CASE REPORT

A case of cough, lymphocytic bronchoalveolitis and coeliac disease with improvement following a gluten free diet

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Chronic cough is a common reason for presentation to a respiratory clinic. In up to 20% of cases the cause remains unclear after investigations. We report one such case where there was bronchoscopic evidence of lymphocytic airway inflammation in association with newly diagnosed coeliac disease. All features improved markedly on a gluten free diet, suggesting a causal relationship between coeliac disease, cough, and lymphocytic bronchoalveolitis.

Chronic cough is one of the most common causes of presentation to respiratory clinics. In most cases a treatable cause can be identified,[1–3] although in up to 20% the cause remains unclear after extensive investigations. We report here a case in whom chronic cough was associated with coeliac disease.

CASE REPORT

A 68 year old retired teacher was referred in June 1999 by his general practitioner with a 1 year history of dry cough with no dyspnoea or wheeze. Oesophagitis diagnosed by endoscopy secondary to oesophageal reflux had been confirmed in 1995 by 24 hour manometry and pH monitoring. His reflux symptoms were partly controlled by regular treatment with H_2 blockers. He had nasal congestion and itchiness suggestive of rhinitis, had never smoked, and kept no pets. His clinical examination and chest radiograph were normal. Initial lung function tests were within normal limits; forced expiratory volume in one second (FEV_1) 3.67 l (104% of predicted), FEV_1/FVC ratio 71%, bronchodilator response 15 minutes after 200 μg inhaled salbutamol 7.9%, total lung capacity 7.33 l (94% of predicted), and corrected carbon monoxide transfer coefficient 3.86 (99% of predicted). Skin prick tests were negative, serum total IgE was marginally raised at 208.7 KU/l (normal 0–122), and methacholine airway responsiveness was normal ($PC_{20}FEV_1$ >64 mg/ml). The differential cell count from an induced sputum sample was normal with a sputum eosinophil count of 0.2% (normal range 0–1%).

His cough was thought to be due to his gastro-oesophageal reflux and rhinitis so he was started on topical nasal steroids and the H_2 blocker was changed to a proton pump inhibitor. On review 4 months later his rhinitis and reflux symptoms had resolved but his cough was worse (46 mm on a 100 mm visual analogue scale (VAS) ranging from "no symptoms" to the "worst symptoms ever"). The concentration of capsaicin causing five coughs (C5) was 32 μM. A bronchoscopic examination was performed which showed macroscopically normal airways. Differential cell count on a 180 ml sample of bronchoalveolar lavage (BAL) fluid from the right middle lobe revealed a high lymphocyte count of 30.6% with a lymphocytic infiltration (table 1). The BAL fluid cells were analysed by flow cytometry using directly and indirectly conjugated monoclonal antibodies and the proportion of T lymphocytes (CD3+) that were CD4/CD8+ are shown in table 1.

The finding of lymphocytic airway inflammation led us to perform a high resolution computed tomographic scan of the thorax which was normal. An autoantibody screen showed positive reticulin autoantibody with a titre of 1:256, endomysial and gliadin IgA autoantibodies were positive with raised serum IgA of 2.08 g/l (normal 0.8–1.4), and other autoantibodies were negative.

Table 1 Cough severity, sensitivity, BAL fluid and bronchial biopsy specimens before and 6 months after a gluten free diet

	Pre-gluten free diet	Post-gluten free diet
Cough VAS (mm)	46	5
Capsaicin cough sensitivity C2 (μM)	4	64
C5 (μM)	32	250
Anti-endomysial antibody	Positive	Negative
BAL recovered volume (%)	30	26
BAL viability (%)	88	90
Total cells recovered ($\times 10^6$)	22.9	5.4
Eosinophils (%) (normal range 0–1%)	0.2	0.5
Neutrophils (%) (normal range 0–8%)	3.3	3
Macrophages (%) (normal range 75–95%)	61.3	87
Lymphocytes (%) (normal range 1–15%)	30.6	6
Epithelial cells (%) (normal range 0–10%)	4.5	3.5
CD4+/CD3 (%)	88	85
CD8+/CD3 (%)	12	15
CD3+ cells/mm^2 subepithelium	92.7	20.6

On further direct questioning the patient alluded to the development of intermittent abdominal bloating and offensive stools over the previous year. Upper gastrointestinal endoscopy showed mild oesophagitis, an atrophic duodenum, and moderate duodenitis. A duodenal biopsy revealed partial villous atrophy and increased numbers of intraepithelial lymphocytes consistent with a diagnosis of coeliac disease.

Following the introduction of a gluten free diet his cough and abdominal symptoms improved over a few weeks. After 6 months on the gluten free diet his cough sensitivity and severity had improved to a C5 value of 250 μM and a VAS score of 5 mm. His anti-endomysial antibody was negative. Repeat bronchoscopy demonstrated a fivefold reduction in the total number of cells recovered in the BAL fluid, and a fivefold reduction in the percentage of lymphocytes with no change in the CD4/CD8 ratio of CD3 positive cells and a decrease in the number of lymphocytes in the bronchial biopsy specimens (table 1).

DISCUSSION

This patient had a chronic cough, a heightened cough reflex, and bronchoscopic evidence of lymphocytic airway inflammation in association with coeliac disease. All features markedly improved on a gluten free diet suggesting a causal relationship between coeliac disease and cough.

Coeliac disease is associated with a number of extragastrointestinal features including dermatitis herpeteformis and ataxia.[4 5] A number of pulmonary complications including diffuse pulmonary nodules, interstitial fibrosis, and alveolitis have been linked to coeliac disease.[6 7] In contrast to these reports, the lymphocytic bronchoalveolitis in our patient was not associated with overt radiological or physiological evidence of airway or lung parenchymal involvement and manifest itself solely as a heightened cough reflex. Similar pathological findings have been reported in subjects with Sjögren's disease[8] and Crohn's disease[9] although, unlike our case, a link with chronic cough and heightened cough sensitivity has not been established.

Our case also differs from previous reports in that the cough and airway inflammation improved with a gluten free diet. The improvement in most parameters was marked and exceeded the known 95% confidence interval for repeat measures suggesting a real change.[10–12] This would be in keeping with a causal association between coeliac disease, cough, and lymphocytic bronchoalveolitis.

Coeliac disease can be viewed as an organ specific autoimmune disease and is associated with other organ specific autoimmune diseases including Grave's disease and juvenile diabetes.[13] A recent case controlled study has shown a strong association between organ specific autoimmune diseases and idiopathic chronic cough.[14] Further studies should be undertaken to investigate the possibility that a similar lymphocytic bronchoalveolitis occurs in a wider population of patients with unexplained cough.

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