Case Report: Cough variant asthma

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Chronic cough is the fifth most common complaint seen by primary care physicians,\(^1\) and for many it is a diagnostic challenge. In a few patients with documented airway hyperresponsiveness (AHR), cough can be the sole presenting symptom of asthma. This uncommon clinical condition is known as cough variant asthma.\(^2\) Despite underlying AHR, it is difficult to diagnose cough variant asthma because these patients typically have normal lung function that does not change in response to bronchodilator challenge.

**Case description**
A 32-year-old woman initially presented with an intermittent nonproductive hacking cough that had lasted several days. She denied having other respiratory, cardiovascular, or constitutional symptoms. Review of systems was unremarkable. Her medical history was negative for atopy, gastroesophageal reflux disease, cancer, tuberculosis, or cardiopulmonary diseases. She was a non-smoker and did not have a history of occupational exposure to respiratory toxins. Results of physical examination were normal. For symptom relief, she had used antitussives including codeine syrup. Despite periods of remission, her cough persisted. Results of physical examination and chest radiograph were normal. Spirometry revealed normal pulmonary function with no reversibility after bronchodilator challenge with a $$\beta_2$$-agonist. Her pulmonary function was further evaluated using a methacholine challenge test. Results showed severe airway hyperreactivity: provocative concentration for a 20% fall in forced expiratory volume in 1 second ($$\text{PC}_{20}$$) was 0.398 $$\mu$$mol/L (normal $$\text{PC}_{20}$$ > 1.4 mmol/L). Cough variant asthma was diagnosed, and treatment was started with a bronchodilator and an inhaled corticosteroid. After initiation of asthma therapy, the patient’s chronic cough resolved and her pulmonary function remained normal.

**Discussion**
MEDLINE was searched for articles related to diagnosis of cough variant asthma. Articles were found using the key words asthma, variant asthma, chronic cough, prevalence, diagnosis, and natural history. The search was limited to investigations completed between 1960 and 2000 of human beings, written in English, and conducted on both sexes. A total of 67 articles were found. Only articles that focused on cough variant asthma and its epidemiology, natural history, diagnosis, and treatment, were used.

The prevalence of adults with cough variant asthma in the general population and more specifically among asthmatic patients is unknown. Studies have not compared the prevalence of cough variant asthma to the symptoms and signs typically associated with classic asthma, namely wheezing, dyspnea, cough, and variable airflow obstruction. One Canadian study has shown that persistent cough and wheezing affect only 6% and 13% of asthmatic children, respectively,\(^3\) supporting the notion that isolated cough is less common than other clinical manifestations of asthma. Since cough variant asthma almost always presents as chronic cough (duration more than 8 weeks),\(^4\) family physicians are faced with the challenge of differentiating it from classic asthma and from other very common causes of chronic cough.

Chronic cough has a lengthy differential diagnosis. Yet asthma, postnasal drip syndrome, gastroesophageal reflux disease, postinfectious cough, or some combination of these are most often responsible.\(^1\)\(^4\)\(^6\) A
comprehensive approach to diagnosing chronic cough is discussed in another paper in this issue (page 1311).

Cough variant asthma is elusive because history, physical examination, and laboratory results are often completely normal, as they were in this case. Among patients with chronic cough, underlying AHR can be the sole manifestation of cough variant asthma. While AHR is not specific for asthma, its absence makes a diagnosis of asthma very unlikely. Consequently, AHR is the key to detecting this occult form of asthma. Both exercise and methacholine challenge tests can evaluate AHR, but methacholine testing is better established. Ultimately, diagnosis of cough variant asthma depends on a positive response to a methacholine challenge test in concert with a favourable response to a brief trial of conventional asthma therapy.

Briefly, methacholine is a cholinergic agent. It can enhance bronchoconstriction and artificially exacerbate potential airway hypersensitivity in healthy people, and to a markedly greater extent in asthmatic patients. A positive test is defined as a 20% reduction in forced expiratory volume in 1 second (FEV$_1$) with a PC$_{20}$ of methacholine less than 1.4 µmol/L. A methacholine challenge test is indicated when asthma is a possibility but when spirometry before and after bronchodilator use is not diagnostic. For this reason, methacholine tests are essential for detecting cough variant asthma. Absolute contraindications for methacholine testing include severe airflow limitation (FEV$_1$ < 50% predicted), recent (within past 3 months) myocardial infarction or stroke, uncontrolled hypertension (systolic blood pressure above 200 mm Hg), and aortic aneurysm.

Methacholine testing has a positive predictive value up to 88% and a negative predictive value of 100% for cough variant asthma. Thus, negative results from a methacholine test preclude a diagnosis of cough variant asthma. A small portion of patients with positive results from a methacholine test have false-positive results (more likely among those with bronchitis, allergic rhinitis, chronic obstructive pulmonary disease, congestive heart failure, and cystic fibrosis). Cough variant asthma is more likely, however, when results of chest x-ray examination are normal and response to a brief trial of asthma therapy is positive.

Most often, patients with cough variant asthma respond well to bronchodilators and corticosteroid drugs. The few patients who are refractory to inhaled therapy often do well with oral corticosteroids. Diagnosis of cough variant asthma is confirmed only with demonstrated AHR during a challenge test when chronic cough responds well to asthma therapy. Current treatment recommendations stress the need for early diagnosis and control of asthma.' The natural history of cough variant asthma underscores the importance of early detection and appropriate treatment, as many patients with cough variant asthma lose lung function and develop additional asthma symptoms.

Conclusion
Cough variant asthma is a diagnostic challenge because history, physical findings, and simple spirometry results often fail to uncover abnormalities in lung mechanics and AHR. Physicians should consider referring patients with undiagnosed chronic cough, normal lung function, and normal results from chest radiographs for methacholine challenge tests. Early introduction of inhaled bronchodilator and anti-inflammatory therapy should prove useful in alleviating cough and slowing the clinical progression of this type of asthma.
Competing interests
None declared

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References