An approach to globus pharyngeus

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Background
Globus pharyngeus, or globus, is characterised by the sensation of a lump or tightness in the throat. Symptoms can be persistent, difficult to treat and often reoccur. Globus is a common issue in the community, with lifetime prevalence occurring in up to 45% of the population.

Objective
This article aims to provide a narrative review of potential causes of globus, as well as a suggested guideline for work-up and management in the primary care setting.

Discussion
Causes for globus remain uncertain; however, current opinion focuses on a mixture of muscle tension and mucosal irritation. It is estimated that globus makes up 4% of all primary care referrals to otolaryngologists. There are a handful of proposed causes, with treatments often able to be initiated in the primary care setting. Although most causes are benign, it is important for clinicians to maintain suspicion for malignancy, because this is often the patient's main concern.

GLOBUS PHARYNGEUS, or the term 'globus' is a general term used to described the sensation of a foreign body sensation, a tightening or a choking feeling.[1] Symptoms can manifest as clearing of the throat, cough, hoarseness and thick secretions.[1,2] Symptoms are persistent, difficult to treat and often reoccur, with community prevalence up to 45% in the general population.[2] Aetiology is uncertain and often multifactorial, with current opinions focusing on muscle tension and mucosal irritation.[3] Globus can be difficult to treat in the primary care setting due to multiple potential treatment pathways that might involve several subspeciality disciplines.[4] This is supported by data indicating that 4% of all referrals to otolaryngologists are related to globus.[4] Several investigations and treatments are often able to be initiated in the primary care setting; however, minimal guidelines exist to guide primary care physicians.[2,4]

Aetiology

Psychological

Historically, globus pharyngeus was thought to be psychosomatic with exacerbations linked to emotional intensity. Previously titled 'globus hystericus' due to occurrence in anxious women, this name was revised given that symptoms affect men equally.[1] It is thought that increased muscle tension and heightened mental state creates a focus on existing sensations, resulting in symptoms.[5] Studies have both supported and rejected the causal relationship between globus and mental health.[6,7] Regardless, it has been formally classified in the International Classification of Diseases, 10th Revision (ICD-10) as a somatoform disorder.[5]

Reflux disorders

Globus is hypothesised to be the sensation of aerodigestive mucosal inflammation and irritation directly from gastric secretions.[2,7] This represents a major target for treatment regimens. Studies have reported symptoms in up to 68% of globus patients[2,7] and patients with gastro-oesophageal disease (GORD) diagnosed by barium swallow studies.[8] Globus has become a recognised manifestation of functional oesophageal disorder, with diagnosis of GORD occurring if globus is present in lieu of objective findings.[9] However, similar rates of globus are reported in asymptomatic patients, and numerous patients still experienced globus regardless of previous and concurrent GORD therapy.[10] Thus, GORD might be a plausible cause in a subgroup of patients, but cannot explain all cases.

Laryngopharyngeal reflux (LPR) exists as a distinct entity to GORD and manifests as globus, hoarseness, persistent cough and dysphagia.[11] LPR is defined by retrograde movement of the gastric contents beyond the upper oesophageal sphincter (UES), causing irritation to laryngeal, pharyngeal and lung mucosa.[11] This occurs directly (via gastric

secretions) or indirectly (repetitive trauma from coughing and throat clearing).

Oesophageal motility

Studies suggest a correlation between globus and elevated UES pressures.[12,13] This has been demonstrated through the improvement of symptoms after injection of botulinum toxin into the pharyngeal musculature.[12] More recent studies debate that higher-resolution manometry contradicts this correlation.[14] Further studies suggest higher UES pressures occur as a result of globus sensation and the patient's hyper-responsiveness to stimuli.[10,15] Although there is no clear causation, globus exists as diagnostic criterion in the Rome IV diagnostic criteria for oesophageal disorders, recognising the correlative relationship.[16]

Other causes

Although rarely presenting primarily as globus, malignancy should be considered as a differential, especially if presenting with other red flag symptoms such as persistent or progressive symptoms, haemoptysis, neck masses, dysphagia for solids, voice changes, weight loss or significant comorbidities (Table 1). This is often a patient's major concern and it is important to address this during consultations.[2,12,16]

It is suggested that globus can represent a form of neuralgia, and an element of visceral hypersensitivity.[17] Limited case reports suggest glossopharyngeal or vagal neuropathies resulting in irritation of the oropharynx and larynx and can be mistaken as LPR.[18] Conversely, there is speculation that persistent acid reflux irritation of mucosa nerve endings can also contribute to the potentially neurogenic cause for globus.[19,20]

Laryngeal sensory neuropathy can manifest as persistent laryngopharyngeal symptoms, such as throat clearing, coughing and globus. Neuropathy can occur following an upper respiratory tract infection or insult to the recurrent laryngeal nerve, superior laryngeal nerve or vagus nerve.[21,22]

Neuropathy can be related to persistent acidic irritation of the reflex laryngeal and digestive reflex arch.[20] Chronic laryngeal neuropathy might also be associated with paradoxical vocal fold movements.[20]

Thyroid disease is commonly found incidentally when investigating globus, with up to 33% of thyroid disease patients initially presenting with globus.[16] Ironically, thyroidectomy patients might experience globus postoperatively, but this is usually short lived. Given that many patients with thyroid disease are asymptomatic of globus, further investigation of this correlative relationship is needed.

Other conditions can cause globus due to irritation and inflammation of the pharynx and larynx to reproduce symptoms, such as pharyngitis, tonsillitis and persistent sinusitis with postnasal drip.[12] Anatomical abnormalities, including tongue base hypertrophy, retroverted epiglottis, cervical osteophytes and Eagle's syndrome, cause globus through physical irritation of the pharynx.[12,16] Salivary hypofunction and hyperviscosity of mucosal secretions can also cause gobus.[16]

Key features of globus are its painless nature, intermittent occurrence, association with swallowing of saliva and often central or suprasternal origin. Specific focus should be placed on symptoms of heartburn, regurgitation or dysphagia, which might suggest gastrointestinal aetiology of reflux disease or oesophageal motility disorders. The use of validated reflux questionnaires might prove useful.[11,13] Consider the role of anxiety or psychological distress, which can be further supported by physical manifestations of palpitations, altered sleep and sensations of panic.[2,13]

Risks factors and red flag symptoms of malignancy, outlined in Table 1, help guide decision making for further investigation or referral for otolaryngology or gastroenterology opinion.

Table 1. Risk factors and red flag history points

Odynophagia/pain on swallowing
Dysphagia/difficulty swallowing
Hoarseness of voice/voice changes
Ipsilateral otalgia/nasal obstruction/epistaxis
Neck/oral cavity/oropharyngeal mass/lesion
Unexplained weight loss/loss of appetite
Haemoptysis/haematemesis
Smoking history/active smoker
History of head and neck malignancy (personal/family)

Initial assessment

Diagnosis is mostly based on clinical history and examination. Aspects such as site, onset, character, duration, exacerbating or relieving factors, severity, progression and impact on quality of life are some key points that should be addressed.

Examination should be focused based on history; however, full examination of the head and neck is still important. The oral cavity and oropharynx should be assessed visually and palpated for elements of masses, ulceration or asymmetry, because these features might suggest malignancy. Palpation of the thyroid gland, cervical lymph nodes and cutaneous masses should be included in examination of the neck. Nasal examination looking for inflamed mucosa, polyps or infective stigmata can also be considered as causes of globus. If suspicions for cutaneous malignancy exist, the examiner should inspect for skin lesions on the neck, face and scalp.[2,23]

Investigations

No formal guidelines exist outlining relevant investigations, and management and workup is often based on practitioner experience and preference. Multiple investigations can be implemented in primary care; however, specialist services might be required for both the interpretation of results and organisation of other testing methods not easily available in the community. Suggested methods of investigation are outlined below:

- **Nasal endoscopy:** Awake transnasal fibre optic laryngoscopy allows for visualisation of the anatomy of the nasopharynx, oropharynx, hypopharynx and larynx.[2,7,12,13,23,24]
- **Upper gastrointestinal endoscopy:** This allows for direct visualisation of the oesophagus, stomach and duodenum and can be useful to investigate lesions or other mucosal processes.[2,7,12,13,23,24]
- **Video fluoroscopy/barium swallow:** These are dynamic imaging studies to assess structural abnormalities and detect oropharyngeal motility dysfunction during swallowing or aspiration disorders.[2,7,12,13,23,24]

- **Oesophageal manometry:** Oesophageal manometry allows for the evaluation of oesophageal pressures. A catheter with pressure sensors detects readings at the upper and lower oesophageal sphincter. Inferences about coordination of oesophageal motility can be made based on variances in pressures at these points.[2,7,12,13,23,24]
- **Ultrasound:** Diagnostic ultrasound can be performed in conjunction with tissue sampling if there is a mass. Ultrasound has difficulty visualising deeper structures, and is highly operator dependant.[2,7,12,13,23,24]
- **Computed tomography:** Computed tomography (CT) localises and defines suspicious lesions and aids in overall cancer staging. The addition of contrast allows for enhanced soft tissue differentiation.[2,7,12,13,23,24]
- **Magnetic resonance imaging:** This is not routinely used as a primary investigation for globus; magnetic resonance imaging (MRI) has better soft tissue contrast than CT, and is an overall more detailed anatomical study for further investigation of masses or the surrounding anatomy.[2,12,13] MRI compared to CT studies are more affected by motion artefacts, are less accessible in the community and are less tolerated by patients due to more claustrophobic conditions.[12,13]

Blood tests have little role as a primary investigation, but specific tests can aid to support related conditions such as *Helicobacter pylori* serology for GORD, thyroid function tests in thyroid disease or inflammatory markers should an underlying autoimmune condition be suspected. Examples include *Helicobacter pylori* serology for GORD,[2,7,12,13,23,24] thyroid function tests in thyroid disease[2,7,12,13,23,24] or inflammatory markers should an underlying autoimmune condition be suspected.[25]

Management

Due to the scarcity of dedicated controlled studies, evidence-based guidelines are limited and there is no universally effective single treatment.

Isolated globus is a benign disorder, and reassurance is often required. Vocal hygiene advice, such as avoidance of cigarette smoke, alcohol and caffeine, as well as avoidance of persistently dry swallowing or clearing of the throat, can reduce symptom burden.[2]

Acid-suppression medications and lifestyle modifications might benefit as an empirical trial of therapy, or if underlying GORD is suspected. Proton pump inhibitors have shown greater symptom control than other medications, but controversy exists as to their dose, frequency and duration of therapy to achieve significant results.[7,17] Neuropathic agents or low-dose antidepressant medications are also an option if neuropathic pain is suspected.[18–20]

Speech therapy, including neck and shoulder exercises and general relaxation techniques, has shown symptom reduction in various studies, especially when paired with vocal hygiene.[11] Patients experienced subjective improvement after several months of focused pharyngolaryngeal tension reduction therapy, but this benefit likely also occurred from persistent attention and reassurance for the patients.[8,12]

Cognitive behavioural therapy (CBT) and antidepressants have been found to be beneficial in patients who have concomitant psychiatric disorders, with specific antidepressants able to address the potential neuropathic component of globus. Generally, CBT itself is emerging as a promising initial treatment for somatoform disorders and symptoms unable to be medically explained, including globus.[2,8,12,13]

Pharmacotherapy aimed at treating potential neuropathy includes neuromodulating agents such as baclofen, gabapentin, amitriptyline or oxcarbazepine.[7,20,21] There are limited studies to support this, and usefulness is often limited by sedating side effects.[7,22]

Surgical intervention in patients with thyroid disorders, retroverted epiglottis or other anatomical causes for globus has been shown to be beneficial.[12] There is limited evidence for surgery in isolated primary globus.[12]

Conclusion

Globus pharyngeus itself is a benign common condition that frequently presents in primary care and can greatly affect patients' quality of life. The exact aetiology remains unclear and currently there is no standard protocol for the assessment or management of this presentation, although it is strongly suggested that GORD is a major contributor. Numerous other disorders have been implicated, but studies looking into causative relationships are lacking. This paper seeks to provide clinicians with suggestions on initial management, and when escalation is required to evaluate for more sinister causes.

Key points

- Globus pharyngeus is a benign condition, with significant community prevalence.
- Limited guidelines exist on assessment and management in the primary care setting.
- Reflux and psychiatric conditions are the most common and treated causes.
- It is recommended for clinicians to always have a suspicion for malignancy.
- The advice of specialist physicians/surgeons can be sought if there are concerns or uncertainties.

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