus Organic Dysphonia

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Objectives/Hypothesis: This is a retrospective study investigating the prevalence of globus pharyngeus in patients with dysphonia.

Study Design: Retrospective chart review.

Methods: The study examined the prevalence of globus pharyngeus in patients presenting with history of dysphonia at the American University of Beirut Medical Center Voice Center. The etiology of dysphonia was categorized as organic in the presence of laryngeal pathology versus functional in the absence of any laryngeal pathology on laryngeal videostroboscopic examination. Functional dysphonia was further stratified as muscle tension dysphonia (MTD) and non-MTD based on the presence or absence of supraglottic muscle tension patterns.

Results: The medical records of 300 patients were reviewed. Total prevalence of globus pharyngeus was 14.33%. There was a significant difference in the prevalence of globus pharyngeus between patients with organic dysphonia and patients with functional dysphonia (P < .001). Out of 43 patients with globus, 41.86% had organic voice disorders versus 58.14% who had functional voice disorders. Among those with functional voice disorders, globus pharyngeus was more prevalent in patients with MTD versus non-MTD patients (P = .19). Out of 25 patients with functional voice disorders and globus, 72% had MTD versus 28% who had no MTD (P = .19).

Conclusions: Globus pharyngeus is significantly more prevalent in patients with functional dysphonia versus patients with organic dysphonia. Moreover, in patients with functional dysphonia, the prevalence of globus was higher in those with MTD despite not reaching statistical significance. Globus pharyngeus may be either the cause or the result of laryngeal aberrant functional behavior.

Key Words: Globus pharyngeus, functional dysphonia, organic dysphonia, muscle tension dysphonia.

Level of Evidence: 4

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INTRODUCTION

Globus is defined as a nonpainful, intermittent, or persistent sensation of a lump or foreign body in the throat. In the past, this condition was referred to as globus hystericus, as it was linked to menopausal women with psychogenic disorders. It was not until 1707 that Purcell first described globus as contractions in the neck strap muscles resulting in pressure on the thyroid cartilage. Later, in 1968, Malcomson defined the term globus pharyngeus in view of the high frequency of pharyngeal symptoms in patients with globus sensation. In 1982, Thompson and Heaton indicated that globus pharyngeus is a common condition that occurs in around 46% of healthy individuals. Men and women are equally affected, yet women tend to seek healthcare more often than men. Moloy and Charter reported that globus pharyngeus accounts for about 4% of general otolaryngology referrals. Although the natural history of globus is yet to be fully established, almost 45% of patients continue to have persistent symptoms at their 7-year follow-up.

The association between globus and dysphonia has always been reported in the context of esophageal motility dysfunction, laryngopharyngeal reflux disease (LPRD), laryngeal sensory neuropathy, muscle tension dysphagia, and in the context of allergy. In the context of esophageal dysfunction, Moser et al. described abnormal esophageal manometry in 67% of patients with globus, and Manabe et al. have attributed ineffective esophageal motility in affected patients to achalasia, esophageal spasm, and abnormal lower esophageal function. Extraesophageal reflux is also believed to be one of the main factors contributing to the pathogenesis of globus pharyngeus. Hoon Park et al. reported LPRD in 71.9% of patients complaining of globus with no organic cause. Similarly, a study by Smit et al. using double-probe pH monitoring on 25 patients with globus revealed pathologic reflux in 72% of the cases. Globus pharyngeus has also been investigated in the context of sensory laryngeal dysfunction. Verrigan et al. looked at the prevalence of laryngeal

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hypersensitivity syndrome using a laryngeal paraesthesia questionnaire and objective testing in a group of 11 patients with globus. The results indicated high-symptom burden and significant impairment in patients versus controls. The authors emphasized the presence of laryngeal hypersensitivity syndrome in a large group of patients with chronic laryngopharyngeal symptoms. In keeping with the aforementioned, globus pharyngeus, in addition to throat clearing and cough, have been thoroughly described in patients with laryngeal sensory neuropathy, which is characterized by the presence of laryngopharyngeal complaints in the absence of laryngopharyngeal reflux, allergy, asthma, psychogenic disorders, and/or the intake of angiotensin-converting enzyme inhibitors. Globus pharyngeus may also be a presenting symptom in patients with muscle tension dysphagia. Kang et al. reported the prevalence of globus in one-third of patients with laryngeal hyperresponsiveness (LHR). The study was conducted on 67 patients with functional dysphagia, 97% of whom had evidence of a muscle tension pattern on laryngeal examination, and 67% had signs and symptoms of LHR. Globus may be associated with allergy as suggested by Jaruchinda et al. A positive skin test was reported in 77.8% of patients with globus (42 out of 54) as compared to 28.6% (eight out of 28) of the control group (P < .001). In addition, globus symptom improved in 64.3% of the cases after the allergy was treated. Functional dysphonia, referred to as “impairment of voice production in the absence of laryngeal structural changes or neurogenic disorders” has been equally associated with etiologies similar to those in patients with globus pharyngeus. Given the cross-cutting in the pathogenesis of globus pharyngeus and functional dysphonia, and the commonality in all the aforementioned etiologies in regard to both disease entities, the authors of this article aimed at investigating the prevalence of globus pharyngeus in patients with functional dysphonia in comparison to patients with nonfunctional dysphonia, referred to in the text as organic dysphonia. The predictive value of globus in patients with functional dysphonia is also reported. The question that the authors attempted to answer is the following: Are patients with dysphonia and globus more likely to have functional dysphonia in comparison to patients with dysphonia and no globus? This information is invaluable to the primary care physician who may lack the facility to perform an indirect laryngeal examination on patients with presenting symptom of dysphonia and globus, and also to otolaryngologists in their workup of patients with dysphonia. The hypothesis set forth is that globus pharyngeus has a positive predictive value in assessing the etiology of dysphonia.

MATERIALS AND METHODS

Participants

Patients who presented with a complaint of dysphonia to the voice unit of a tertiary referral center between 2013 and 2016 and whose electronic medical records were available were included in this study. Dysphonia was defined as a change in voice quality in relation to timber, loudness, or pitch. All patients had undergone laryngeal videostroboscopy examination using the Rhino-Laryngeal Stroboscope (RLS 91008; PENTAX Medical, Tokyo, Japan) in addition to history taking and system inquiry.

Data Collection

After having obtained the institutional review board approval, a retrospective chart review of all patients with the chief complaint of dysphonia and available electronic records was conducted. A total of 300 electronic medical records were reviewed. Patients were stratified according to the etiology of dysphonia, namely organic or functional. Organic etiology was characterized by the presence of either mucosal lesions or inflammation, exudative lesions of the lamina propria (nodules, cysts, Reinke’s edema, polyps), or by the presence of a neurogenic disorder such as impaired mobility of the vocal folds (paresis or paralysis). Patients with no organic etiology were labeled as functional dysphonia. These were further stratified into having functional dysphonia with muscle tension (muscle tension dysphonia (MTD)) or functional dysphonia with no muscle tension. MTD was diagnosed based on the presence of laryngeal muscle tension, which can be in the form of posterior glottic chink, mediolateral compression of the false vocal folds, anteroposterior shortening of distance between interarytenoid area and petiole, and in the form of sphincter-like closure of the supraglottic structures.

Statistical Method

Frequencies and means (± standard deviation [SD]) were used to describe categorical and continuous variables, respectively. Categorical variables were analyzed using the Pearson χ² test, whereas continuous variables were analyzed using an independent t test. The Pearson χ² test, which is a nonparametric test, was used to analyze the difference in the categorical variables between two groups and to calculate the odds ratio and P value. A two-tailed P value of <.05 was considered statistically significant. All analyses were conducted using Statistical Package for the Social Sciences version 24 software (IBM, Armonk, NY).

RESULTS

Demographic Data

A total of 300 patients were included. They were divided into 156 males (52%) and 144 females (48%). Two hundred thirty-two patients had organic etiology for dysphonia, and 68 patients had functional etiology. The group with organic dysphonia had a mean age of 49.46 years (SD = 15.36 years), whereas the functional group had a mean age of 42.35 years (SD = 16.32 years) (P = .517) (Table I).

Patients With Organic Dysphonia

Among patients with dysphonia of organic etiology (N = 232), the most common pathologies were laryngitis/inflammation of the vocal folds (N = 50) (21.55%), polyps (N = 44) (18.97%), and Reinke’s edema (N = 42) (18.10%).

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Less common pathologies included leukoplakia (N = 30) (12.93%), paresis or paralysis (N = 32) (13.79%), and nodules (N = 19) (8.19%) (Table II).

Prevalence of Globus Pharyngeus in Functional Versus Organic Dysphonia

Globus pharyngeus was present in 14.33% of patients presenting with dysphonia (43 out of 300), with no significant predilection to gender (25 [58.14%] were males vs. 18 [41.86%] females, P > .05). Prevalence of globus pharyngeus was found to be significantly higher in patients with functional dysphonia (36.76%) as compared to those with organic etiology (7.76%) (P < .001). Out of 43 patients with globus, 41.86% had organic voice disorders versus 58.14% with functional voice disorders (Table III). Regarding the odds ratio (OR), patients with globus sensation were 6.91 times more likely to have functional dysphonia compared to those without globus (OR = 6.91, 95% confidence interval [CI]: 3.471-13.76).

Based on numerous reports including that of Morrison et al., mucosal changes such as nodules and polyps, in addition to abnormal laryngeal muscle tension, may be observed in patients with functional dysphonia.24 To that end, further analysis that took into account vocal fold nodules and polyps as functional causes of dysphonia was conducted and revealed a statistical significance between the functional group, inclusive of polyps and nodules, and the organic group (P < .01). The odds ratio, despite having decreased, showed a positive correlation, with a value of 3.564 (95% CI: 1.775-7.158). Thus, patients with functional dysphonia had 3.564 times the odds of having globus sensation as compared to patients with organic causes of dysphonia.

Prevalence of Globus in Relation to MTD in Patients With Functional Dysphonia

Out of the 25 patients with functional dysphonia complaining of globus sensation, 18 (72.0%) had MTD. The prevalence of globus pharyngeus was found to be higher in patients with functional dysphonia and MTD in comparison to patients with functional dysphonia and no MTD. The difference, however, did not reach statistical significance (P = .19). Patients with functional dysphonia and globus sensation were almost twice as likely to have MTD compared to those with no globus (OR = 2.04, 95% CI: 0.71-5.88). The lack of significant difference may be attributed to the small number of cases.

DISCUSSION

Globus pharyngeus is a common complaint in otolaryngology practice. More often than not it is associated with other symptoms related to the laryngopharyngeal complex, such as dysphagia, throat clearing, cough, and change in voice quality. When present, clinical diagnosis of LPRD, allergy, laryngeal sensory neuropathy, or muscle tension dysphagia is suspected.

Given the aforementioned, namely the broad pathogenic background of globus pharyngeus and its significance in diverse clinical contexts, the authors of this study have been intrigued with investigating the clinical significance of globus in the context of dysphonia and its predictive value in patients with organic versus functional dysphonia. The latter refers to a group of patients who present with impaired voice production and normal laryngeal exam, namely lack of neurologic or structural pathologies of the larynx.1−3,5 Based on numerous investigations, functional dysphonia accounts for 10% to 40% of cases referred to voice clinics,6,7,25 and the vocal history of affected patients is presumed to be similar to those of organic etiology. The results of this investigation showed a statistically significant difference in the prevalence of
globus in patients with functional dysphonia versus organic dysphonia (36.76% as compared to 7.76%) \( (P < 0.001) \). Patients with dysphonia and globus were almost seven times more likely to have functional dysphonia compared to patients with dysphonia and no history of globus sensation. Even after including patients with vocal folds nodules and polyps in the functional group, the prevalence of globus pharyngeus was significantly higher in the functional group.

The results of this investigation are not surprising given that most of the etiologies of globus that were thoroughly discussed in the Introduction have also been incriminated in patients with functional dysphonia. LPRD, for instance, has been estimated to be present in one out of two patients with dysphonia, and more so in patients with nonspecific laryngeal findings. As such, it has been listed as a main complaint in the reflux symptom index described by Belafsky et al. An alternative diagnosis to LPRD in patients with dysphonia, globus, and normal laryngeal findings is allergy. This seems to be an important confounding factor in the context of the unified airway model described by Rubin et al. and Krouse et al. With the increasing susceptibility of the laryngeal structures to environmental allergens, recent reports indicate that the prevalence of allergic laryngitis can reach up to 70% in patients with laryngeal complaints, with 50% being positive for at least one allergen. Laryngeal sensory neuropathy has also gained popularity recently as an etiologic factor in patients with globus, dysphonia, and normal laryngeal and pharyngeal examination. As noted by Cobeta et al., patients with laryngeal sensory neuropathy invariably present with chronic cough, associated dysphonia, and globus sensation. Vertigan et al. reported that these patients were more likely to have dysphonia, globus, and increased sensitivity to triggers of cough. After excluding the aforementioned confounders, patients are started on neuromodulators with promising results. Other suggested etiologies of functional dysphonia are psychological disorders, namely conversion disorders, anxiety, and depression, all of which have been implicated in patients with globus sensation. Anxiety and depression are considered as predisposing and confounding diseases for globus. Stress has been reported as a pathogenic factor in 96% of patients with globus sensation, with exacerbation of their symptoms during periods of high emotional intensity.

In summary, the findings of this investigation imply that patients with dysphonia and globus are less likely to have laryngeal pathology in comparison to patients with dysphonia and no history of globus sensation. In a primary care setting, this information is important in deciding on the urgency for referral to a specialist, while keeping in mind the need for early laryngeal evaluation in high-risk smokers and or patients with comorbid diseases such as neurogenic disorders. The findings also indicate that patients with functional dysphonia and globus are twice as likely to have MTD on laryngeal examination in comparison to patients with functional dysphonia and no globus. In the laryngology practice, physicians should be more on the lookout for laryngeal muscle constriction in patients with dysphonia, globus, and nonspecific laryngeal examination.

The higher prevalence of globus in patients with functional dysphonia, and in particular those who exhibited a laryngeal muscle tension pattern, in comparison to patients with organic dysphonia, alludes to the pathogenic role of laryngeal muscle hyperactivity in this group of patients. Whether globus is the cause or effect of this laryngeal behavior remains to be determined in a prospective study looking at the prevalence of dysphonia and abnormal laryngeal muscle tension in a group of patients with globus pharyngeus as the presenting symptom.

The main limitation of this study is its retrospective nature, which did not allow us to exclude important confounding diseases in patients with functional and organic dysphonia, most common of which is laryngopharyngeal disease. The presence of LPRD may blur the true predictive value of globus as a symptom in the absence of other symptoms of extralaryngeal reflux disease. It would be valuable to investigate the predictive value of globus, as one of the many ill-defined symptoms related to the laryngopharyngeal complex, in patients with normal 24-hour double-probe pH monitoring. Another major limitation to this study is the lack of a quantitative measure or scoring for globus, namely standardized questionnaires such as the ones described by Lyberg-Åhlander et al. and Catheart et al.

CONCLUSION

Globus pharyngeus is a common symptom in patients with dysphonia presenting to the otolaryngology clinic. Its prevalence is higher in patients with functional dysphonia in comparison to those with organic dysphonia. Its etiology seems multifaceted and includes both organic and functional etiologies. Future investigation taking into consideration other comorbidities is warranted.

BIBLIOGRAPHY
