

Globus

Current Concepts and Dilemmas

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Abstract: Globus is an area of interest for many medical specialists including otorhinolaryngologists, gastroenterologist, allergists, and psychiatrists. It may be caused by an organic disease, but it is not uncommon that an underlying etiology remains unidentified even after a full workup has been performed. Patients who suffer from globus usually visit several physicians from different specialties without finding a solution for their symptoms. Identifying the underlying cause of globus is not always a simple task; therefore, structural or functional abnormalities of the thyroid, larynx, pharynx, and esophagus should be investigated. Gastroesophageal reflux disease is commonly considered to be the underlying cause after being identified in an otorhinolaryngeal (ear, nose, and throat) evaluation, which is usually the first diagnostic step. In the last few years, an inlet patch in the proximal esophagus has been shown to be associated with globus, and its elimination has resulted in symptom resolution in some patients. Finally, globus can be associated with psychiatric disorders as well as oropharyngeal hypersensitivity that could be either chemical or mechanical. Treatment is directed toward an identified organic cause; in those with a functional disorder, the mainstay of therapy includes neuromodulators and psychiatric/psychological interventions.

Key Words: globus, heartburn, gastroesophageal reflux, esophageal hypersensitivity, esophageal motor disorders

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Globus is the sensation of a lump in the throat. It is usually described as the sensation of a foreign body, itching, or even mucus sticking in the throat and improves with swallowing. Globus is not generally painful and might be intermittent, occurring with dry swallows and disappearing with meals. Globus might be sensed from the cricoid region down to the upper edge of the sternum. It can be associated with other symptoms or may present alone as a single symptom. The prevalence of globus varies from 0.1% to 21%, depending on the population studied and the definition used.

Globus is a frequently encountered but poorly understood disorder, and it is managed by different specialties such as otorhinolaryngology, gastroenterology, allergy, and psychiatry. Consequently, the terminology tends to vary across

different medical specialties, such as “globus hystericus” in the psychiatry literature and “globus pharyngeus” in the otorhinolaryngology and gastroenterology literature.

In most cases, even in patients without alarm symptoms, globus is so bothersome that it impacts their quality of life significantly. There are various structural causes for globus, but gastroesophageal reflux disease (GERD) is commonly suspected first because ear, nose, and throat (ENT) evaluation is often the initial diagnostic step. In the last few years, an inlet patch in the proximal esophagus has been shown to be associated with globus, and in some patients its elimination has resulted in symptom resolution. In the absence of GERD, an inlet patch, major esophageal motor disorder, or other structural and functional mechanisms, globus is considered a functional esophageal disorder. Globus, the functional esophageal disorder, is commonly associated with psychiatric disorders and visceral or oropharyngeal hypersensitivity to either chemical or mechanical stimuli.

This update is intended as an overview of the literature on globus and includes current definitions, alarm symptoms, pathophysiologic mechanisms, diagnostic algorithm, and treatment options.

DEFINITION

Globus is defined as a persistent or intermittent non-painful sensation of a lump or foreign body in the throat.¹ The symptom is commonly episodic and is located in the midline between the thyroid cartilage and the sternal notch. It is not associated with dysphagia or odynophagia, and it frequently improves with eating and swallowing.

Diagnosis of globus per Rome IV criteria requires the absence of pharyngeal, laryngeal, and esophageal structural lesions, esophageal mucosal abnormalities (eg, inlet patch), GERD, eosinophilic esophagitis, or major esophageal motor disorders (distal esophageal spasm, esophagogastric junction outflow obstruction, achalasia, jackhammer esophagus, and absent contractility). Criteria must be fulfilled for the previous 3 months with symptom onset at least 6 months before diagnosis and frequency of at least once a week.²

EPIDEMIOLOGY

Globus is a common symptom. Nearly half of the general population has reported intermittent symptoms resembling globus, while more severe and distressing symptoms have comprised up to 4% of the referrals to ENT specialists.³ Globus is reported by up to 46% of healthy individuals.⁴ The prevalence of globus has been estimated in the literature to be between 0.1% and 21.0%, depending on the population studied and the definition used.^{5–10}

Globus can be associated with other symptoms including dysphagia,¹¹ odynophagia,¹² chronic cough,¹³ and heartburn,¹⁴ or it can present without any of these symptoms.

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Globus has a peak onset at middle age and is equally prevalent in both sexes, but women are more likely to seek medical attention for this complaint. Thompson et al¹⁵ reported that 46% of 147 healthy volunteers had experienced globus sensation at least once during their lifetime. The symptom was 3 times more common in women than in men who were younger than 50 years of age, while there was no difference in prevalence between men and women over the age of 50 years.

Globus is commonly a chronic disorder, and symptoms typically persist for > 3 years in 75% of patients, although as many as 50% have persistent symptoms after 7 years.¹⁶ A recent study that included 3006 subjects found a lifetime prevalence of 21.45%, with a peak onset at the age range between 35 and 54 years. It was higher in urban areas. There is no predilection by sex, but there is a higher incidence in patients with anxiety, depression, and sleep disorders as compared with subjects without globus.¹⁷

PATHOPHYSIOLOGY

Presently, many causes for globus sensation have been suggested, and it has been linked to several medical conditions including organic and functional disorders (Table 1).

Structural Causes

Various organic disorders have been shown to be associated with globus including Zenker diverticulum, esophagogastric junction stenosis, esophageal webs, esophageal strictures, esophageal cancer, pharyngitis, tonsillitis, chronic sinusitis, upper respiratory tract malignancy, hypertrophy of the base of the tongue, retroverted epiglottis, cervical heterotopic gastric mucosa (inlet patch), inflammatory or malignant thyroid disease, dysfunction of salivary secretion, laryngopharyngeal tumors, cervical osteophytes, spondylolisthesis, lingual tonsillar hypertrophy, and dental malocclusion. While, Chen et al¹⁸ found no anatomic abnormality in 23 subjects with globus, a more recent study by Nagano et al¹⁹ showed that up to 36.5% of 52 consecutive subjects with globus and no associated laryngeal or hypopharyngeal findings had esophageal diseases including 10 cases of reflux esophagitis, 5 with esophageal candidiasis, 3 with esophageal cancer, and 1 with herpetic esophagitis. Tsutsui et al²⁰ found that 13 (3.7%) of 350 subjects complaining of globus sensation had endoscopic evidence of organic disease including 10 patients with esophageal cancer, 2 patients with pharyngeal cancer, and 1 patient with Zenker diverticulum. The last 2 papers suggest that the esophagus needs to be evaluated for potential causes of patient symptoms in the absence of laryngeal or hypopharyngeal findings.

Several recent papers have shown that globus has also been linked to the presence of cervical heterotopic gastric mucosa or the inlet patch. Acid secretion might be the possible cause of globus.^{21–24} Inlet patch is found most frequently in the postcardiac area of the esophagus at or just below the upper esophageal sphincter (UES). Although the reported prevalence of an inlet patch generally varies from 0.1% to 10%,²⁵ the incidence has been reported to be up to 70% in autopsy studies.²² Globus, hoarseness, odynophagia, dysphagia, or oropharyngeal burning may occur in 6.2% to 20% of patients with inlet patch.²⁶ In a recent study, Alagozlu et al²⁷ reported that the endoscopic prevalence of an inlet patch in the population studied was 1%. The authors also found that all the subjects showing

TABLE 1. Causes for Globus

Structural
Oropharyngeal
Polyps
Cysts
Pharyngitis, tonsillitis
Retroverted epiglottis
Pharyngeal diverticula or pouches
Vocal fold nodules
Granuloma
Lingual tonsillar hypertrophy
Laryngopharyngeal tumors
Esophageal
GERD/inlet patch/cancer/diverticula/rings/webs
Other
Thyroid inflammatory and malignant disease
Cervical osteophytes
Cervical spondylolisthesis
Dental malocclusion
Malignant lesions of neck and head
Nonstructural
Oropharyngeal
Laryngeal sensory dysfunction
Laryngeal neuropathy
Esophageal
Esophageal sensory dysfunction (visceral hypersensitivity)
Esophageal motor dysfunction (UES and body)
Other
Dysfunction of salivary secretion
Use of anticholinergic drugs
Psychological comorbidity

GERD indicates gastroesophageal reflux disease; UES, upper esophageal sphincter.

Helicobacter pylori infection of the cervical heterotopic gastric mucosa presented with globus, suggesting an association; further studies are needed to confirm this intriguing finding.

While structural causes are not frequent in globus patients, they should be excluded first in patients with persistent symptoms.

Nonstructural Causes

When an underlying structural cause is excluded, the following disorders should be considered: GERD, laryngeal dysfunction/neuropathy, UES dysfunction, esophageal body motility disorder, esophageal and laryngeal hypersensitivity, and psychiatric or psychological disorders. Globus has also been noted to be associated with anticholinergic medication use.²⁸

Gastroesophageal reflux (GER) is thought to be the leading cause of globus, representing 23% to 68% of cases.²⁹ Currently, 2 main mechanisms are believed to lead to globus in patients with GERD. The first is the presence of acidic reflux that reaches the distal esophagus and induces a vagovagal reflex. The second is direct contact of refluxate with the laryngeal mucosa, resulting in local laryngeal inflammation and consequent globus sensation.³⁰ A population-based study demonstrated that typical symptoms of GERD such as heartburn or regurgitation were commonly associated with globus (odds ratio, 3.9; 95% confidence interval, 1.5–9.7).³¹ It was also reported that proximal esophageal acid exposure occurred in half of patients with laryngeal symptoms including globus or abnormal laryngoscopic findings.³² Although GER is often associated

with globus, its treatment with a proton pump inhibitor (PPI) commonly generates disappointing results, especially in the absence of typical reflux symptoms.

Laryngopharyngeal Dysfunction

Laryngeal and pharyngeal dysfunctions such as vocal cord palsy, laryngeal neuropathy, and increased pharyngeal peak pressures are some of the findings described in patients with globus.³³ Arts et al,³⁴ observed a high prevalence of laryngeal neuropathy in up to 85% of 40 subjects with globus, using electromyography examination.

Esophageal Motor Disorders

Multiple studies^{35–44} have demonstrated several esophageal motor disorders. Abnormal UES function has been suggested to be an important cause of globus. Kwiatek et al⁴⁵ quantified the timing and magnitude of respiratory variation in UES pressure with high-resolution esophageal manometry in subjects with globus, normal controls, and GER subjects without globus. The authors found that respiration-related changes in resting UES pressure were significantly amplified in globus subjects and that this hyperdynamic UES was not associated with other abnormalities of esophageal motor function. Elevated UES basal pressure (UES pressure > 118 mm Hg) has also been found to be significantly more frequent in subjects with globus than in controls (28% vs. 3%, $P < 0.05$).⁴⁶ In another study that included 57 globus subjects, investigators were unable to demonstrate an association between UES pressure, contractile front velocity, proximal contractile integral, distal contractile integral, and globus. However, increased length of the transition zone was found to correlate with globus.⁴⁷ Another recent study found that secondary peristalsis was triggered less frequently after rapid air distension in globus subjects as compared with healthy controls (40% vs. 60%, $P = 0.001$). Whether these findings have therapeutic implication in the management of patients with globus remains to be elucidated.⁴⁸ A study that evaluated the esophageal motility function of subjects with globus resistant to PPI treatment showed that 47.9% had abnormal esophageal motility. Of those, 66.4% had ineffective esophageal motility, 14.4% achalasia, 9.6% diffuse esophageal spasm, 8% nutcracker esophagus, and 1.6% hypertensive lower esophageal sphincter, suggesting significant differences in esophageal body peristalsis between subjects with PPI-resistant GERD complaining of globus and healthy controls matched by age and sex.²⁰

A recent study compared esophageal motility among 57 consecutive GERD subjects with ($n = 27$) and without ($n = 30$) globus.⁴⁹ GERD subjects with globus were found to have a higher UES residual pressure, longer LES length, higher LES basal pressure, and greater esophageal dysmotility than typical GERD subjects. The authors concluded that evaluating esophageal motility in GERD patients with globus is highly useful, although treatment outcome in this setting was not evaluated.

Nevalainen et al⁵⁰ studied 30 subjects with globus using transnasal esophagoscopy, high-resolution esophageal manometry and 24-hour multichannel intraluminal impedance plus pH monitoring. Subjects with reflux symptoms served as controls. The authors found that globus subjects without reflux symptoms did not have abnormal acid or nonacid reflux on impedance+pH monitoring, and the UES mean basal and residual pressures were not elevated on manometry. However, the authors demonstrated that supragastric belching was more

common in subjects with globus sensation as compared with subjects with reflux symptoms, suggesting the possible role of supragastric belching in generating globus sensation.

All esophageal motility findings that have been described in subjects with globus are summarized in Table 2.

Laryngeal and UES Sensory Dysfunction

Vertigan and colleagues compared symptoms and sensory function among subjects with different diseases associated with laryngeal dysfunction such as chronic refractory cough ($n = 33$), paradoxical vocal fold movement ($n = 28$), muscle tension dysphonia ($n = 18$), globus ($n = 11$), and controls ($n = 13$). The authors found that the case groups showed a similar pattern of symptoms and significant sensory impairment compared with controls, supporting a laryngeal hypersensitivity syndrome and suggesting a role for central sensitization of an afferent reflex.⁵²

UES hypersensitivity has been proposed as one of the mechanisms for globus based on the lower perception thresholds for pain noticed during UES distention with a balloon.⁵³ Rommel et al⁵¹ demonstrated in 58 globus subjects that UES compliance, change in esophageal body compliance, and somatization explain 40% of the variance in globus symptom severity when globus subjects were compared with healthy controls. The authors concluded that globus is a complex disorder of the brain-gut axis rather than a psychosomatic or peripheral esophageal disorder.

Chen and colleagues evaluated subjects with globus sensation using esophageal balloon distension and electrical stimulation protocols. The authors found that subjects with globus sensation demonstrated esophageal hypersensitivity to mechanical distension.⁵⁴

Functional Globus

Functional esophageal disorder globus is suspected in a significant subset of patients with globus in whom structural or functional abnormality cannot be found. In these patients, esophageal hypersensitivity and abnormal central processing of peripheral stimuli, as seen with other functional esophageal disorders, are likely to be the underlying mechanisms for symptoms.

Historically, globus has been considered a type of psychopathology associated with somatization and referred to as globus hystericus. Psychiatric diagnoses are prevalent in globus patients. Increased reporting of stressful life events preceding symptom onset has been observed in several studies, suggesting that life stress might be a factor in symptom generation or exacerbation.^{55,56} Up to 96% of sufferers reported symptom exacerbation during periods of high emotional intensity. Deary et al⁵⁷ studied 54 globus subjects and controls and reported that globus subjects were characterized by increased levels of obsessive-compulsive personality traits and neuroticism. Several authors found higher anxiety and depression scores^{58–60} in subjects with globus using a range of validated scales. Rommel et al⁵¹ found that somatization ($P = 0.003$), panic disorder ($t = 3.04$; $P = 0.004$), and posttraumatic stress severity ($P = 0.005$), were associated with globus symptom severity.

Selleslagh et al⁶¹ suggested an integrated model for globus in which a peripheral neuronal dysfunction could be the main underlying mechanism resulting in altered sensory and motor responses. The resultant hypersensitivity could cause increased perception of normal physiological events such as GER or bolus passage during swallowing. Psychological

TABLE 2. Esophageal Motor Disorders Findings Among Patients With Globus

References	N	Method	Findings %
Tang et al ⁴⁹	57	HRM	Higher UES residual pressure, longer LES length, higher LES basal pressure and greater esophageal dysmotility
Lei et al ⁴⁸	35	4 channel solid-state catheter	Defective triggering of secondary peristalsis during rapid air distension
Nevalainen et al ⁵⁰	30	HRM	Increased supragastric belching
Rommel et al ⁵¹	58	Barostat	UES compliance and changes in UES compliance
Choi et al ⁴⁷	57	HRM	Increased length of transition zone
Tsutsui et al ²⁰	119	HRM catheter	Normal (52), IEM (30), achalasia (8), DES (5), nutcracker (4), LES hypercontraction (10)
Yanova et al ³⁵	27	HRM	Normal (33), NSEMD (47), nutcracker esophagus (37)
Chen et al ³⁶	25	5 channel solid state	Normal (52), IEM (48)
Kwiatek et al ⁴⁵	131	HRM	Hyperdynamic UES pressures changes
Arts et al ³⁴	40	Not specified	Normal (60), NSEMD (20), nutcracker esophagus (5), hypoperistalsis (15)
Sinn et al ³⁷	64	Not specified	Normal (55), IEM (22), nutcracker esophagus (11), isolated hypertensive LES (6), other (6)
Knight et al ³⁹	12	4 channel solid-state catheter	Normal (25), IEM (58), hypertensive LES (17)
Moser et al ⁴⁰	88	3/5 strain-gauge pressure sensors	Normal (34), NSEMD (34), achalasia (27), DES (1), nutcracker (3)
Corso et al ⁴⁶	650	Stationary esophageal manometry	2%/28% of patients with UES elevated basal pressure
Hill et al ⁴¹	26	Nonperfused catheter	Normal (77), NSEMD (19), DES (4)
Färkkilä et al ³⁸	21	Low-resolution manometry	Normal (33), IEM (29), achalasia (5), DES (14), LES dysfunction (5), hypoperistalsis (5)
Moser et al ⁴²	30	3 strain-gauge pressure sensors	Normal (13), NSEMD (10), achalasia (23), DES (3), nutcracker (13), hypoachalasia (33), LES low pressure (3)
Wilson et al ⁴³	41	4 channel perfused manometry	Normal (98), diffuse esophageal spasm (2)
Flores et al ⁴⁴	12	Assembly of 3 open-tip catheters	Normal (25), disordered esophageal motor dysfunction (75), incomplete LES relaxation (8)

DES indicates diffuse esophageal spasm; HRM, high-resolution manometry; IEM, ineffective esophageal motility; LES, lower esophageal sphincter; NSEMD, nonspecific esophageal motility disorders; UES, upper esophageal sphincter.

factors increase esophageal hypersensitivity by an increased perception threshold for pain via central mechanisms.

DIAGNOSIS

Diagnosis of globus is primarily made clinically by eliciting a typical history. Initial steps require a workup to identify a structural or functional cause such as GERD, an inlet patch, or a major esophageal motor disorder. If there is no evidence for the above causes and alarm features (Table 3) are absent, functional esophageal disorder should be considered.

Physical examination of the neck followed by laryngoscopic examination of the pharynx and larynx are advised for an initial evaluation.

Sanyaolu et al⁶² evaluated the role of transnasal esophagoscopy—a safe and accurate technique that does not require sedation—in the diagnosis of globus. In a retrospective study of 60 consecutive subjects with globus and 68 subjects with nonprogressive dysphagia, they found normal studies in 65%, with the more common positive findings being laryngeal erythema in 13% and esophagitis in 10%.

Transnasal flexible laryngoscopy is the preferred diagnostic test with which otorhinolaryngologists assess

laryngeal symptoms and also establish a diagnosis of GERD.^{63–65} There are different classifications and scores used to diagnose GERD including several endoscopic findings such as subglottic, laryngeal, or vocal fold edema, ventricular obliteration, laryngeal erythema or hyperemia, posterior commissure hypertrophy, granuloma, and thick endolaryngeal mucus.⁶⁶

Herbella et al⁶⁷ studied 79 subjects in whom ENT symptoms including globus (n=14) were assumed to be secondary to GERD transnasal laryngoscopy, esophageal manometry, and dual sensor pH monitoring off PPI treatment. The authors found that laryngoscopy, as a diagnostic test for GERD, had a sensitivity of 86%, specificity of 9%, positive predictive value of 46%, positive likelihood ratio of 0.95, and negative likelihood ratio of 1.49. This study showed higher sensitivity and much lower specificity than previous studies^{68–70} and concluded that ENT symptoms were unreliable and that laryngoscopy had a low positive predictive value for the diagnosis of GERD.

Once localized structural or inflammatory causes are excluded, an empiric trial of double-dose PPI therapy for 8 to 12 weeks should be started. If the patient does not respond to an aggressive antireflux therapy, endoscopy with possible mucosal biopsies is indicated to assess for reflux-related esophagitis, Barrett esophagus, an inlet patch, or other esophageal mucosal abnormalities that could explain a patient's symptoms.

In those with normal endoscopy, esophageal manometry may be helpful to rule out a major esophageal motor disorder; however, there are limited data to support a distinct motor pattern that is specifically associated with globus. Esophageal manometry has revealed motor abnormalities in as many as 67% of patients with globus sensation,

TABLE 3. A List of Alarm Symptoms

Gastrointestinal bleeding
Dysphagia
Odynophagia
Chronic vomiting
Weight loss
Iron-deficiency anemia
Anorexia

with nonspecific esophageal motility disorder being the most frequent finding.³⁷ Subsequently, a reflux monitoring test (either impedance+pH on PPI treatment or wireless pH capsule off PPI treatment) should be considered although the role of pathologic esophageal acid exposure in globus patients has been an area of persistent controversy.^{71,72} Patients who do not respond to PPI treatment and fail to demonstrate no identifiable cause in the oropharynx, larynx, and esophagus are likely to have functional globus.

At any time, the clinician should evaluate the patient for signs of somatization or psychiatric comorbidity as the cause of globus sensation or the result of chronic unresolved globus.

TREATMENT

Treatment success essentially depends on resolving the cause that is responsible for the patient's globus.

Organic Causes

Specific treatment could be delivered to patients with the following underlying causes of globus: Zenker diverticulum, esophageal cancer, pharyngitis, tonsillitis, chronic sinusitis, upper respiratory tract malignancy, hypertrophy of the base of the tongue, retroverted epiglottis, inflammatory or malignant thyroid disease, dysfunction of salivary secretion, laryngopharyngeal tumors, cervical osteophytes, spondylolisthesis, lingual tonsillar hypertrophy, and dental malocclusion.

GERD Therapy

Because GERD has been shown to be a major cause for globus sensation, empirical therapy with PPIs for those without alarm symptoms is a reasonable initial approach. However, like any other extraesophageal manifestation of GE-dose PPI (morning and evening) treatment is given for at least 2 to 3 months. A recent study that investigated the effectiveness of double-dose PPI (rabeprazole sodium 20 mg twice daily for 4 wk) in GERD patients with globus sensation demonstrated a 44.4% symptom response rate.²⁰ Importantly, 55.6% of GERD patients with globus sensation did not respond to PPI therapy, among them being 47.9% with abnormal esophageal motility (mostly with ineffective esophageal motility). The study suggests that the globus symptoms may not be related to acid reflux in half of GERD patients with globus sensation.

Ezzat et al⁷³ randomized 100 subjects with laryngopharyngeal reflux (LPR) to PPI plus itopride or PPI plus placebo for a period of 8 weeks. The authors found that adding a prokinetic to PPIs improved the subjects' outcome, shortened the need for oral medication, and reduced the recurrence of symptoms including globus sensation.

Inlet Patch

Several recent studies showed that an ablation of cervical heterotopic gastric mucosa with argon plasma coagulation resulted in improvement in chronic globus symptoms.^{74,75} More recently, radiofrequency ablation was used to eradicate large (>20 mm diameter) heterotopic gastric mucosa in 10 globus patients demonstrating significant improvement in globus sensation ($P < 0.001$), increase in mental health scores ($P = 0.007$), and decrease in LPR, ($P = 0.005$).⁷⁶ Therefore, ablation of the inlet patch with argon plasma coagulation or radiofrequency ablation is considered to be one of the therapies for patients with globus sensation that is resistant to medical treatment.

Laryngeal Dysfunction

Speech therapy has been used to treat patients with persistent globus sensation in order to relieve vocal discomfort and tension.³³ Khalil and colleagues randomized globus pharyngeus subjects to treatment with speech therapy (study group) and reassurance by a nurse practitioner (control group) for 3 months. The authors found significant improvement in the globus symptom scores in the speech therapy group ($P < 0.001$) compared with preintervention scores and controls.⁷⁷

UES/Gastric Dysfunction

A study that evaluated the effectiveness of injecting botulinum toxin into the cricopharyngeal muscle in subjects with both globus sensation and high UES pressure showed that a decrease in UES pressure led to resolution of the globus sensation.⁷⁸ A recent study showed that a 4-week treatment with rikkunshito, a Japanese herbal compound, significantly improved globus sensation in 22 subjects with PPI-refractory LPR, either alone or with PPI. The authors also found that rikkunshito improved delayed gastric emptying and that there was a significant positive correlation between improvement in globus sensation and in gastric emptying ($P < 0.05$). This study suggests for the first time that improvement in globus could be related to stimulation of gastric emptying.⁷⁹

Functional Globus and Psychological Comorbidity

Because psychological comorbidity has been shown to contribute to globus generation and its presentation, medical and behavioral therapies have been proposed but scarcely studied.⁸⁰ Hypnotically assisted relaxation was evaluated with the aim of decreasing the perception of globus sensation and its effect on interdeglutitive UES pressure. The authors studied 10 subjects with globus sensation who did not respond to PPI and included a 7-session clinical protocol. Nine of the subjects reported a reduction in symptoms. Thus, the authors concluded that hypnotically assisted relaxation could be a useful intervention in globus patients.⁸¹ A small study demonstrated that antidepressants were beneficial for globus subjects with concomitant psychiatric comorbidity such as panic disorder, somatization, major depression, and agoraphobia.⁸² Intuitively, cognitive-behavioral therapy and antidepressants should be helpful in patients with globus sensation and psychological comorbidity or those with functional globus; randomized controlled trials, however, are still lacking. Kirch et al⁸³ investigated the effectiveness of PPIs for at least 2 months or gabapentin for a period of at least 2 weeks in 87 subjects. In this study, 67% of subjects with globus improved after PPI treatment, and 66% improved after gabapentin. Eight of 14 subjects who did not respond to PPI improved on gabapentin. According to the result of the study, the authors concluded that a trial of gabapentin may be considered for patients who do not respond or only respond partially to antireflux treatment.

Overall, given the benign nature of globus, the likelihood of long-term symptom persistence, the multiple pathophysiologic mechanisms involved, and the absence of highly effective pharmacotherapy, the mainstay of treatment rests with explanation to the patient and reassurance. Expectation for prompt symptom resolution should be low because symptoms persist in up to 75% of these patients at 3-year follow-up.

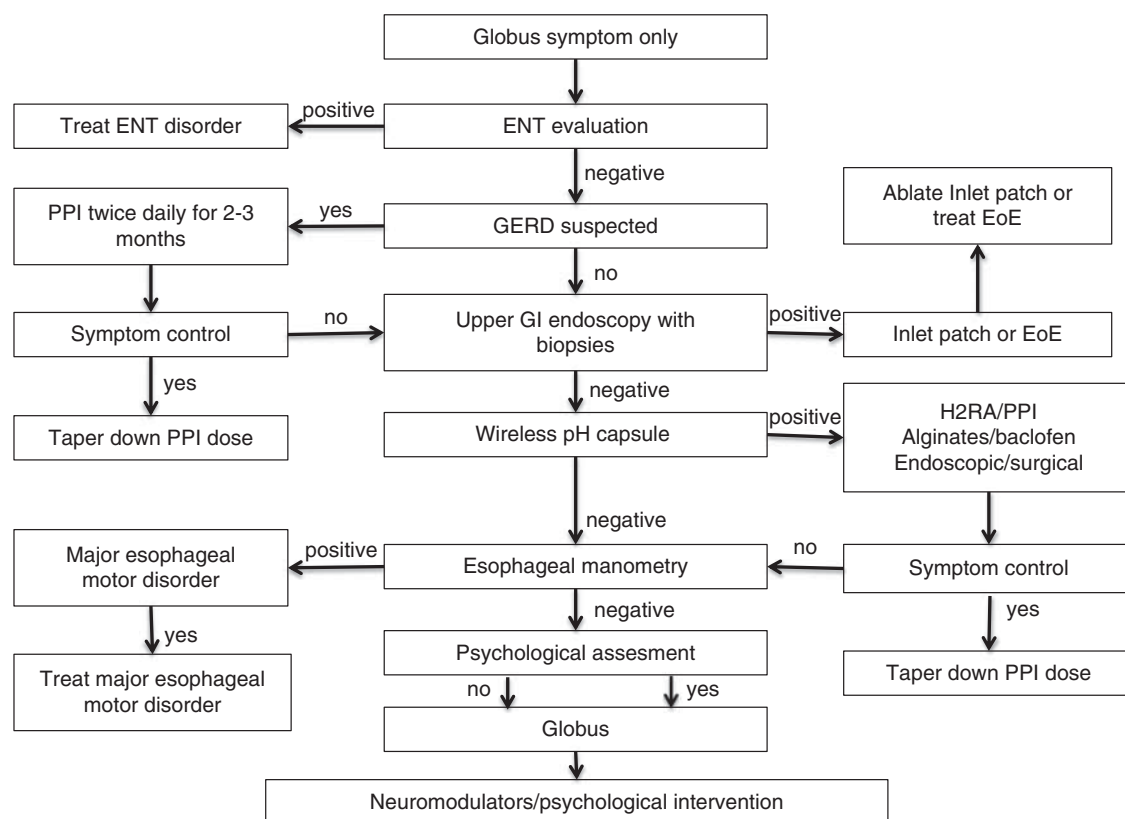


FIGURE 1. Proposed management algorithm for patients with globus. ENT indicates ear, nose, and throat; EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; PPI, proton pump inhibitor.

SUMMARY

Globus is a frequent and troublesome symptom that is treated by different types of physicians including those in primary care, otorhinolaryngology, and gastroenterology. Understanding how to differentiate between organic and functional causes will allow better management and consequently improve the likelihood of resolving the patient's symptoms. GERD is often a factor when structural causes are excluded. If GERD is still present, start the patient on a PPI trial. If globus persists, perform or refer the patient for upper endoscopy. If the endoscopy is negative, perform or refer the patient (off antireflux therapy) for esophageal manometry and wireless pH monitoring. Supportive care and neuromodulators can be helpful for those patients with functional globus, in whom hypersensitivity and psychological disorders are commonly present. A diagnostic and therapeutic algorithm is proposed in Figure 1.

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