Gastroesophageal reflux as a cause of chronic cough, severe asthma, and migratory pulmonary infiltrates

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Abstract
Gastroesophageal reflux (GER), asthma-type cough and upper airway disease are the most common causes of chronic cough syndrome. We present a case in which impedance–pH monitoring indicated severe mixed acid–nonacid esophageal reflux reaching the upper third of the esophagus in 75% of nonacid events. GER and the associated aspiration episodes were shown to be the cause of severe asthma attacks and migratory pulmonary infiltrates. GER was caused by a sleeve gastrectomy, which seriously disabled the mechanisms preventing reflux from reaching the airways. Respiratory symptoms improved notably after abdominal surgery to correct the GER, suggesting a close causal relationship between GER and all the symptoms, including asthma. However, this issue remains unresolved in the literature.

Introduction
In the management of patients with recent respiratory symptoms and predominant chronic cough, it is important to consider gastroesophageal reflux (GER) and its complications: laryngopharyngeal reflux when it reaches the upper airway, or asthma and pneumonia aspiration when it reaches the lower airway [1]. A sleeve gastrectomy producing serious incompetence of the anti-reflux barrier may cause the reflux to move to the airway. Respiratory disease deriving from GER comprises three syndromes: chronic cough syndrome, asthma, and reflux laryngitis. It develops directly through aspiration, and indirectly through esophageal–bronchial vagal reflexes [2].

Case Report
A 44-year-old woman was admitted for chronic cough syndrome and refractory asthma criteria. The patient had a history of hypertension and morbid obesity with body mass index of 42 despite gastric reduction surgery 11 months earlier by means of sleeve gastrectomy. Since surgery, she had reported chronic cough with 10 recurrent exacerbations of dyspnea and wheezing requiring visits to the emergency services. In one of the visits, pneumonic infiltrates were observed in lung bases; after 12 days, they reappeared at another site and were therefore defined as migratory (see Figs. 1, 2). Blood tests revealed a total IgE of 5.54 kU/L (n = 150 kU/L), and blood eosinophils of 225 (n < 400/\text{mm}^3). Given the repeated asphyxial episodes, and despite inhaled corticosteroids and high-dose long-acting beta-adrenoceptor agonists, she was readmitted for further study. During her stay, she presented several asthma attacks with declines in peak flow exceeding 20%, and two sudden decreases of 40% and 60%, respectively. During the periods between attacks, the spirometric pattern remained within normal limits. Brittle asthma was diagnosed [3].

Using laryngeal fibroscopy, the reflux finding score was 8 points (n < 7). Given these results and the lack of improvement with the addition of proton pump inhibitors (40 mg/bid), impedance–pH monitoring was performed. This test detected the existence of a severe mixed acid–nonacid esophageal reflux, with 75% of the events reaching the upper third of the esophagus and a significant increase in nonacid or weakly acid GER episodes. For all refluxes, there was a symptomatic association probability of 100%.
Given the evidence of uncontrolled GER with a clear temporal association between the onset of extraesophageal symptoms and the gastric reduction surgery performed 11 months earlier, the digestive tract was reoperated by open gastric bypass with incisional surgical repair and conversion from sleeve to bypass. A few days after surgery, and at 2 and 6 months after surgery, the patient presented no respiratory symptoms.

**Discussion**

This patient suffered a severe GER, which also produced chronic cough, refractory asthma (with characteristics of brittle asthma), and repeated aspiration pneumonias. All the symptoms appeared after sleeve gastrectomy, and disappeared with the surgical correction of the reflux. The persistence of chronic cough over time should alert physicians to the possible involvement of GER. Morice maintain that chronic cough is part of a broader syndrome, termed cough hypersensitivity syndrome (CHSS), characterized by troublesome coughing often triggered by low levels of thermal, mechanical, or chemical exposure. According to the author, its pathophysiological basis is acid or nonacid liquid and gaseous reflux, and it comprises several phenotypes such as airway eosinophilic inflammation, GER, and upper-airway involvement [4].

Until recently, pH-metry was accepted as the gold standard for establishing GER as the cause of respiratory symptoms. But it has now been rendered obsolete by studies such as R. Tutuian et al. that confirmed the role of nonacid reflux in patients with chronic cough receiving antacids [5]. In this patient, the high frequency of acid and nonacid refluxes

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**Table 1.** Results of pH–impedance monitoring in our patient opposed to those expected in a normal individual.

|                                    | Normal values | Patient | Proportion of refluxes that reach proximal esophagus (%) |
|------------------------------------|---------------|---------|----------------------------------------------------------|
| Number of acid refluxes (pH < 4)   | <55           | 100     | 36                                                       |
| Number of weakly acid refluxes (pH 4–7) | <26           | 37      | 75                                                       |
| Number of nonacid refluxes (pH > 7) | <1            | 4       | 75                                                       |
| Number of all refluxes             | <73           | 141     | 74                                                       |
| Bolus exposure in distal esophagus measured by impedance monitoring (percent of total time recorded) | <2.1 | 8.20 | – |
| Acid exposure in distal esophagus measured by pH monitoring (percent of total time recorded) | <4.5 | 23 | – |
| DeMeester score*                   | <14.72        | 76.2    | –                                                       |

*DeMeester score is a global measure of esophageal acid exposure.*
reaching the upper esophagus (35% and 75%, respectively) suggested a direct relationship between the symptoms and GER [6]. Remedial gastric surgery was indicated to control severe GER since fundoplication eliminates reflux of any kind. As has been previously mentioned in patients with extraesophageal symptoms, a positive symptom index responds well to anti-reflux surgery [7].

In this patient, the cause of the GER was gastric surgery for obesity. This association draws attention to the disruption that this surgical procedure may cause in the mechanism preventing the massive and recurrent increase in gastric reflux and its potentially severe consequences in the airways.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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