Interstitial Pneumonia Accompanying Ulcerative Colitis

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Abstract

We report a patient with ulcerative colitis complicated with idiopathic interstitial pneumonia, in whom the etiology of interstitial pneumonia was unknown, but immunological disturbance might have been involved. There are many complications with ulcerative colitis, but interstitial pneumonia is quite rare and its prognosis is quite poor. Antibiotic and steroid treatment were given under respiratory supported therapy, but no response could be obtained. In the treatment of patients with ulcerative colitis, we must be mindful of interstitial pneumonia because the prognosis is quite poor.

Introduction

Ulcerative colitis (UC) can be associated with a variety of extraintestinal manifestations, but the lung is rarely involved. Bronchopulmonary disease in patients with UC has sometimes been considered as an adverse reaction to sulfasalazine (SASP) therapy. We report a non-smoker UC patient with interstitial pneumonia, in whom a trans bronchial lung biopsy was performed and the causal relationship between drug and pulmonary manifestations could not be established.

Case Report

A 55-year-old man suffered from UC from the age of 35. At the age of 35, maintenance therapy was begun with oral SASP and prednisolone, with resolution of symptoms. He had never smoked and had no history of allergic or respiratory disease. In December 1998, he developed bloody diarrhea, abdominal pain and was admitted to our hospital at the end of that month. Endoscopic examination on the 8th day after admission showed diffuse erosions and ulcers in the rectum, sigmoid, descending and transverse colon (Fig. 1). Barium enema study on the 30th day after admission showed barium flecks in the descending and transverse colon with lead pipe appearance (Fig. 2), and barium flecks were also observed in the rectum and sigmoid colon. After admission treatment was started with intensive regimen therapy (prednisolone, 50 mg) and SASP was discontinued because aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were elevated (AST 49 U//, ALT 132 U//); on the 16th day after admission, we suspected drug-induced liver function disorders. The response to the intensive regimen therapy was not satisfactory, diarrhea with blood was being passed 5 or 6 times a day. So leukocytapheresis therapy with a leukocyte removal filter was started on February 10, 1999. That therapy was performed once a week, 7 times in total, until April 7, 1999 with prednisolone therapy. But the response to that therapy was not satisfactory, either. He abruptly developed a high fever (38.5°C) on April 10, 1998, and other respiratory symptoms such as cough were not observed before the fever rose. The chest roentgenogram revealed a reticular shadow in the lower lobe of the left lung (Fig. 3). The shadow spread rapidly over almost the entire lung (Fig. 4). Chest computed tomographic (CT) films showed parenchymatous shadow over most of the lung field, with small regions of reticular shadows (Fig. 5). Eosinophilia was not found in peripheral blood. An arterial blood sample showed severe hypoxia (PO2, 36.6 torr, PCO2, 32.6 torr) on April 23, 1999. Intra-trachial intubation was performed and mechanical ventilation was started. Klebsiella pneumonia was found in the culture of sputum on April 21, 1999. We made the diagnosis of bacterial pneumonia complicated with interstitial pneumonia. We treated him with antibiotics and steroid pulse therapy (methyl prednisolone 1,500 mg/day x3). The pneumonia caused by cytomegalovirus or pneumocystis carinii shows an interstitial shadow. In this case, anti-cytomegalovirus IgM was negative. Transbronchial lung biopsy was performed on May 11, 1999. The specimen showed that the majority of the lung parenchyma had been replaced by fibrous tissue, accompanied by a moderate infiltration of lymphocytes (Fig. 6). In this specimen, there was no cytomegalovirus nuclear or cytoplasmic inclusions, nor was there any foamy, amorphous material composed of proliferating protozoas and cell debris, typically observed in Pneumocystis carinii pneumonia, in the alveolar spaces. We
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Figure 1. Endoscopic examination showing diffuse erosions and ulcers (January 4, 1999).

Figure 2. Barium enema study revealed barium flecks in the descending and transverse colon with lead-pipe appearance (January 27, 1999).

Figure 3. Chest X-ray films showing reticular shadow in the lower field of the left lung (April 10, 1999).

treated him with sulfamethoxazole-trimethoprim as a diagnostic therapy, but the response was not satisfactory. We therefore concluded that the pneumonia was not caused by cytomegalovirus or Pneumocystis carinii. We established the diagnosis as idiopathic interstitial pneumonia. We repeated the steroid pulse therapy several times. Unfortunately, his pulmonary function deteriorated because of pulmonary opportunistic infection, and he died on June 21, 1999.

Discussion

A variety of bronchopulmonary diseases have sporadically been reported in patients with UC, including those related to SASP (1-3), 5-aminosalicylic acid (5-ASA) (4), such as eosinophilic pneumonia, fibrosing alveolitis and interstitial pneumonitis (5). In most patients, signs and symptoms of bronchopulmonary complications usually disappear after therapy is discontinued. The etiology of such bronchopulmonary lesions during SASP or 5-ASA therapy remains unknown. However, one cannot always attribute bronchopulmonary disease in patients with UC to SASP or 5-ASA therapy. Several reports have described various bronchopulmonary complications unrelated to SASP or 5-ASA (6, 7), which include interstitial pneumoni-
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Figure 4. Chest X-ray films showing reticular shadow spread over most of the lung field (April 22, 1999).

Figure 5. Chest computed tomographic film showing parenchymatous shadow over most of the lung field, with small regions of reticular shadows (April 27, 1999).

Figure 6. Specimen of the transbronchial lung biopsy stained in hematoxylin-eosin. It revealed that the majority of the lung parenchyma had been replaced by fibrous tissue, accompanied by a moderate infiltration of lymphocytes (×100).

tis. In the present case of interstitial pneumonia accompanied with ulcerative colitis an etiologic role of SASP appears unlikely, as the patient had discontinued the drug about 3 months before the onset of pulmonary symptoms and eosinophilia was not found in the peripheral blood. Investigations into the etiology of interstitial pneumonia have focused on several areas, including immunologic abnormalities, genetic abnormalities, and viral infection. The etiopathogenesis of the lung involvement in patients with UC is far from clear, but the lungs are frequently sites of involvement in systemic immunological diseases, as the immune system of the gastrointestinal tract shows features common to all mucosal surfaces. The association of UC and lung disease may well be the result of an immunological mechanism. Both organs are vulnerable to autoantibodies (8, 9), both interstitial pulmonary disease and ulcerative colitis have been associated with circulating immune complexes (10–13), and altered effector-cell function has been described in both disorders (14–16). One hypothesis concerning the pathophysiology of idiopathic interstitial pneumonia includes a stimulus active on the cell surface, perhaps immune complexes, lymphocytes and macrophage activation and cytokine release (10, 14, 17). Cytokines, such as macrophage growth factor, platelet-derived growth, and/or fibronectin, may then stimulate mesenchymal cells, such as fibroblasts, to proliferate and synthesize and release collagen into the pulmonary interstitium (18–20).

In the majority of these cases steroids were very effective (7), because they inhibit the production of some cytokines and also inhibit cellular effects by reducing receptor binding or expression (21, 22). But in several patients with severe airway inflammation or chronic bronchiolitis, steroids lacked effectiveness (7). We treated the patient with a high dose of steroids several times as pulse therapy, but the response was not satisfactory. Leukocytapheresis exerts an immunosuppressive or immunomodulating effect in patients with UC (23), so it is hard to say that this therapy is connected with interstitial pneumonia. No severe adverse effect was observed in this therapy (24), such as infection. However, steroids have an immunosuppressive effect, and patients treated with them for a long time sometimes suffer from opportunistic infections. In this patient, bacterial pneumonia complicated with interstitial pneumonia
deteriorated the condition. Interstitial pneumonia is quite a rare complication of ulcerative colitis, but the prognosis is quite poor. We must be mindful of this complication.

References