

Bronchiolitis in a Patient with Ulcerative Colitis Treated with Erythromycin

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Abstract

A 47-year-old man was referred to our hospital with an abnormal shadow on a chest X-ray. He had a history of untreated chronic sinusitis and suspected ulcerative colitis (UC). Chest CT revealed a diffuse centrilobular granular shadow, while laboratory tests demonstrated an increased proportion of neutrophils; however, no microorganisms were detected in bronchoalveolar lavage fluid. Therefore, sinobronchial syndrome or small airway disease associated with UC was diagnosed, and the patient was treated with long-term erythromycin therapy. Small airway disease associated with UC is usually treated with steroids. Our experience shows that airway involvement in patients with inflammatory bowel disease can be treated with macrolides.

Key words: inflammatory bowel disease, macrolides, bronchitis, sinobronchial syndrome, diffuse panbronchiolitis

(Intern Med 53: 875-877, 2014)

(DOI: 10.2169/internalmedicine.53.1826)

Introduction

Extraintestinal manifestations of inflammatory bowel diseases (IBD) commonly include ulcerative colitis (UC) and Crohn's disease. Airway inflammation is the most common form of respiratory manifestations of IBD, and the advent of high-resolution CT has led to more frequent detection of small airway diseases (1). Such manifestations in patients with IBD are usually treated with inhaled or systemic steroids (2); however, the effects of inhaled and systemic steroids have not been sufficiently evaluated. We herein describe the case of a patient with UC accompanied by small airway disease that was treated with long-term erythromycin therapy.

Case Report

A 47-year-old Japanese man was referred to our hospital for a further assessment of an abnormal shadow on a chest

X-ray discovered five years previously (Figure a) that had gradually deteriorated. Pulmonary symptoms, such as coughing, sputum production and dyspnea were absent. An otolaryngologist had diagnosed chronic sinusitis 15 years previously, which had remained untreated. One year before the present referral, colonoscopy for positive fecal occult blood demonstrated nonspecific enteritis, and the patient was treated with mesalazine. He had quit smoking at the age of 40 years.

A physical examination performed on admission revealed the following findings: temperature, 36.7°C; blood pressure, 112/60 mmHg; regular pulse, 62 beats/min. Lung auscultation demonstrated normal vesicular sounds in both lungs. The laboratory findings were as follows: white blood cells, 6,700/ μ L; hemoglobin, 14.4 g/dL; total protein, 7.1 g/dL; C-reactive protein, 0.07 mg/dL; cold agglutinin, \times 256; and immunoglobulin-G, 1,136 mg/dL. Arterial blood gases assessed on room air were normal (pH 7.416; PaCO₂ 39.3 Torr; PaO₂ 85.5 Torr). Sputum microbiology identified normal flora. Pulmonary function tests showed the following

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Received for publication September 26, 2013; Accepted for publication November 24, 2013

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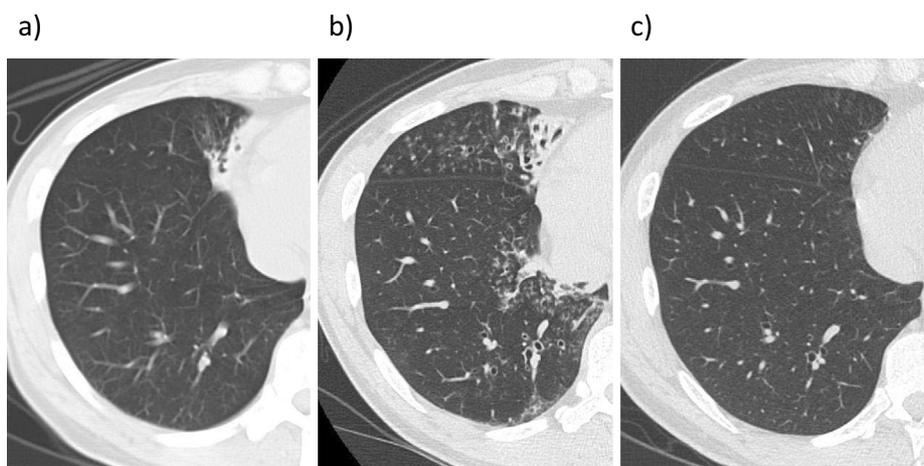


Figure. Chest CT performed five years before admission, on admission and after the administration of erythromycin therapy for two years. Partial bronchiectasis and atelectasis in the right middle lobe five years before admission (a). A diffuse centrilobular granular shadow primarily in the right lung with partial atelectasis in the middle lobe of the right lung on admission (b). The centrilobular granular shadow reduced in size and the atelectasis disappeared after two years of erythromycin treatment (c).

results suggestive of peripheral airway obstruction: %VC, 125.8%; FEV1.0/FVC(%), 75.7%; $\dot{V}_{50}/\dot{V}_{25}$, 4.3; %RV, 118%; and RV/TLC, 92.6%. A chest X-ray disclosed consolidative and nodular shadows primarily in the right lower field; however, no volume loss was evident. Chest CT demonstrated a centrilobular granular shadow primarily in the right lung with partial atelectasis in the middle lobe of the right lung (Figure b), whereas that performed five years previously had shown only partial atelectasis in the middle lobe of the right lung (Figure a). An increased number of cells ($25.0 \times 10^5/\text{mL}$) and a proportion of neutrophils of 95% were identified in the bronchoalveolar lavage fluid recovered from the right B⁵ lobe, although microorganisms, including mycobacteria, were undetectable. A transbronchial lung biopsy was not performed because the considerable amount of secretions observed in the bronchoscopic findings indicated infection. The patient was diagnosed with sinobronchial syndrome or airway disease associated with nonspecific enteritis. Treatment with erythromycin (EM; 600 mg/day) was started and maintained for two years, which improved the nasal symptoms and chest CT findings (Figure c). However, the colonoscopic findings worsened following the discontinuation of mesalazine, and a colonoscopic biopsy confirmed UC, which improved after resuming this drug.

Discussion

Pulmonary manifestations of IBD are considered rare; however, two reports have suggested that such manifestations are more frequent than previously thought (2, 3). Although the mechanisms underlying the association between pulmonary involvement and IBD remain unclear, an embryological origin and the similarity of the mucosal immune systems of the lungs and gastrointestinal tract may explain the link between pulmonary involvement and IBD (4). The

detection of small airway diseases associated with IBD has increased with the recent advent of high-resolution CT. Small airway diseases, such as granulomatous or necrotizing bronchiolitis, bronchiolitis obliterans and diffuse panbronchiolitis (DPB), are associated with IBD (2, 5). These diseases are usually treated with inhaled and systemic steroids in affected patients (2). Camus and Colby reported that small airway diseases are usually refractory to inhaled steroids, the effects of oral steroids range from slight to modest and the role of macrolide antibiotics has not been sufficiently evaluated (3). The present patient had both sinusitis and bronchiolitis (sinobronchial syndrome; SBS), which involves coexisting chronic rhinosinusitis and chronic lower airway inflammation, such as that observed in patients with chronic bronchitis or DPB (6). Long-term treatment with macrolides has become a common strategy for SBS, including DPB, after Kudoh et al. described the positive effects of long-term erythromycin therapy against DPB (7). Therefore, the SBS observed in the present case was treated with long-term EM because UC had not yet been diagnosed at that point. The long-term EM therapy improved the patient's nasal symptoms and chest CT findings. Mitsui et al. reviewed eight patients with bronchiolitis associated with UC. Two of three patients treated with EM responded to the therapy (8). Reports describing these three patients have been published in Japan, with the pathological lung findings described as reflective of DPB (8). The pathological status of our patient was not defined; however, the complicating sinusitis and high ratio of neutrophils in the bronchoalveolar lavage fluid suggested neutrophilic inflammation in the upper and lower airways, similar to that observed in DPB, a predominant chronic inflammatory disease of unknown origin in East Asian countries, including Japan (9), that is routinely considered in the differential diagnosis of bronchiolitis in East Asian patients with UC. The predominance of this disorder

suggests that the characteristics of the bronchiolitis observed in patients with UC differ between those from East Asia and elsewhere; thus, strategies for treating bronchiolitis in UC patients may differ depending on the individual's background.

Macrolide antibiotics, including EM, now possess anti-inflammatory properties, and the effects of long-term treatment with these agents on several chronic inflammatory respiratory diseases, including DPB, cystic fibrosis, post-transplant bronchiolitis obliterans and chronic obstructive pulmonary disease, have been investigated (10). Precisely how EM therapy exerts beneficial effects on bronchiolitis associated with UC is unknown; however, the actions of macrolides are generally thought to be due to immune-modifying, rather than direct antimicrobial, activities (11). Our experience with the present patient supports the notion that the immune-modifying effects of macrolides improved his nasal symptoms and chest CT findings, as microorganisms were undetectable in the bronchoalveolar lavage fluid.

Treatment with long-term macrolides should be considered in UC patients with small airway diseases, especially those with features of DPB.

The authors state that they have no Conflict of Interest (COI).

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