



Challenging Clinical Cases

A curious case of cough

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A 41-year-old woman presented to a private practice allergy/immunology office with 1 year of persistent cough. The cough was often productive of yellow sputum in the morning and clear sputum throughout the day. At other times, the cough was dry and associated with wheezing, but she denied any shortness of breath. The cough woke her up from sleep most nights and was worse with exertion. In addition, the patient had symptoms for the past 5 years of perennial clear rhinorrhea, postnasal drip, nasal pruritus, and sneezing with occasional ocular pruritus and erythema without any significant nasal congestion or obstruction. She did not have cough before the onset 1 year ago. There was no seasonal variation of her symptoms. She had tried over-the-counter antihistamines, which partially controlled her symptoms. She had also tried a combination inhaled corticosteroid and long-acting β -agonist (ICS-LABA), with no improvement of her cough. She had not tried nasal sprays or nasal irrigation. She had recently seen an otolaryngologist and had unremarkable rhinolaryngoscopy findings. She had not required any antibiotics during the last year. She had 2 dogs and 1 cat, which all slept in her bed. She smoked cigarettes socially. She had no recent changes in the home or work environment.

In a patient with persistent dry cough associated with wheeze, nocturnal awakenings, and exertion, asthma or bronchospasm is initially considered. Typically, asthma symptoms improve with appropriate therapy, such as inhaled corticosteroids or β -agonists. However, other factors may be at play, such as adherence, administration technique, environmental exposures, and comorbid conditions. In such a patient, asthma is the first condition considered, with pulmonary function tests (PFTs) performed and then a trial of a short-acting β -agonist alone or with an ICS, depending on results of the workup and clinical picture. This patient's rhinoconjunctivitis symptoms were likely contributing to the cough and represent an allergic or nonallergic origin. However, with nasal pruritus and sneezing and a partial response to oral antihistamines, allergy to a perennial

exposure is perhaps most likely. The patient had not yet tried a nasal spray. As such, after evaluating for potential environmental allergens and providing education on environmental controls, a nasal corticosteroid was prescribed. In addition, the patient was questioned about a history of heartburn and reflux symptoms and asked whether she was using an angiotensin-converting enzyme inhibitor (ACE-I).

The patient's medical history included gastroesophageal reflux disease (GERD) and obesity for the past 10 years. She had undergone gastric banding surgery 3 years before presentation. Reflux symptoms were well controlled with famotidine. She had no history of hypertension and was not using an ACE-I. She had one nephew with asthma but otherwise no family history of atopy. Physical examination findings were notable for obesity (body mass index of 34.7), clear rhinorrhea with postnasal drainage, clear lungs, and a nonproductive cough. The PFT results were normal without a significant bronchodilator response. Forced expiratory volume in 1 second (FEV₁) was 2.60 L (89% predicted), forced vital capacity (FVC) was 3.07 L (89% predicted), FEV₁/FVC was 0.85, and forced expiratory flow between 25% and 75% (FEF_{25%-75%}) was 3.21 L/s (95% predicted). Percutaneous skin test results were positive only for cat and dog. Chest radiography results were normal. The patient was diagnosed as having allergic rhinitis, cough, obesity, and GERD. Environmental controls were discussed, particularly removing pets from her home, which she was not willing to do. She was prescribed a nasal corticosteroid and trial of albuterol to use as needed despite the normal PFT results because of the history of wheezing. She continued to take cetirizine and famotidine. She was encouraged to stop smoking.

Sensitization to dog and cat and history of both pets sleeping in her bed at night are consistent with perennial allergic rhinitis as a cause of nocturnal cough and rhinorrhea, but she also had wheezing. Initiating use of a nasal corticosteroid is appropriate treatment for this diagnosis, along with environmental controls, such as removing pets from the home. Although normal PFT results without a bronchodilator response are reassuring against significant airway obstruction, they do not exclude asthma as an underlying diagnosis. A trial of albuterol and monitoring a patient's response can be diagnostic, as well as therapeutic, for bronchospasm. In the differential diagnosis of asthma, particularly with

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nocturnal symptoms, it is important to assess for reflux symptoms, which may actually be the main or a contributing diagnosis. This patient's allergic rhinitis and potential bronchospasm were treated with close follow-up to monitor her response to therapy and recommended smoking cessation.

At the patient's 1-month follow-up visit, rhinitis was improved during the day but continued at night. The cough was waking her up from sleep 5 nights per week, was often wet, and was not responsive to albuterol. She had removed the cat from the bedroom, but the dogs continued to sleep in her bed. She continued to smoke occasionally. Nasal irrigation, a nasal antihistamine, and montelukast were added to her medication regimen. The patient elected to start allergen immunotherapy for cat and dog.

Because of multiple missed and rescheduled follow-up visits, the patient presented 10 months later. She had 6 weeks of cough productive of thick yellow mucus, chest tightness, dyspnea with exertion, and nightly awakenings due to cough. Her cough had varied in severity since her previous follow-up. She was using albuterol frequently, up to twice daily in the evening, with partial relief of symptoms. She continued to have clear anterior rhinorrhea despite good adherence with her medications. She had stopped smoking in the previous weeks. She continued to have animals in her home but reported overall improvement in rhinitis symptoms since starting immunotherapy. In the interim, she had been transitioned from famotidine to omeprazole, 20 mg/d, which she reported was controlling reflux symptoms well. Her PFT results revealed a 17% decrease in FVC and a 21% decrease in FEV₁ compared with her initial visit, along with a partial bronchodilator response (10% increase in FEV₁). She was prescribed azithromycin, a prednisone burst, and an ICS for maintenance. Use of all other medications was continued. Symptoms initially resolved but returned within 3 weeks. Subsequent PFT results were improved, but FEV₁ was still 15% decreased from the time of initial presentation. Use of the ICS was discontinued, and she was stepped up to an ICS-LABA for maintenance. Her cough improved with the ICS-LABA, but she did not keep her scheduled follow-up visit.

The patient's decrease in FEV₁ with partial bronchodilator response and improvement with oral and inhaled corticosteroids and an ICS-LABA supports asthma as a contributing factor for the cough, although this recent episode may have been complicated by bronchitis or sinusitis. The persistence of rhinorrhea despite good adherence with medications is unsettling but can be attributed to having animals in her home and potentially having a component of perennial nonallergic rhinitis. However, her overall improvement in rhinitis symptoms after starting immunotherapy is encouraging and consistent with an underlying allergic cause.

Once again, the patient missed several follow-up appointments. She returned to the clinic 12 months later. She was experiencing nocturnal awakenings each night, dyspnea on exertion, and persistent rhinitis symptoms. She denied GERD symptoms and continued taking omeprazole, but she was now taking 40 mg/d. She was using albuterol nightly but had run out of her ICS-LABA. She continued to report overall improvement of her rhinitis symptoms with immunotherapy. The PFT results were decreased from the year before and significantly decreased from her initial presentation; FVC was 68% predicted, FEV₁ was 61% predicted, FEV₁/FVC was 0.76, and FEF_{25%-75%} was 47% predicted. These findings represented a 24% decrease in FVC and a 33% decrease in FEV₁ from her first visit. She also had a significant bronchodilator response with a 14% increase in her FVC, a 23% increase in her FEV₁, and a 43% increase in her FEF_{25%-75%}. Fractional exhaled nitric oxide was not assessed because it was not available in the office. She restarted use of her asthma medications and was encouraged to follow-up regularly.

The history of a bronchodilator response, improvement in symptoms with oral corticosteroids, and worsening of symptoms and PFT results once use of maintenance asthma medications was

stopped continued to support a diagnosis of asthma as a cause of her cough. Bronchial challenge to methacholine was not performed because lung function testing revealed a significant response to albuterol. Immunotherapy was again reported to be helpful in controlling rhinitis symptoms. Still, the worsening obstruction and persistence of rhinitis symptoms are concerning for diagnoses other than asthma and allergic rhinitis that may be playing a role, for example, chronic sinusitis, GERD, or a nonasthma pulmonary process. Because of the patient's nonadherence to medications and her high no-show rate, she was again prescribed her medications and strongly encouraged to adhere to her medication protocol and attend follow-up appointments. If the patient's symptoms do not improve with asthma therapy, sinus and possibly chest imaging and full PFTs will need to be performed. The patient should also see a gastroenterologist for further evaluation.

One month later, the patient had worsening of her sinus symptoms. PFT results were mildly improved, with a 13% increase in FEV₁. She was prescribed a 2-week course of antibiotics, and her subsequent sinus computed tomography (CT) results were normal.

Three months later, she had increased cough and dyspnea, with progressive worsening of a wet cough at night associated with a viral upper respiratory tract infection. PFTs revealed a continued decline (FVC, 47% predicted; FEV₁, 46% predicted). An immune workup was performed, the results of which were normal except for decreased IgG3. Total IgE level was 71 IU/mL. She was prescribed omalizumab and inhaled beclomethasone. She continued to receive an ICS-LABA, montelukast, and albuterol. GERD was again assessed and reported to be well controlled with omeprazole, 40 mg/d, except for diet-related symptoms once per week.

Five months later, she developed an acute upper respiratory tract infection with further worsening of her PFT results (FVC, 42% predicted; FEV₁, 36% predicted) and a significant bronchodilator response of 23% in FEV₁. After a prednisone burst, she had both subjective (less dyspnea) and objective improvement (subsequent PFTs revealed an FVC of 72% predicted and an FEV₁ of 71% predicted). However, she had persistence of her rhinitis symptoms, especially at night, and persistence of a marked cough that continued to be worse in the evening and caused nocturnal awakenings each night. The omeprazole dosage was increased to 40 mg twice daily despite her denial of significant GERD symptoms. She had not scheduled an appointment with a gastroenterologist.

During the next several months, her PFT results again worsened (FVC, 61% predicted; FEV₁, 58% predicted), and she was prescribed daily prednisone. As in the past, prednisone helped dyspnea and cough, but she continued to experience nightly awakening due to cough.

The patient now has persistent rhinorrhea and cough, both worse at night, with progressive worsening of PFT results despite maximum treatment of allergic rhinitis and asthma. The lack of improvement in rhinorrhea with oral corticosteroids suggests allergic disease is not the main cause of the rhinitis symptoms. The patient had no history of facial trauma or sinus surgery (cribriform plate fracture), and this would not explain worsening PFT results. Additional workup needs to be performed. The differential diagnosis includes worsening asthma, GERD, malignant tumor, emphysema, and interstitial or restrictive lung diseases. Chest imaging was ordered, and a pulmonologist was consulted for bronchoscopy. The patient was again advised to see a gastroenterologist for further evaluation of her GERD.

Full PFTs with diffusing capacity of the lungs for carbon monoxide were performed, which revealed evidence of restrictive lung physiologic features (FVC, 60% predicted; FEV₁, 65% predicted; FEV₁/FVC, 0.87) with moderate improvement after an inhaled bronchodilator (increase in FVC of 12% and FEV₁ of 11%). The diffusing capacity of the lungs for carbon monoxide was modestly reduced. Ambulatory pulse oximetry ranged from 93% to 97%. A chest CT revealed increased interstitial markings bilaterally

presumed to represent scarring, with discrete linear scars and probable nodular scarring present in both lower lungs. Fluid distension was noted in the thoracic esophagus, which represented an abnormal finding because of the degree of distension and amount of fluid present. On bronchoscopy, erythema was found throughout the transbronchial tree. Bronchoalveolar lavage (BAL) results were unavailable. Esophagogastroduodenoscopy (EGD) revealed candida esophagitis and food in her esophagus, despite the patient taking nothing by mouth the night before the procedure.

The findings of distention in the thoracic esophagus on CT and food remaining in her esophagus on EGD are suspicious for uncontrolled GERD because the EGD did not report evidence of eosinophilic esophagitis or a mass obstructing the gastroesophageal junction. The scarring in her lungs and abnormal PFT results may be due to aspiration. The BAL results were not available; however, a finding of lipid-laden alveolar macrophages in BAL would support aspiration. Although the initial chest radiography results were normal and subsequent decreases in her PFT results were associated with respiratory infections or nonadherence with medications, in hindsight, performed chest CT at an earlier time may have facilitated the correct diagnosis. Persistent reflux could explain nocturnal rhinorrhea and cough refractory to rhinitis and asthma medications. Despite GERD symptoms being repeatedly assessed at each visit, it seems likely that the patient's symptoms are due to ongoing, unrecognized reflux.

On further discussion with the patient, it was determined that her gastric band was inflated 1 to 2 years before her initial presentation, and she had not since followed up with her general surgeon because of his retirement. She also recalled 2 episodes in the last several months in which she coughed up food she had eaten 24 to 48 hours earlier. Her gastric band was subsequently deflated, with marked improvement of her symptoms. Her cough and rhinorrhea resolved and PFT results improved. She was able to discontinue use of prednisone and maintenance asthma medications. She continued to use albuterol as needed.

The marked improvement in the patient's symptoms and PFT results confirm that persistent nocturnal rhinorrhea, cough, and progressive dyspnea were due to reflux and aspiration caused by overinflation of her gastric band.

Commentary

Chronic cough is a common reason adult patients seek medical attention in the United States. The cause of a patient's chronic cough cannot be identified in up to 46% of cases.¹ Physicians often assess for postnasal drip, asthma, GERD, and medications such as ACE-Is as potential causes. However, when symptoms do not respond as expected to attempted therapies and complications arise, such as worsening pulmonary function, additional investigations should be explored.

Chronic cough and rhinorrhea are potential complications of the gastric banding surgery that may be underrecognized outside the general surgery community. A literature search revealed only one other case report of cough and copious nocturnal rhinorrhea after gastric banding surgery. In that case, the patient had normal PFT results and negative allergy test results. Her cough and rhinorrhea (described as "abundant liquid mucous emanating from her right nostril, sometimes to the point of having to get up at night to change her bed sheets and clothes") started 8 months after the surgery.² Symptoms were noted to disappear immediately after deflation of her gastric band.

Our patient initially presented with persistent cough and perennial clear rhinorrhea, both worse at night. Clinical history and objective data appeared to support diagnoses of allergic rhinitis and asthma. For example, skin test results were positive for dog and cat, to both of which she had nocturnal exposure, and symptoms

overall improved with immunotherapy. Certain characteristics of her cough, particularly the history of it sometimes being dry and associated with wheeze, and her nocturnal and exertional symptoms were in line with asthma. This diagnosis was further supported by decreased PFT results with bronchodilator response and interval improvement on maintenance asthma medications and oral corticosteroids bursts. This patient likely had a component of allergic rhinitis and underlying asthma or bronchospasm. However, her persistent, significant nocturnal cough, often productive, and copious clear nocturnal rhinorrhea were red flags that additional diagnoses needed to be investigated. At each visit, the patient reported that reflux symptoms were controlled, but in this case, earlier evaluation by a gastroenterologist may have more quickly elucidated the diagnosis. For a few years, our patient received antihistamines (nasal and oral), corticosteroids (nasal, inhaled, and oral), nasal irrigation, high-dose proton pump inhibitors (PPIs), antibiotics, montelukast, allergy immunotherapy, omalizumab, an immune workup, sinus CT, and a bronchoscopy before the diagnosis was ultimately revealed after performing chest CT and EGD.

GERD-related cough can be seen in 10% to 55% of patients who present with chronic cough. Multiple randomized, double-blind, placebo-controlled, parallel studies have found no significant differences between placebo and PPIs in treating chronic cough, likely because of the contribution of nonacid refluxate vs acid refluxate to chronic cough. Of note, even in patients who do respond, it can take 3 to 6 months of use of a high-dose PPI with an added histamine₂-blocker at night before symptoms improve.³

Obesity affects more than 78.6 million adults in the United States.⁴ With the increasing epidemic, more patients are exploring various procedures to help with weight loss. There are known complications associated with gastric banding surgery, such as infection, band slippage, or band erosion.⁵ A study by Gamagaris et al⁶ found that abnormal manometric evaluations of patients after undergoing gastric banding surgery had significant increases in their lower esophageal sphincter residual pressures and increases in peristaltic wave durations. They also noted that esophageal dilatation is a complication of gastric banding surgery. Their findings support esophageal motility, not refluxate, as an effect of gastric banding surgery.⁶ This finding may be a further explanation of why the patient's esophagus was dilated as noted on CT. Many physicians outside the general surgery and gastrointestinal surgery communities may not be well acquainted with the potential complications, routine maintenance, or recommended follow-up schedules.

Cough and rhinitis are frequent concerns of patients presenting to allergists-immunologists. This case highlights gastric banding surgery as an important cause of persistent cough and rhinitis refractory to medical management. Recognition that overinflation of a gastric band, leading to reflux and possibly aspiration, may present as chronic cough and rhinitis is critically important among allergists-immunologists to ensure prompt diagnosis and to avoid unnecessary therapies.

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