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OBSERVATION

Gastroesophageal reflux disease and the airway-essentials for the surgeon

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Abstract

Gastroesophageal reflux disease (GERD) has many protean manifestations. Some of the most vexing have to do with the airway. GERD affects the tracheobronchial tree directly, leading to aspiration pneumonia and asthma, or exacerbating existing pulmonary disease, such as asthma or chronic obstructive pulmonary disease. In addition to the respiratory manifestation of GERD, there are unique pharyngeal and laryngeal manifestations. These include voice hoarseness, throat-clearing, chronic cough, globus, and "post-nasal drip". Linking these symptoms to GERD is challenging and frequently the diagnosis is that of exclusion. Despite proton pump inhibitor therapy being the mainstay of treatment, with anti-reflux surgery being reserved for intractable cases, there is no definitive evidence of the superiority of either.

Key words: Gastroesophageal reflux disease; Laryngopharyngeal reflux; Reflux-induced asthma; Aspiration pneumonia; Chronic obstructive pulmonary disease; Chronic cough; Reflux laryngitis

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INTRODUCTION

Gastroesophageal reflux (GER) is the normal physiologic reflux of gastric contents into the esophagus. Various physiologic mechanisms protect the esophagus from injury, including minimizing reflux itself through the lower esophageal sphincter, reflex peristaltic clearing of the esophagus to minimize the time exposure of the esophagus to the acidic contents, a mucus layer on the esophageal epithelium to act as a barrier to the acidic contents, and alkalinization of the acidic contents with saliva. When one or more of these defense mechanisms breaks down, pathologic reflux occurs, leading to symptoms severe enough to affect quality of life and/or cause pathologic changes in the esophagus such as inflammation, ulceration, stricture, Barrett's esophagus and possible adenocarcinoma. Heartburn and regurgitation are the most common symptoms of gastroesophageal reflux disease (GERD), and are therefore, referred to as the "typical" symptoms of GERD. However, GER can affect the upper aerodigestive tract including the hypopharynx, pharynx, larynx, and tracheobronchial tree. These lead to symptoms involving these structures which are different than the typical symptoms of GERD. These symptoms are referred to as the "atypical" or "extra-esophageal" symptoms of GERD, or when specifically associated with the pharynx or larynx, "laryngopharyngeal reflux disease" (LPRD).

RESPIRATORY MANIFESTATIONS OF GERD

Prevalence and magnitude

Because the respiratory manifestations of GERD are so varied, and because different authors have different definitions of what, in fact, constitute respiratory manifestations, the exact prevalence is hard to determine. The best studied prevalence, however, relates to GERD-induced asthma[1], the effects of GERD on chronic obstructive pulmonary disease (COPD)[2], and aspiration pneumonia[3].

Havemann *et al*[1] have performed a systematic review of the prevalence studies of GERD and asthma. The studies have focused on the association of patients with GERD symptoms also having asthma symptoms, abnormal pH monitoring studies, endoscopically-determined esophagitis, and hiatal hernia. Their meta-analysis found an overall odds ratio (OR) of 2.26 with a 95% confidence interval (CI) of 1.81 to 2.83 for the presence of asthma in GERD patients. Alternatively, when evaluating the presence of GERD symptoms in asthmatic patients, they determined an OR of 5.5 with a 95% CI of 1.9 to 15.8.

Although not a cause of COPD, GERD can affect lung function in these patients. Terada *et al*[2] demonstrated that COPD patients were more than twice as likely to suffer from GERD than normal controls (OR 2.13, 95% CI 0.88-5.25), and those COPD patients who suffer from GERD were more than twice as likely to suffer exacerbations of their COPD in any 6 month period (OR 1.93, 95% CI 1.32-2.84). Lastly, in a study of death related to GERD, Rantanen *et al*[3] found that 41 of the 213 deaths related to GERD in Finland from 1987 to 2000 were due to aspiration pneumonia. Therefore, respiratory complications of GERD may be potentially fatal.

Symptoms

The respiratory symptoms and conditions associated GERD include asthma, chronic cough, chronic bronchitis, pulmonary aspiration complications (lung abscess, bronchiectasis, aspiration pneumonitis), idiopathic pulmonary fibrosis, COPD, and obstructive sleep apnea[4]. However, it should be emphasized that a causal, or even an associative, relationship has not been fully determined and controversy exists for many of these conditions[4].

Pathophysiology

The pathophysiology of respiratory symptoms of GERD has not been fully elucidated. Two basic mechanisms have been proposed[1,4]. These include microaspiration of either/both acidic and nonacidic gastric contents into the airway and nervous system-mediated responses. Specifically, with respect to asthma, vagally-mediated bronchospasm has been proposed as an explanation linking asthma and GERD in the absence of aspiration[4]. For cough, in addition to aspiration, normal or abnormal stimulation of afferent nerves, the stimulation of abnormally sensitive afferent nerves, and the abnormal integration of stimulation within the central nervous system have been proposed[4].

Diagnosis

The diagnosis of GERD-related respiratory manifestations can be difficult and is primarily a diagnosis of exclusion. There are many potential causes of these conditions and establishing the causal relationship to GERD can be vexing. Anecdotally, it seems reasonable to place more credence in the diagnosis if the respiratory symptoms appeared or worsened after the onset of GERD symptoms. However, frequently patients will have respiratory symptoms without the typical symptoms of reflux. Therefore, the use of gastrointestinal, laryngeal, and tracheobronchial endoscopy, esophageal manometry, duel channel 24 h pH monitoring, and impedance manometry have been used to supplement the diagnosis[5].

Medical management

Medical management for GERD-related respiratory symptoms has proven to be disappointing. Many studies have been done using a variety of medical acid suppression therapies with proton-pump inhibitors, H_2-blockers, and promotility agents with mixed results. A systematic review of the data has demonstrated no convincing evidence that medical management improves symptoms[4].

Surgical management

Surgical management has been with antireflux operations, specifically laparoscopic Nissen fundoplication. Most of these reports have been uncontrolled studies in highly selected patients. The only prospective comparative study showed that 74% of patients improved with surgery, while only 9% of medically-treated and 4% of controls improved[6].

LARYNGOPHARYNGEAL REFLUX

Prevalence and magnitude

Because the symptoms related to LPRD are common and non-specific, it is difficult to determine the prevalence and magnitude of this condition. In a study of patients presenting with hoarseness, by Cohen *et al*[7] found that over 50% had "secondary" laryngopharyngeal symptoms and over 50% had diagnoses other than LPRD or GERD.

Symptoms

Symptoms of LPRD include dysphonia (voice hoarseness), globus, chronic throat-clearing, chronic cough, sore throat, paroxysmal laryngospasm, idiopathic subglottic stenosis, and postnasal drip[8,9].

Pathophysiology

LPRD is caused by reflux of gastric contents into the hypopharynx and larynx. Reflux of acidic contents into the upper aerodigestive tract is a rare event, with a total time that the pH < 4 is < 0.01%, compared to 4% in the distal esophagus[8]. In addition, it has become increasingly clear that pepsin, in addition to acid, has a role in LPRD[10]. Therefore, patients may manifests symptoms of reflux without exposure to acid. However, the basic defect in the lower esophageal sphincter appears similar

in patients with GERD, LPRD, and mixed GERD/LPRD symptoms[11].

Diagnosis

As with GERD-related respiratory symptoms, LPRD can be a difficult diagnosis to secure. The signs and symptoms are non-specific and can be attributed to several disease conditions. Usually, a combination of laryngoscopy, esophageal manometry, duel-channel 24 h esophageal pH monitoring and, recently, impedance manometry has been used. Some advocate a trial of proton pump inhibitor therapy as a means of diagnosis[8].

Medical management

Several trials have been conducted evaluating the effectiveness of PPI therapy in relieving the symptoms of LPRD. The results have been mixed. A meta-analysis of the existing trials shows a modest, but not statistically significant, result favoring PPI treatment (OR 2.0, 95% CI 0.84-3.16).

Surgical management

Studies evaluating the effectiveness of surgical fundoplication on LPRD are surprisingly lacking. The only controlled trial available assessed the symptom relief of laparoscopic Nissen fundoplication in patients who were not responsive to PPI therapy. In this group of patients, fundoplication also did not improve symptoms[12]. However, it is unclear how these data relate to patients with LPRD as a whole.

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