A broad spectrum of extra-intestinal manifestations can be associated with inflammatory bowel disease (1). Although pulmonary involvement is very rare, there were only six cases of unexplained bronchopulmonary disease in a review of 1,400 patients (2). However, recently, a variety of airway-related disorders, interstitial and pleural diseases have been reported in ulcerative colitis (3–26). The occurrence of these complications underscores the fact that inflammatory bowel disease is a systemic illness. We herewith describe two new cases of lung disorders with underlying ulcerative colitis.

Case Reports

Case 1

A 30-year-old woman, a non-smoker, had a 6-year history of ulcerative pancolitis which was being treated initially with sulfasalazine and prednisolone. Two years after persistent exacerbations of intestinal symptomatology she was admitted to Mie University Hospital Surgery Department where a total colectomy with protective loop ileostomy was carried out. Four months after her operation she started complaining of cough, purulent sputum (200–300 ml/day), dyspnea on exertion and anal bleeding. She was then admitted to our department. The patient looked chronically ill. Her temperature was 39.5°C, pulse rate 102 and 30 respirations per minute. Chest examination revealed diminished respiratory excursion and coarse crackles more intense in both lung bases. Rhinological examination revealed a chronic sinusitis. Laboratory data on admission were as follows: hemoglobin 11.9 g/dl, white blood cell count 16.8 × 10³/μl, 0.83 segmented cells, 0.12 lymphocytes, 0.04 monocytes and 0.01 eosinophils. The erythrocyte sedimentation rate was 110 mm/h, C-reactive protein was 6 mg/dl and cold hemagglutinins were positive at titer of 1:126. There was hypoalbuminemia with hyperimmunoglobulinemia. The serum level of lactic dehydrogenase was 479 IU/l (Normal range: 100–230), and of alkaline phosphatase 154 IU/l (Normal range: 30–105). The blood gas test revealed the following values: pH 7.48, oxygen pressure 62 mmHg, carbon dioxide 32 mmHg and arterial saturation 96%. Serological studies of antinuclear antibody, rheumatoid factor and syphilis gave negative results. Tuberculin skin test was negative. The conventional chest X-ray (Fig. 1a) revealed diffuse reticulo-nodular shadows with bilateral lower zone bronchial thickening and dilated bronchi. The chest radiography before her operation was normal. The CT scanning (Fig. 1b) showed bilateral and extensive bronchiectasis with micronodular shadowing in the interstitium, more preponderant in the middle and the lower lobes. Gallium scanning disclosed diffuse irregular distribution of the radioactive substance bilaterally. Pulmonary function test results (percentage of predicted values) were the following: vital capacity 86.9%, forced expiratory volume in one second 68%, DLco 62.8%.
Fig. 1. a) Chest X-ray on admission of the first case, revealed diffuse reticulo-nodular shadows with bilateral bronchial thickening and dilated bronchi in the lower bronchi. b) CT scanning showed extensive bronchiectasis with micronodular shadowing in the interstitium.

Fiberoptic bronchoscopic study showed bilateral bronchitis and the biopsic material taken during this procedure (Fig. 2) revealed thickness and fibrosis of the alveolar wall with lymphocyte and neutrophil infiltrations in the interstitium. She was treated with a regimen of postural drainage, antibiotics, prednisolone 30 mg/day and sulfasalazine 4 g/day. She responded satisfactorily to the therapy and was discharged with marked clinical and radiological improvements after one month (Fig. 3).

Case 2

A 72-year-old man was admitted to Mie University...

Fig. 2. Histological microphotograph (H.E.; x300) revealed thickness and fibrosis of the alveolar wall with interstitial lymphocyte and neutrophil infiltrations.

Fig. 3. a) left: first case, and b) right: second case. Improvement of chest radiological findings in both patients after one month of steroid therapy.
Lung Involvement in Ulcerative Colitis

Fig. 4. a) Chest X-ray of the second case showing diffuse infiltrates with predominant apical distribution. b) CT showing diffuse interstitial infiltrates and alveolar patchy shadows.

Hospital because of persistent high fever, abdominal pain and melena. He was diagnosed as having ulcerative pancolitis by endoscopic, barium-enema and biopsic studies. Conventional chest X-ray on admission (Fig. 4a) showed diffuse infiltrates in both lungs with predominant apical distribution. The computerized tomography on admission (Fig. 4b) showed interstitial infiltrates and alveolar patchy shadows diffusely distributed in both lung fields. He was being treated irregularly with non-steroidal antiinflammatory agents because of arthritis of the left knee and tarsometatarsal joints. There was no history of industrial exposure to dusts, chemical fumes or animals. Pulmonary symptomatology was absent. On examination the patient appeared chronically ill. The temperature was 39.0°C rectally, pulse rate 63 beats per minute and respirations 18/minute. Chest examination revealed a diffusely diminished breath sound in both lung fields; moist rales were absent. There were no cyanosis, finger clubbing or edema. Laboratory data on admission included the following: hemoglobin 9.8 g/dl, white blood cell count 14,31 × 10^3/μl, with 0.83 segmented cells, 0.13 lymphocytes, 0.02 monocytes and 0.02 eosinophils. The erythrocyte sedimentation rate was 135 mm/h, and the C-reactive protein, 15 mg/dl. Blood gas analysis revealed the following results: pH, 7.45, oxygen pressure, 61.6 mmHg; carbon dioxide pressure 35.2 mmHg and oxygen saturation 91.5%. The serum albumin was low with hyperimmunoglobulinemia. Serum level of lactic dehydrogenase was 165 IU/l (Normal range: 100–230), and of alkaline phosphatase 208 IU/l (Normal range: 30–105). Results of pulmonary function test were as follows: vital capacity 78% (percentage of predicted value), forced expiratory volume in one second 76%. Hemodynamic study revealed normal intracardiac pressures. Studies of antinuclear antibody, LE, rheumatoid factor, tests for syphilis and for viral infection were all negative. The tuberculin test produced no induration. Bronchoscopic study disclosed normal findings of both bronchial trees. Cytology and bacteriological studies of the bronchial lavage were negative for malignant cells, acid-fast bacilli and bacteria. Histological examination (Fig. 5) of the transbronchial biopsy showed alveolar wall thickening, interstitial fibrosis with lymphocyte and histiocyte infiltrations. The patient was followed up with sulfasalazine (4 g/day) and prednisolone (30 mg/day) while work-up of his fever and lung abnormality was carried out. Fever, colonic symptomatology and pulmonary infiltrates improved remarkably (Fig. 3b) after one month of therapy and the patient was discharged from the hospital. He was followed up in the out-patient clinic where a gradual tapering of steroid and sulfasalazine dosages was initiated. Seven months later an acute
deterioration of his ulcerative colitis without relapse of the interstitial disease occurred, necessitating the resumption of high daily doses of prednisolone therapy. He responded well again and over the subsequent months he was given maintenance doses of prednisolone 10 mg and sulfasalazine 3 g with good clinical evolution.

Discussion

Although numerous and varied systemic extraintestinal manifestations have been described during the course of inflammatory bowel disease, bronchopulmonary lesion is an infrequent complication of this disease (1–2). To date, including one case reported in the Japanese literature, there has been a total of 50 cases of pulmonary involvement in ulcerative colitis (3–26). The airway was the most commonly affected area with 33 cases (3–12). Interstitial pulmonary disease was diagnosed in 12 cases and pleuritis in the remaining 5 cases (13–26). Among the 33 reported cases of pulmonary involvement with airway disorders, there were 16 cases of bronchectasis, 13 with supplicative bronchitis, 1 with fibrotic obliterative bronchitis, 1 with sclerosing peribronchiolitis, and another case with diffuse panbronchiolitis (3–12). Women were more frequently affected than men, and age varied from 7 to 72 years old (4, 5). Cough and sputum were the most common symptoms that brought patients to consultation. Conventional chest X-ray disclosed infiltrative and cystic shadowing more prominent at bases in 20 cases, at both lung apices in 1 and normal findings in 12 cases. Pulmonary function test was carried out in 31 patients; the obstructive or mixed pattern with diminished values of transfer factor for carbon monoxide were more commonly encountered. While in 12 patients the pulmonary symptomatology appeared after the surgical treatment of the ulcerative colitis with an interval varying between 3 weeks and 12 years, in 5 cases the lung disease preceded the colonic presentation of inflammatory bowel disease (5, 6, 12). Other extraintestinal manifestations were also frequently found including arthritis in 9, skin lesions in 8, sinusitis and liver disease in 2 cases (3, 5, 7, 8). Twenty-three patients temporarily experienced clinical improvement with steroid therapy, whereas 2 patients improved after colectomy. The present first case was a young woman who complained of cough with bronchial and sinus suppuration 7 months after a total colectomy, diffuse bronchi and granular shadows preponderantly basilar and with a functionally obstructive lung. Histological findings of the transbronchoscopic biopsy were consistent with chronic interstitial pneumonia. Considering the time relationship between the exacerbation of her proctitis and the appearance of the pulmonary symptomatology, the lack of other causative factors of her lung disease and the good long-term clinical evolution after steroid therapy, we believe this case corresponded to another example of multi-systemic manifestation associated with ulcerative colitis.

To our knowledge interstitial lung disease has been reported in only 12 cases of ulcerative colitis (13–23). Among these cases, 6 presented pulmonary vasculitis, 6 diffuse interstitial lung fibrosis and another case of apical pulmonary fibrosis. Histological confirmation of the lesion was obtained in only 10 cases (13–15, 17–22). Of these, 2 cases showed pathological description compatible with Wegener's granulomatosis. Pulmonary function test was performed in 5 cases, of which 4 presented characteristic restrictive pattern (19–23). Diverse chest radiological findings were described. Diffuse pulmonary infiltrates more conspicuous in the lower zones of the lungs were observed in 8 cases, bilateral pulmonary nodular lesions in 2, pleural effusion or thickening in 5 and unilateral apical pulmonary fibrosis in 1 case. In each of 8 patients there was a history of sulfasalazine therapy for their colonic affection. Of these, 6 patients were taking this drug when the pulmonary symptoms appeared, and though withdrawal of sulfasalazine was carried out, the pulmonary lesions did not regress (14, 20, 21). Pulmonary lesions did regress in 5 patients with the administration of corticosteroids, in 1 after the surgical treatment of ulcerative colitis and in another case the improvement was spontaneous. In the second case of the current report, the pulmonary disorder commenced coincidentally with his ulcerative colitis and ameliorated dramatically with the corticosteroid therapy. Our diagnosis was ulcerative colitis-related lung interstitial disease.

The occurrence of pulmonary disorders in patients with inflammatory bowel disease poses a controversial issue of whether these entities are truly associated or they only represent the casual occurrence of two unrelated disorders. In the current report, the onset of lung complications paralleled flares of ulcerative colitis and, thus, favored the idea that true association might have existed between them. A review of the literature shows also the presence of temporal correlation between the states of activity of both diseases (3, 5, 9). Furthermore, in some of the reported cases, clinical and laboratory improvements were seen following colectomy as was mentioned before (5). The simultaneous beneficial effects of corticosteroid therapy for ulcerative colitis and pulmonary lesion experienced in the present two cases and in others previously described, are likewise suggestive that they respond to the same etiopathogenetic mechanism (5, 22).

The significance of the coexistence of these diseases was also the object of various clinical investigations. Eade et al reported a significant reduction of carbon monoxide transfer factor as the only abnormality in inflammatory bowel disease patients in an age-matched control study. The results were not related to either sulfasalazine therapy or disease activity (27). Pasquis et al with a similar study design, found greater values of functional residual capacity during the attack than in
remission of intestinal disease (28). It is also of interest to note that Bonnier et al found a persistent increased lymphocytosis in the bronchoalveolar lavage of those patients with normal clinical or radiological studies. The degree of this lymphocyte alveolitis was uncorrelated with abnormalities in functional tests of the lung (29).

Based upon these studies, there appears to be a latent lung involvement that might somehow be linked to the changes occurring in the underlying bowel disease. The demonstration of this subclinical lung damage lays the basis for the hypothesis that both disorders might represent the expressions of the same systemic disease resulting from the host’s response to a common etiological agent.

In brief, considering the therapeutic and prognostic implications in the occurrence of lung disorders, we believe that there is justifiable rationale to advocate a periodical work-up for earlier diagnosis of this potential complication in inflammatory bowel disease patients, even though the pathogenetic mechanism of both disorders as well as their interrelationship are, as yet, unestablished. New reports of cases with such as association should encourage further investigation to enlighten this challenging aspect of inflammatory bowel disease.

References


