



Endoscopic investigation and evaluation of anxiety for the management of globus sensation

Naoki Oishi^a, Koichiro Saito^{a,*}, Yutaka Isogai^b, Haruna Yabe^a, Koji Inagaki^a, Hideki Naganishi^a, Hiroyuki Kimura^c, Kaoru Ogawa^a

^a Department of Otolaryngology – Head and Neck Surgery, Keio University School of Medicine, Tokyo, Japan

^b Department of Speech and Hearing Sciences, International University of Health and Welfare, Tochigi, Japan

^c Kimura Medical Clinic, Tokyo, Japan

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ABSTRACT

Objective: To verify whether the severity of globus sensation would be affected by the results of investigations on possible underlying serious pathology in the head, neck and esophagus.

Methods: Thirty-six patients with globus sensation were enrolled in this study. All the patients suffered relatively persistent globus sensation which remained after conventional laryngoscopy at their family doctors. These patients were investigated for possible underlying oropharyngeal and esophageal lesions using fiberoptic endoscopy. The severity of globus was evaluated by the visual analog scales (VAS), and the degree of anxiety was evaluated by the state section of State Trait Anxiety Inventory (STAI-s). The questionnaires were administered at their first visits, and 9.6 ± 3.2 months after endoscopy. The follow-up data obtained from 22 patients were incorporated in the further evaluations. Multiple regression analysis was used to evaluate the relationship between the improvement of VAS scores and that of STAI-s scores. Afterwards, Pearson product-moment correlation coefficient was measured. The recorded images of fiberoptic endoscopy were retrospectively verified by an expert of upper gastrointestinal endoscopy.

Results: No malignancies were observed in the endoscopic examination. Despite no treatment administered during the follow-up period, significant improvement of VAS scores was observed from the initial scores (40 ± 21) to follow-up scores (27 ± 27, $p = 0.014$) in the patients examined in this study. The multiple linear regression analysis proved that the improvement of STAI-s scores was the only factor significantly affected the improvement of VAS scores ($p = 0.029$) among the dependent variables. The retrospective evaluation of the recorded images revealed comorbid esophagitis in 10 out of the 22 patients. When patients were stratified with the presence of comorbid esophagitis, significant improvement of VAS scores was observed only in the group without comorbid esophagitis at their follow up (17 ± 20, $p = 0.026$) compared with their initial scores (36 ± 17). The multiple linear regression analysis proved that the improvement of VAS scores was significantly affected by the improvement of STAI-s scores ($p = 0.047$) in this group. Moreover, significant positive relationship between the improvement of VAS scores and that of STAI-s scores was observed only in the group without comorbid esophagitis ($r = 0.61$, $p = 0.047$).

Conclusion: Proper investigation to prove no underlying serious pathology may lead to the improvement of globus sensation in the patients without comorbid esophagitis through the reduction of their anxiety even when their symptoms are relatively persistent. Our results also indicated that some treatments against esophagitis may be helpful for the improvement of globus sensation in the patients with this comorbid disease.

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1. Introduction

A patient with globus pharyngeus (globus) feels an abnormally persistent and distressing sensation (globus sensation) in the throat [1]. Globus is a common condition affecting 6% of the

population [2], and accounts for about 4% of new referrals to an otolaryngology clinic [3]. In spite of such high prevalence, the cause of globus is still unknown [4], and no standard protocol is yet established for managing this distressing condition [5]. Furthermore, more than 40% of globus patients had persistent symptoms for approximately 8 years after diagnosis [6], and no distinct prognostic indicator has been identified yet [6,7]. Thus, proper management of globus is highly demanded in a daily outpatient clinic.

* Corresponding author at: Division of Laryngology, Department of Otolaryngology – Head and Neck Surgery, Keio University School of Medicine, 35 Shinanomachi Shinjuku, Tokyo 160-8582, Japan. Tel.: +81 3 3353 1211; fax: +81 3 3353 1261.

E-mail address: koichiro@ja2.so-net.ne.jp (K. Saito).

Although the exact cause of globus remains to be elucidated, this disease is considered to be multifactorial in origin [5,8]. One possible etiology of globus is gastroesophageal reflux disease (GERD) or laryngopharyngeal reflux (LPR) [8]. A number of studies have suggested an association between globus symptom and GERD or LPR [9]. High incidence of globus symptom was reported among patients with GERD [10], and the globus symptom score was significantly higher in patients with GERD than in those without GERD [11]. However, proton pump inhibitor (PPI) therapy was unable to show the significant symptom reduction in a meta-analysis of randomized controlled trials for GERD-related chronic laryngitis [12], and the role of GERD or LPR in globus sensation still needs to be elucidated. Even for the patients with acid reflux symptoms, the risk of masking malignancy should be kept in mind when applying empirical PPI therapy without performing endoscopy [13].

Psychological factors may also play important roles in the etiology of globus. Recently, it has been shown in 4240 U.S. veterans that globus sensation was associated with a wide range of psychopathology including depression, somatization disorder, and anxiety [14]. Although another study has yielded contradictory results that psychological characteristics might not be relevant for the globus sensation's origin and course [15], multiple studies have implied associations between globus and comorbid psychological distress including anxiety [1,16]. It has also been reported that the presenting globus symptoms themselves could induce the anxiety for patients [9], and suggested that simple reassurance could be the first and foremost therapeutic option against this disease [2].

As there has been no established pharmacological treatment so far, it should be helpful if adequate investigations, even with negative results, could reassure the patients and improve their globus symptoms. In this study, we performed endoscopic evaluation through hypopharynx to esophagus as minimally invasive, simple, and highly reliable procedure on the patients with relatively persistent globus sensation which remained after conventional laryngoscopy at their family doctors. This clinical study was carried out to verify the impact of endoscopic examination for serious pathologies on the patients with globus. We hypothesized that negative endoscopic study could reassure the patients and reduce the severity of their globus sensation as long as the psychological factors play some roles in the etiology of this multifactorial disease.

2. Methods

2.1. Patient sample and physical examination

Thirty-six patients (20 males and 16 females; mean age, 60 ± 14 years; range, 26–85 years) were referred to our institution with globus sensation between December 2008 and November 2009. All of them still complained persistent symptoms even after conventional flexible laryngeal fiberoptic had shown negative results at their family doctors. Further endoscopic re-examinations of oropharyngeal-to-laryngeal regions, as well as external cervical examinations were performed at our institution on the first day of their visits to confirm the negative results. Subsequently, fiberoptic endoscopy using flexible hooded video-endoscope (EH-1530T2, Pentax, Tokyo, Japan) [17] was performed on the globus patients considering of their persistent symptoms. The hooded video-endoscopy enabled us to examine their hypopharynx and esophagus on their second visits [18]. These routine examinations were performed by otolaryngologists to screen potentially lethal lesions. All images were video recorded and the patients were allowed to view the recorded images after examinations. This process has been reported to support the reassuring of the patients with globus [2]. The recorded images were retrospectively reevaluated by an expert of upper gastrointestinal

endoscopy (H.K.) for precise diagnosis and verification of comorbid lesions in this study.

No further investigation was planned when endoscopy did not prove any finding suggestive of malignancy in the patient. Patients with a history of malignant tumors in the head and neck region or the upper gastrointestinal tract, as well as the patients currently receiving treatment for GERD were excluded from this study.

2.2. Questionnaires

To evaluate the severity of globus sensation, the visual analog scales (VAS) were administered at their first visits to our clinic [19]. VAS is a self-report scale which consists of a 100-mm straight line with a phrase listed at each end of the line. The phrases used in this study were 'I feel no discomfort' and 'I feel overwhelming discomfort'. The severity of globus sensation measured by the VAS was associated with the results of multiple psychological tests in our country [19,20].

To measure the levels of anxiety in the patients, we conducted the state section of the validated Japanese version of State Trait Anxiety Inventory (STAI-s) [21,22]. Initial STAI-s scores were compared with the scores measured at their follow-up. The questionnaire is the definitive instrument for measuring anxiety which is composed of 20 items. The higher the score is, the more anxious the patient is, and the highest possible score is 80. The average score (\pm SD) of normal controls is $39 (\pm 10)$ in our country [21].

2.3. Follow-up evaluation

To evaluate prognosis of their symptoms, follow-up evaluation was performed in 9.6 ± 3.2 months after endoscopic examination of hypopharynx and esophagus. Questionnaires were mailed to the patients and 22 patients (12 males and 10 females; mean age, 62 ± 12 years; range, 34–85 years) out of the 36 patients replied to the follow-up inquiries. These data were further evaluated in this study. Of the 22 patients, the initial STAI-s score of one patient was not available. Thus our data enabled the assessment of changes in VAS and STAI-s scores out of 22 patients and 21 patients, respectively.

2.4. Statistical analysis

The data are expressed as the mean \pm SD. Paired *t* tests were used to compare the scores of questionnaires obtained at their first visits and at their follow-up in each patient. Subsequently, multiple linear regression analysis by forward selection was performed to evaluate the factors responsible for the improvement of VAS scores. The relationships were assessed between the improvement of VAS scores and the following factors: age, gender, duration of globus sensation, and the improvement of STAI-s scores. Additional Pearson product-moment correlation coefficient was measured to evaluate the relationship between improvement of VAS score and that of STAI-s score. The significance level was set at $p < 0.05$. All analyses were performed using JMP version 8.0.1 (SAS Institute Inc., Cary, NC).

This study was approved by the institutional review board of Keio University, School of Medicine.

3. Results

Fiberoptic endoscopy did not show any findings suggestive of malignancies through oropharynx, larynx, and esophagus. None of the 22 patients complained of typical symptoms of GERD/LPR such as heartburn or regurgitation, and therefore, no medication was prescribed for the patients in this study. Despite no treatment during the follow-up period, significant improvement of VAS scores was observed in the 22 patients from their initial scores (40 ± 21) to their

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