An autopsy case of diffuse panbronchiolitis accompanying rheumatoid arthritis

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Introduction

Diffuse panbronchiolitis is a clinicopathological entity with the characteristics of chronic recurrent sinopulmonary infection, respiratory bronchiolitis, and peribronchiolitis that are diffusely disseminated throughout the bilateral lungs, especially in the lower lobes (1,2). This disorder is prevalent in Japan but rare in America and Europe. Chronic cough, copious sputum and dyspnoea on exertion are frequent complicating symptoms. The radiographic findings consist of diffusely disseminated fine nodular shadows in the lower lung fields, and hyperinflation of the lungs. Slight bronchiectasis, which appears as tramlines, usually develops in the middle lobe and lingula. In advanced cases, bronchiectasis sometimes extends throughout all lung fields. The respiratory function tests reveal marked obstructive and slight restrictive impairment.

In patients with rheumatoid arthritis, various lung involvements have been described, including rheumatoid nodules, lymphoid hyperplasia (follicular bronchitis/bronchiolitis), usual interstitial pneumonia, desquamative interstitial pneumonia, cellular interstitial pneumonia, bronchiolitis obliterans with organizing pneumonia, and diffuse alveolar damage (3). We report herein an autopsy case of diffuse panbronchiolitis accompanied by rheumatoid arthritis.

Case Report

A 67-year-old Japanese woman, a non-smoker, was admitted to our hospital because of abundant yellow sputum, chronic cough and exertional dyspnoea. It was her eighth admission. About 15 yr previously, she had noted bilateral knee joint pain and swelling, and morning stiffness of the bilateral knee joints and fingers. At that time, rheumatoid factor was positive and she had been diagnosed as having classical rheumatoid arthritis. She was thereafter treated with non-steroidal anti-inflammatory drugs, prednisolone (5–15 mg day⁻¹), D-penicillamine and gold. For the 5 yr preceding her most recent admission, she had had chronic yellow sputum and cough, and she had been diagnosed with chronic bronchitis. Haemophilus influenzae had been detected in her sputum 2 yr previously, and, at this admission, Pseudomonas aeruginosa was found. Physical examination disclosed a dyspneic and deteriorated woman with muscle atrophy and ulnar deviation of the fingers. Course crackles and wheezes could be heard in her bilateral lungs on auscultation.

Her chest X-ray film revealed hyperinflation of both lungs. The laboratory data were as follows: white blood cell count, 11 000 mm⁻³; erythrocyte sedimentation rate, 97 mm h⁻¹; and C-reactive protein, (+ + + +). Pulmonary function tests revealed a mixed type impairment with VC, 1.19 l (57.9% of predicted); FEV₁, 0.55 l; FEV₁/FVC, 66.3%; RV, 1.57 l; RV/TLC, 56.9%. Arterial blood gas analysis disclosed hypoxaemia with pH of 7.459, PaCO₂ of 33.3 Torr, and PaO₂ of 64.0 Torr. During the hospitalization, prednisolone, diuretics, antibiotics, albumin and oxygen were administered. Her respiratory insufficiency continued to progress and she died 1 month after admission.

PATHOLOGICAL FINDINGS FOR THE AUTOPSIED LUNGS

The lungs were well aerated and soft (left, 250 g; right, 340 g). No pleural adhesion was observed. On the cut surfaces, miliary-sized yellowish foci, which are the characteristic gross feature of diffuse panbronchiolitis, were found diffusely scattered in both lungs, being especially dense in the left lower lobe. No fibrotic nodules were seen. Occasional mild ectasis of the subsegmental bronchus was found.
Plate 1 The respiratory bronchiolar wall is thickened with lymphocytic infiltration. The bronchiolar lumen is obliterated by a purulent plug. Small polypoid granulation tissues are seen at the junction of the respiratory bronchiole and alveolar duct. Marked anthracosis and slight foam cell accumulation are observed in the peribronchiolar interstitium. No remarkable change is noted in the alveolar wall. (HE, magnification × 26.4)

Plate 2 A polypoid granulation tissue is formed in the constricted lumen of the respiratory bronchiole. Marked foam cell accumulation is seen in the peribronchiolar interstitium and associated with centrilobular emphysema. (HE, magnification × 32)

Histologically, the respiratory bronchiolar walls were thickened with round cell infiltration and fibrosis. Their lumina were constricted and/or obliterated by granulation tissue and purulent plugs. Accumulation of foamy histiocytes and anthracosis were prominent in the peribronchiolar interstitium and focally associated with moderate centrilobular emphysema (Plates 1, 2). The inflammatory lesions were restricted to the bronchiolo-alveolar junction, or transitional zone of the lung (1). Neither alveolitis nor peribroncho-bronchiolar lymphoid follicle were observed. These histological findings established the diagnosis of diffuse panbronchiolitis. The pathological findings could be distinguished from other pulmonary manifestations of rheumatoid arthritis, i.e. follicular bronchitis/bronchiolitis, usual interstitial pneumonia, desquamative interstitial pneumonia, bronchiolitis obliterans with organizing pneumonia, and diffuse alveolar damage (3).
OTHER NECROSCOPIC FINDINGS

The heart (350 g) showed mild left ventricular hypertrophy. There was no endocarditis. Congestion and centriobular cell necrosis of the liver with nutmeg appearance was found. The kidneys (left, 80 g; right, 80 g) presented arteriolosclerotic contraction with fine-granular surface. Ulnar flexion of the bilateral wrist joint due to absorption of the ulnar head was found. Ulceration of the joint cartilage of the femur and tibia was also found.

Discussion

This case is the first reported case to our knowledge of histologically confirmed diffuse panbronchiolitis in a patient with rheumatoid arthritis. Diffuse panbronchiolitis is a unique disease, which is found mainly in Japanese and rarely in other ethnic groups (4). The characteristic findings of this disease are chronic sino-pulmonary infection with obstructive or mixed type pulmonary function test impairment, and the characteristic histological feature of bronchiolitis without alveolitis (1,2).

Diffuse panbronchiolitis can be accompanied by various diseases including ulcerative colitis (5). Recently, rheumatoid arthritis was also recognized as a disease accompanied by diffuse panbronchiolitis. We reported two such cases together with HLA analysis (6). In our HLA analysis, both cases showed the same haplotype, A24-B54-Cw1-DR4, and this haplotype is recognized as a common haplotype in both diffuse panbronchiolitis (4) and rheumatoid arthritis (7) in Japan. Since both of these diseases have the same HLA haplotype in common, it may not be surprising to find the two diseases in association with each other.

On the other hand, almost all patients with diffuse panbronchiolitis have continuous elevation of cold haemoagglutinin (a kind of auto-antibody) titre. The characteristic histological feature of diffuse panbronchiolitis is the infiltration of lymphocytes around the respiratory bronchioli. Thus, it might be suggested that diffuse panbronchiolitis is in some respects an immunological disease, particularly in its pathogenesis.

Rheumatoid arthritis is accompanied by various lung involvements. Yousem et al., in a report describing the open lung biopsy results in 40 patients with rheumatoid arthritis, noted that the main histologic pattern was classic rheumatoid nodules, lymphoid hyperplasia, usual interstitial pneumonia, cellular interstitial pneumonia, bronchiolitis obliterans with organizing pneumonia, and diffuse alveolar damage (3). The pathological findings in our case could be distinguished from these conditions. In this case, gold and penicillamine therapy had been administered. Gold is known to induce diffuse interstitial pneumonitis and fibrosis (8). Bronchiolitis obliterans has been reported following penicillamine therapy (9). These conditions could also be distinguished.

Rheumatoid arthritis is a disease widely distributed throughout the world, but diffuse panbronchiolitis is a very rare disease except in Japanese, Chinese and Korean individuals (4). This may explain why no cases of rheumatoid arthritis accompanied by diffuse panbronchiolitis have yet been described in the English literature. Our analysis revealed that 4 (7.1%) of our 56 cases of diffuse panbronchiolitis were accompanied by rheumatoid arthritis (6). Diffuse panbronchiolitis should be kept in mind as a pulmonary complication of rheumatoid arthritis in individuals with Japanese, Chinese, and/or Korean heritage.

References