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Case report

A case of cough variant asthma undiagnosed for 16 years

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A 64-year-old female patient presented with a 16-year history of persistent dry cough that was undiagnosed after workups at several healthcare facilities. The patient denies wheezing, shortness of breath or sputum production. Previous workups include chest imaging, transthoracic echocardiogram (TTE), laryngoscopy, spirometry and bronchoscopy, all of which were unremarkable. During her current evaluation, spirometry was ordered again for the patient, which showed a post-bronchodilator improvement in the FEV1 by 13%, strongly suggestive of asthma. The patient was started on pharmacological therapy for severe persistent asthma, which led to sustained symptomatic improvement per evaluation at follow-up after 2 months. Spirometric findings, clinical presentation and resolution of symptoms with adequate therapy for asthma suggest that this is a case of cough variant asthma that went undiagnosed for several years. This case report summarizes the workup for chronic cough and how the diagnosis of cough variant asthma can be missed.

INTRODUCTION

Chronic cough is defined by the presence of unremitting cough symptoms for a minimum of 8 weeks in adults. It is very distressing for affected patients and although it is one of the most common complaints in the primary care setting, it is also one whose etiology is commonly misattributed or misdiagnosed [1]. This particular case is important because it demonstrates how cough variant asthma can be missed as the cause of chronic cough as it does not present with classic asthma symptoms such as wheezing, shortness of breath or excess sputum production. Spirometry is also less sensitive for cough variant asthma compared with classic asthma and more often requires methacholine challenge testing to establish the diagnosis. The case presented here highlights how cough variant asthma can be missed due to its atypical clinical presentation and deceptively normal appearing diagnostic workup.

CASE REPORT

A 64-year-old female presented to the allergy immunology clinic as a self-referral complaining of a persistent cough since 1996, almost 17 years to date. The patient stated that the cough occurs most days of the week with no seasonal changes or obvious provoking factors except for exercise and physical exertion. She reported minimal sputum production and denied associated wheezing, shortness of breath, night-time symptoms or snoring. Review of symptoms was otherwise unremarkable.

The patient's medical history was significant for erosive esophagitis documented by esophagogastroduodenoscopy (EGD) in 2007 for which the patient was started on omeprazole 40 mg daily at that time; however, this did not help with her coughing symptoms and was discontinued after 2–3 months. Her only current medication was aspirin 81 mg daily. The patient endorsed seasonal rhinosinusitis with history of a positive skin prick test, which showed reaction to dust mites, weed and grass but she stated these seasonal exacerbations were unrelated to her persistent cough symptoms. She denied smoking, use of tobacco products and recreational drugs. She denied family history of atopic disease and any other health conditions. There were no pertinent positive physical examination findings. Notably, there was no cobblestone appearance of the nasopharyngeal mucosa and no wheezes, rales or rhonchi on pulmonary examination. Previous evaluations in the late 1990s and early 2000s included chest imaging, TTE,

laryngoscopy, spirometry and bronchoscopy, which were all unremarkable. She never underwent a methacholine challenge. Spirometry was ordered to evaluate the possibility of cough variant asthma with plans to order methacholine challenge if the test was negative. Spirometry showed pre-treatment forced expiratory volume in 1 s (FEV1) of 82% predicted and post-treatment FEV1 of 93% predicted with a 13% change from baseline with >200 ml increase in FEV1, thus meeting criteria for 'significant reversibility' suggestive of asthma [2].

Spirometric finding of reversible bronchopulmonary obstruction are consistent with the diagnosis of asthma. The diagnosis of the cough variant subtype of asthma was made based on the clinical picture of chronic cough in the absence of wheezing, shortness of breath or excess sputum production. Post-nasal drip, acid reflux and post-infectious cough are important causes of chronic cough that were considered in this evaluation [1, 3].

The treatment for cough variant asthma is no different than the treatment of classic asthma. Combination medium-dose inhaled corticosteroid and long-acting beta-2 agonist mometasone/formoterol 100/5 μg, one puff twice per day, was started with short-acting beta-2 agonist for rescue. Given a history of acid reflux, the patient was also started on omeprazole 40 mg twice per day for 3 months pending future EGD surveillance.

DISCUSSION

Asthma is an important etiology to consider in the evaluation of chronic cough. In a recent study examining 131 cases of chronic cough, cough variant asthma was the most common cause (24%) [3]. Patients with cough variant asthma usually present with chronic cough as their only symptom. In this particular case, the patient underwent evaluation for her chronic cough for several years and many potential causes were ruled out appropriately. She was assessed for post-nasal drip secondary to rhinosinusitis and treated for acid reflux, both of which are common etiologies for chronic cough. The patient even underwent spirometry for evaluation of asthma several years ago, which was negative. However, there is a higher false-negative rate associated with spirometric evaluation of cough variant asthma than there is for classic asthma [4]. Therefore, the patient may have benefited from methacholine challenge following negative spirometry since bronchoprovocation is a more definitive assessment with a positive predictive value (PPV) of 88% and negative predictive value (NPV) of 100% for cough variant asthma [5]. Contraindications to methacholine challenge include FEV1 <50% predicted, myocardial infarction or stroke within the past 3 months, systolic blood pressure over 200 mmHg and aortic aneurysm, none of which are problems for this patient.

Despite the utility of spirometry and methacholine challenge in diagnosing cough variant asthma, positive tests do not necessarily prove that asthma is the etiology of the chronic cough. In fact, one study demonstrated that positive spirometry falsely attributed asthma as the cause of chronic cough in 33% of cases and methacholine challenge did so in 22% of cases. These false-positive cases are more common in the setting of comorbidities including congestive heart failure, chronic obstructive pulmonary disease, bronchitis and allergic rhinitis [1, 6]. Resolution of chronic cough symptoms in the setting of adequate control of underlying asthma is the most definitive way to establish cough variant asthma as the etiology of chronic cough [7]. Therefore, an appropriate follow-up with patients reporting chronic cough following an intervention is essential. As with classic asthma, patients refractory to this regimen may benefit from leukotriene receptor antagonists and/or a short course of oral corticosteroids per treatment guidelines for severe persistent asthma [1, 2].

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