

EDITORIAL

Eosinophilic bronchitis – what is it and why is it important?

Chronic cough is one of the most common causes of presentation to general practice. At any one time 20% of the population have a troublesome cough and sufferers consume 75 million doses of over the counter antitussive medication [1]. Most cases are acute and self-limiting although a significant minority are referred for a specialist opinion with an isolated persistent chronic cough. This is traditionally defined as a cough lasting for more than 3 weeks with no overt clinical and radiological evidence of lung disease. In many cases a treatable cause can be identified using a simple 'anatomical diagnostic' protocol originally proposed by Irwin *et al.* 18 years ago [2]. Rhinitis with postnasal drip, cough variant asthma and gastro-oesophageal [2–4] are the most important causes of isolated chronic cough and one or more of these conditions may be responsible for as many as 90% of cases where a cause is identified.

Over the last 10 years there has been a growing interest in assessing airway inflammation in patients with chronic cough [5]. This interest has been stimulated by the development of simple noninvasive methods to assess airway inflammation using induced sputum [6,7]. One of the more interesting early observations was that sputum evidence of an eosinophilic bronchitis identical to that seen in asthma can occur in patients with an isolated chronic cough and no evidence of the variable airflow obstruction and airway hyperresponsiveness that characterize asthma [8,9]. Eosinophilic bronchitis has since emerged as a common cause of cough with an incidence of 10–15% in patients referred for a specialist opinion [5,10]. Patients typically present in middle age with a cough occasionally productive of small amounts of tenacious mucoid sputum. Atopy is not prominent and smoking is unusual [10], perhaps reflecting a selection bias since primary care physicians are likely to attribute a chronic cough in smokers to chronic bronchitis. Both the cough and sputum eosinophilia improve [8–11] and the increased capsaicin cough sensitivity returns towards normal [11] following treatment with inhaled corticosteroids.

The patients reported by Fujimara *et al.* in this issue of *Clinical and Experimental Allergy* presented with a bronchodilator-resistant cough, which responded to treatment with corticosteroids and antihistamines [12]. Spirometric values and airway responsiveness were normal but capsaicin cough sensitivity was increased and many had been previously shown to have a sputum eosinophilia [13]. This condition therefore has many features in common with eosinophilic bronchitis although atopy is more prominent (Table 1). The authors suggested the diagnostic label 'atopic cough'.

Neither condition should be confused with cough variant asthma [14], which is associated with variable airflow obstruction, airway hyperresponsiveness, normal [15] or mildly increased [16] capsaicin cough sensitivity and improvement in the cough with bronchodilator therapy (Table 1).

Why are eosinophilic bronchitis and atopic cough important? The most obvious reason is that both are treatable causes of cough and are thus important to recognize, yet recognition is not straightforward since it requires assessment of airway inflammation. Most cases would become apparent with a trial of corticosteroid therapy and it is likely that many are erroneously assumed to have cough variant asthma or given the unsatisfactory label of corticosteroid responsive cough. However, it has been suggested that a trial of corticosteroids is restricted to those with a positive histamine or methacholine challenge [4], so there is clearly the potential for these patients to be denied effective treatment. We suggest assessment of airway inflammation or at the very least a trial of corticosteroids should be incorporated into the diagnostic algorithm of chronic cough whether there are features of asthma or not. The natural history of unrecognized or under-treated eosinophilic bronchitis is unknown. Up to 40% of patients with chronic obstructive pulmonary disease have sputum evidence of an eosinophilic airway inflammation [17] so one possibility is that such patients develop irreversible structural changes to their airways and fixed airflow obstruction. In support of this we have reported a patient with eosinophilic bronchitis who had a good symptomatic response to inhaled corticosteroids but had sputum evidence of persistent eosinophilic airway inflammation and developed fixed airflow obstruction over 3 years [18].

As well as being interesting in its own right, understanding more about the pathogenesis of eosinophilic bronchitis might provide some insight into the pathophysiology of asthma. The association of asthma with a TH2 type of mucosal inflammation characterized by an eosinophilic bronchitis [19] is well established but much less is known about how this inflammatory process relates to the abnormality of airway function that underlies much of the morbidity of asthma [20]. It is therefore of considerable interest that apparently similar airway pathology can lead to quite different pathophysiological consequences in eosinophilic bronchitis. Possible explanations for the different functional consequences of the airway inflammatory process in eosinophilic bronchitis and asthma include involvement of different parts of the bronchial tree or differences in the state of activation of the inflammation. Alternatively,

Table 1. The characteristics of cough variant asthma, eosinophilic bronchitis and atopic cough

	Asthma	Cough variant asthma	Eosinophilic bronchitis without asthma	Atopic cough
Symptoms	Dyspnoea, cough, wheeze	Isolated cough	Cough and often associated upper airway symptoms	Isolated cough
Atopy	Common	Common	Same as general population	Common
Variable airflow obstruction	Present	Present	Absent	Absent
Airway hyperresponsiveness	Present	Present	Absent	Absent
Cough reflex hypersensitivity	Normal or increased	Normal or increased	Increased	Increased
Sputum eosinophilia	Usually	Usually	Always at diagnosis	Invariably at diagnosis
Bronchial biopsy eosinophilic infiltration	Yes	Yes	Unknown	Yes
Bronchoalveolar lavage eosinophilia	Yes	Yes	Yes	No

airway responsiveness may be increased by the airway inflammation in eosinophilic bronchitis but stays within the normal range because baseline airway responsiveness is far to the right of the normal range. We have recently observed such a phenomenon in a patient with eosinophilic bronchitis who developed worsening symptoms and airway hyperresponsiveness during an exacerbation of eosinophilic airway inflammation [21].

A number of researchers have begun to investigate the site and state of activation of the airway inflammation in eosinophilic bronchitis. We [10] and others [8] have noted that upper airway symptoms are common in patients with eosinophilic bronchitis and have speculated that inflammation may be confined to the upper airway. However, eosinophilic bronchitis is not typically associated with a nasal wash eosinophilia or upper airway hyperresponsiveness [22]. Gibson *et al.* [23] have shown a similar degree of bronchoalveolar lavage eosinophilia and GM-CSF and interleukin-5 gene expression in patients with asthma and eosinophilic bronchitis. These observations would not support a predominant upper airway inflammation and suggest that the site and underlying cytokine mechanisms of the eosinophilic airway inflammation is similar in asthma and eosinophilic bronchitis. In contrast Fujimura *et al.* [12] found biopsy evidence of eosinophilic tracheobronchitis but no excess eosinophils in the bronchial wash in their patients with atopic cough. The significance of these findings and of the apparent difference between atopic cough and eosinophilic bronchitis is unclear although it is possible that they are distinct conditions.

Further detailed and systematic comparison of the immunopathological features and consequences of the

eosinophilic airway inflammation in asthma, eosinophilic bronchitis and atopic cough would seem worthwhile and might identify particular features of the inflammatory process that are functionally important.

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