CASE REPORT

Combined Pulmonary Fibrosis and Emphysema Preceding Lupus Pleuritis

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Abstract

An 83-year-old man, who was a former smoker, with anti-ribonucleoprotein (RNP) antibody-positive combined pulmonary fibrosis and emphysema presented with a cough and dyspnea. A chest radiograph showed bilateral pleural effusions. His laboratory data showed proteinuria and elevated levels of anti-nuclear antibodies, anti-double strand DNA antibodies, and CA125, with decreased serum complement levels. Thoracentesis showed an exudative pleural effusion with an increased lymphocyte count and elevated CA125 levels. A thoracoscopic biopsy specimen showed proliferation of CA125-positive mesothelial cells. Systemic lupus erythematosus was diagnosed. His symptoms and pleural effusion resolved after the initiation of systemic corticosteroid therapy. The detection of anti-RNP antibody and CA125 levels are helpful in the diagnosis of lupus pleuritis.

Key words: combined pulmonary fibrosis and emphysema, systemic lupus erythematosus, lupus pleuritis, anti-ribonucleoprotein antibody, CA125


Introduction

It is known that interstitial pneumonia can precede various connective tissue diseases such as rheumatoid arthritis, microscopic polyangiitis, and systemic sclerosis (1, 2). However, interstitial pneumonia preceding systemic lupus erythematosus (SLE) is rare (3). We herein describe a case of anti-ribonucleoprotein (RNP) antibody-positive combined pulmonary fibrosis and emphysema (CPFE) which preceded SLE. In addition, the significance of the detection of anti-RNP antibody and the serum and pleural fluid levels of CA125 in the diagnosis of lupus pleuritis is discussed.

Case Report

An 83-year-old man was referred to our hospital for a detailed examination after abnormal shadows were detected on chest radiography as part of a mass screening examination. The patient was asymptomatic; however, he had a 30-pack-year history of smoking. His personal history included gastric cancer and postoperative ileus. On physical examination, he had digital clubbing, and fine crackles were audible in both lungs. The laboratory data showed normal urinalysis and arterial blood gas analysis and elevated serum levels of immunoglobulin G (2,145 mg/dL), KL-6 (808 U/mL), surfactant protein (SP)-D (214.0 ng/mL), antinuclear antibody (×40, speckled pattern), and anti-RNP antibody (14.4 U/mL). The results of respiratory function testing were as follows: vital capacity, 2.90 L (predicted: 92.9%); forced expiratory volume in 1 second, 2.70 L (predicted: 128%); and diffusion capacity of the lung for carbon monoxide, 8.18 mL/min/mmHg (predicted 57.5%). A chest radiograph showed hyperinflation and reticular shadows in both lung fields (Fig. 1A). Chest computed tomography showed upper lobe emphysema (Fig. 1B) and bilateral basilar honeycombing (Fig. 1C), suggesting CPFE with the usual interstitial pneumonia (UIP) pattern. Bronchoalveolar lavage showed neutrophilia (16.1%) with normal counts of other cells. A transbronchial lung biopsy did not yield a diagnosis. Based on the diagnosis of CPFE, he was followed up without any treatment because he was elderly and asymptomatic. How-

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ever, 8 months later, he began to complain of cough and dyspnea, and he was referred to our hospital again. The physical examination was similar to that at the initial presentation, and no edema was observed. The laboratory data showed proteinuria (1.0 g/day) with granular casts, elevated serum levels of C-reactive protein (1.1 mg/dL), immunoglobulin (Ig) G (2,797 mg/dL), antinuclear antibody (×320, cytoplasmic pattern), and anti-double strand DNA antibody (13 IU/mL), with decreased serum levels of complement (22.5 U/mL), complement C3 (84 mg/dL), and C4 (11 mg/dL). The serum levels of KL-6, SP-D, and anti-RNP antibody were elevated to the same degree as at the initial presentation, and his renal function was normal. A chest radiograph (Fig. 2A) and chest computed tomography (Fig. 2B, C) showed bilateral pleural effusions. On diagnostic thoracentesis, a yellowish cloudy exudative pleural effusion was observed, with predominant lymphocytes and elevated levels of adenosine deaminase (99.0 U/L), antinuclear antibody (×320, cytoplasmic pattern), IgG (2,770 mg/dL), and CA125 (2,030.0 U/mL) and decreased levels of complement (<12.0 U/mL), C3 (25 mg/dL), and C4 (2 mg/dL). No malignant cells were observed. A thoracoscopic biopsy specimen obtained from the right parietal pleura to exclude tuberculosis revealed the proliferation of mesothelial cells and mild lymphoplasmacytic cell infiltration (Fig. 3A). The cytoplasm of the mesothelial cells was immunohistochemically positive for IgG, C3, and CA125 (Fig. 3B-D). The patient was diagnosed with SLE according to the 1997 American College of Rheumatology classification criteria for SLE, and corticosteroid therapy (prednisolone 30 mg/day) was initiated. His symptoms and pleural effusion gradually disappeared, and his prednisolone dose was tapered. The serum levels of CA125, IgG, C3, C4, KL-6, and SP-D, normalized.

**Discussion**

Concomitant idiopathic pulmonary fibrosis (IPF) and emphysema have been reported and characterized as a distinct entity, the syndrome of CPFE (4). The syndrome of CPFE is not an established disease, it deserves to be considered as a syndrome due to the associated symptoms and clinical manifestations, with the probability of each being present increased by the presence of the others. The syndrome of CPFE results from the association of distinct features, including tobacco smoking, severe dyspnea, unexpected subnormal spirometry findings, severely impaired transfer of carbon monoxide, hypoxemia with exercise, and characteristic imaging features (emphysema of the upper lobes and fibrosis of the lower lobes).

Previous reports have demonstrated that interstitial pneumonia can precede various connective tissue diseases (CTD) such as rheumatoid arthritis, microscopic polyangiitis, and systemic sclerosis (1, 2). In addition, Tzouvelekis et al. reported that, in comparison to IPF patients, significantly higher number of CPFE patients had autoantibody positivity, and that the massive infiltration of clusters of CD20-positive B cells forming lymphoid follicles within the fibrotic lung was more frequently observed in CPFE patients with a positive serum immunologic profile than in those with a negative profile (5). They speculated that repetitive injurious stimuli including smoking and/or viruses might cause this process, and that it might last for prolonged periods of time.

![Figure 1](image_url)

**Figure 1.** A chest radiograph taken at the patient’s initial presentation showing hyperinflation and reticular shadows in both lungs (A). Chest computed tomography showing upper lobe emphysema (B) and honeycombing changes in the lower lobes of both lungs (C).
even after the cessation of smoking, leading to antibody production and the development of CTD in some patients with CPFE. In the present case, several serum autoantibodies were detected, and computed tomography of the chest showed emphysema and UIP pattern; however the symptoms and findings of connective tissue diseases were not evident.
at the initial presentation. Therefore, the patient, who fulfilled the criteria of lung-dominant CTD at the time, could be also diagnosed with CPFE (6). SLE developed 8 months later. To the best of our knowledge, this is the first reported case of CPFE preceding SLE. The relationship between CPFE and SLE may be coincidental, because interstitial pneumonia preceding SLE is rare, and CPFE was not aggravated when the lupus pleuritis was evident. Although immunohistochemical studies of lung biopsy specimens were not performed in this case, ongoing chronic inflammation that consists mainly of B cells that can switch isotype and which produce autoantibodies in the fibrotic lung of CPFE patients might be involved in the development of SLE, as described by Tzouvelekis et al. In regard to these points, CTD may develop in a patient with CPFE, but CPFE does not appear to be a lung manifestation of CTD.

Previous studies have demonstrated a relationship between autoantibody profiles and the specific disease manifestations of SLE (7-9). Some reports demonstrated a possible association between anti-RNP antibodies and lupus serositis (7, 8). The findings suggest that the development of lupus serositis should be considered in patients with anti-RNP antibody-positive interstitial pneumonia. Information about the pathogenesis and histological findings of lupus pleuritis is still limited. A few studies demonstrated the pleural deposition of immunoglobulin and C3 (10). Similarly, the deposition of IgG and C3 in proliferated mesothelial cells was observed in the present case. In addition, CA125, which is reported to be elevated in the serum and the serofluid of lupus serositis (11, 12), was detected in the proliferated mesothelial cells. Based on these observations, the elevation of CA125 levels in both the serum and the serofluid of patients with lupus serositis may be attributable to the proliferation of mesothelial cells, probably resulting from chronic pleural inflammation through an immunological process in lupus serositis.

In conclusion, we herein reported a case of lupus pleuritis following CPFE. Physicians might need to consider the development of lupus serositis in patients with anti-RNP antibody-positive interstitial pneumonia. Determining both the serum and serofluid CA125 levels is thus considered to be helpful in the diagnosis of lupus serositis.

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

References