

Beyond Heartburn: Extraesophageal Manifestations of Gastroesophageal Reflux Disease

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Presentation Summary

A variety of extraesophageal manifestations of chronic acid reflux can be encountered in practice, and it is important to diagnose and manage them appropriately. Some of these patients are asymptomatic; others have symptoms most commonly associated with pulmonary or otolaryngologic disease. An aggressive trial of antireflux medication can often improve or resolve these symptoms, indicating that gastroesophageal reflux disease is the primary contributing component. In such medication trials, several diagnostic methods may be used to determine the source of the symptoms.

difficulty for clinicians is to determine which symptoms are truly GERD related and which may require additional diagnostics and management by an ENT specialist. GERD-related symptoms are often adequately managed with antireflux medication. This approach may also reduce the severity of many pulmonary and ENT symptoms.

Summary

Atypical presentations of gastroesophageal reflux disease (GERD) pose a challenge for clinicians and investigators and are primarily categorized as having pulmonary or otolaryngologic characteristics (Table). Diagnosis of GERD in patients with these symptoms can be difficult because they are completely asymptomatic. Symptoms of heartburn and regurgitation. In the latter case, proton pump inhibitors (PPIs) are not as effective.

In addition, many other patients may have acid reflux, but it is unclear whether it is related to their symptoms or whether there is a concomitant, contributing pulmonary or ear, nose, and throat (ENT) process. The

prevalence. Asthma is the pulmonary disorder most often associated with GERD, and acid reflux disease is found in 30% to 89% of asthmatics.¹⁻³ In a study of 105 asthmatic patients presenting at an allergy clinic, 24-hour pH monitoring diagnosed 32% with GERD.³ Half of these patients reported no classic acid reflux symptoms, and endoscopy revealed erosive esophagitis in less than one fourth of the GERD patients, illustrating the diagnostic difficulty physicians face. In another study, erosive esophagitis was found in only one third of older asthmatics, whereas 82% were positively diagnosed with GERD.² A third study found that 77% of 109 asthma patients presenting at research units and outpatient pulmonary clinics complained of heartburn; 55% reported regurgitation; 24% had swallowing difficulties; and 37% were taking at least 1 antireflux medication. Although there was no overall

increase in GERD symptoms associated with asthma medications, beta-agonist inhaler use for asthma correlated with increased severity of heartburn and regurgitation.¹

The presence of GERD appears to be particularly related to asthma that is difficult to control with traditional asthma therapy. A study of 32 such patients showed that the addition of reflux medication in 20 patients rendered their asthma controllable.⁴ In some cases, GERD medication, when combined with other treatment enhancements such as inhaled steroid medication, increased compliance, environmental control, and improved medication delivery techniques, significantly improved asthma control with conventional asthma medication.

The mechanism of GERD in asthma is unclear, but the most convincing explanation from both human studies and animal models is that microaspiration of small amounts of acid in the larynx causes bronchospasm. Another mechanism may be a vagal mediated neural reflex, whereby acid refluxing into the esophagus stimulates pulmonary receptors designed to protect the airway from acid aspiration.⁵⁻⁷ Conversely, asthma may have mechanical effects that reduce lower esophageal sphincter pressures and can worsen GERD, which had been previously unobservable. Furthermore, some asthma medications may relax smooth muscle to cause a worsening of GERD symptoms.⁷

Diagnosis. There are limitations to using 24-hour pH testing alone to diagnose GERD in asthma patients with symptoms suggestive of reflux because although it determines the presence of acid reflux, it does not help elucidate the relationship between GERD and the asthma. Other tests are rarely useful. A therapeutic trial using GERD medication for at least 3 months may be the most

realistic approach in patients with asthma and other GERD-related pulmonary problems regardless of 24-hour pH testing results. A review of 12 studies involving 326 asthma patients showed that antireflux therapy can improve asthma symptoms and may reduce asthma medication use but should not be expected to improve lung function.⁸ However, patients with negative 24-hour pH testing results may require barium esophagrams, endoscopy, or gastroesophageal scintigraphy in addition to an anti-reflux medication trial to rule out other causes.

Good results with a PPI trial were seen in a study of 30 consecutive asthma patients with symptomatic reflux confirmed by 24-hour pH monitoring. They received an initial daily dose of 20 mg omeprazole, which was titrated to 40 or 60 mg daily as needed until acid suppression was achieved. They remained on the suppressive dose for 3 months. Acid suppression was documented with 24-hour pH testing. Response was defined by an asthma symptom reduction greater than 20% and/or a peak expiratory flow rate increase of greater than 20%. Twenty-two patients responded and 75% of these required only the 20-mg omeprazole dose. The mean dose needed to con-

Table. Atypical Presentations of GERD

Pulmonary	ENT
■ Asthma	■ Hoarseness
■ Bronchitis	■ Cough
■ Aspiration pneumonia	■ Globus
■ Apnea	■ Halitosis
■ Atelectasis	■ Vocal cord granulomas/ulcers
■ Pulmonary fibrosis	■ Laryngeal stenosis
	■ Laryngeal cancer
	■ Loss of dental enamel

GERD = gastroesophageal reflux disease; ENT = ear, nose, throat.

trol asthma was 27 mg daily, and after 3 months, asthma symptom scores dropped from 37 to 15 among the responders. Among non-responders, asthma symptom scores increased from 17 to 25 during the trial period.⁹ For most patients, a therapeutic trial dose of 20 mg twice daily is recommended for best outcomes and, although a response may be seen during the first month, an adequate trial of at least 3 months is needed to verify a response.

If an aggressive treatment trial fails to resolve symptoms, surgery may be considered. There have been no direct comparison trials between surgery and PPI therapy. An analysis of 24 studies including a total of 417 asthma patients with GERD who underwent open or laparoscopic surgery between 1966 and 1998 showed that 90% experienced lessened GERD symptoms; 88% used fewer asthma medications; 79% had improved asthma; and 27% showed improvement on pulmonary function tests.¹⁰

ENT Complaints

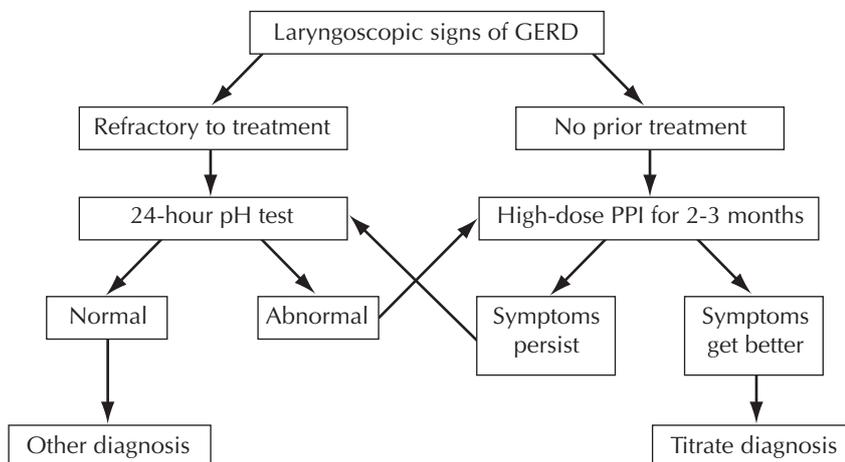
Diagnosis. ENT patients also have a wide range of GERD symptoms. Of 182 patients referred to an ENT practice, 18% reported mild heartburn, regurgitation, or dysphagia; 18% had moderate GERD symptoms; and 13% suffered severe levels of these classic symptoms.¹¹ After asthma and post-nasal drip, chronic cough is most often associated with GERD, and up to half of patients with refractory hoarseness are estimated to have acid reflux. Posterior laryngitis, tonsillitis, subglottic stenosis, otitis media, contact ulcers, laryngeal cancers without smoking and alcohol use history, granulomas, and polyps may also be related to GERD.¹² Dental erosions have also been linked to GERD.¹³

When the percentage of various laryngeal signs found in 105 healthy volunteers were compared with those found in a small group of confirmed GERD patients, arytenoid medial wall erythema, vocal fold abnormalities, and posterior cricoarytenoid wall abnormalities were significantly more frequent in GERD patients. Treatment with a PPI improved or resolved these abnormalities in the majority of patients, further indicating an association with GERD.¹⁴

Endoscopy can often identify some abnormalities that are linked with GERD, and 24-hour pH monitoring may be somewhat useful. However, GERD-related ENT symptoms can be intermittent, and pH monitoring may not detect reflux and should not be used to exclude GERD in these patients.

Treatment. When laryngoscopic findings suggest an association with GERD, a PPI trial is indicated before extensive diagnostic testing. If there is little response or if the patient presents with symptoms despite already taking a PPI, initial eval-

Figure. Approach to GERD-Related ENT Abnormalities



GERD = gastroesophageal reflux disease; ENT = ears, nose, throat; PPI = proton pump inhibitor.

uation with pH monitoring may be helpful. Monitoring in these patients should be conducted while maintaining the antireflux medication to more accurately determine if reflux is present (**Figure**).

Patients with ENT symptoms secondary to GERD do well on PPI therapy. In a trial comparing ENT symptoms before and after therapy with omeprazole, the incidence of heartburn was reduced from 38% to 10%, bad taste complaints from 45% to 29%, throat clearing from 85% to 43%, globus from 80% to 35%, cough from 55% to 25%, dysphagia from 35% to 8%, odynophagia from 5% to zero, and hoarseness from 60% to 35%. In addition, the severity of laryngoscopic findings including edema, nodularity, erythema, ulceration, and granuloma was significantly reduced after treatment.¹⁵ A PPI trial of 2 to 3 months' duration is necessary because ENT symptoms may take time to resolve after acid suppression.

Conclusion

The primary manifestations of chronic acid reflux in some patients may be those of pulmonary or otolaryngologic disorders, most notably asthma, chronic cough, and hoarseness. A trial of antireflux medication can often resolve these atypical symptoms and should be undertaken prior to extensive pulmonary or ENT diagnostic tests. A medication trial of 3 months' duration is recommended.

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