Acute Pulmonary Thromboembolism Associated with Interstitial Pneumonia

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Abstract

A 68-year-old woman, who had been diagnosed as idiopathic interstitial pneumonia, complained of progressive dyspnea on exertion for a week. Although her chest radiograph did not worsen, arterial blood gas findings were markedly worsened. Contrast-enhanced chest computed tomography showed filling defects of the right upper and middle lobe branches of the pulmonary artery. She was diagnosed as having acute pulmonary thromboembolism (APTE). Clinical symptoms and contrast-enhanced chest computed tomography findings were remarkably improved after the treatment with heparin and urokinase. APTE should be considered as a differential diagnosis in patients with interstitial pneumonia who have worsening of respiratory symptoms with unchanged chest radiograph.

Key words: interstitial pneumonia, acute pulmonary thromboembolism, pulmonary infarction

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Introduction

Acute pulmonary thromboembolism (APTE) has been reported to be one of the causes of clinical deterioration in patients with interstitial pneumonia (1). Recent studies have demonstrated that patients with interstitial pneumonia may have coagulation-fibrinolytic disorders (2, 3). Here, we report a case of APTE associated with interstitial pneumonia. We also describe possible mechanisms of thrombus formation in patient with interstitial pneumonia.

Case Report

A 68-year-old woman, who had been diagnosed as fibrotic non-specific interstitial pneumonia according to findings of video-assisted thoracoscopic lung biopsy, complained of progressive dyspnea on exertion for a week. She was observed carefully without systemic corticosteroid therapy. Physical examination revealed a body mass index of 21.5 kg/m², a respiratory rate of 20 breaths/min, a pulse rate of 66 beats/min, and a blood pressure of 136/84 mmHg. Ausculation of the heart and lung showed an enhancement of the second heart sound and bibasilar fine crackles on the back. Her jugular veins were distended. Laboratory examinations disclosed increased levels of lactate dehydrogenase (318 IU/L), C-reactive protein (0.6 mg/dl), KL-6 (2,330 U/ml), SP-D (412 ng/ml), D-dimer (5.6 μg/ml), and TAT (3.1 ng/ml). However, KL-6 level remained high compared with 1 month earlier (2,270 U/ml). PaO₂ and PaCO₂ changed from 84 mmHg and 37.3 mmHg to 51 mmHg and 31.9 mmHg, compared with 1 month previously. Echocardiography demonstrated dilatation of the right atrium and ventricle with normal wall thicknesses, a leftward shift of the interventricular septum, and lack of inferior vena cava collapse during inspiration. Color doppler echocardiography demonstrated mild tricuspid regurgitation and the estimated pulmonary artery systolic pressure was 47 mmHg, suggesting mild pulmonary hypertension. Electrocardiography demonstrated T wave inversion in leads V₁-V₄ and III and S wave in leads V₅ and V₆ (Fig. 1). Chest radiograph 3 months before admission showed diffuse bilateral reticulo-nodular opacities predominantly in the lower lung fields, and enlargement of the proximal portion of the pulmonary artery (Fig. 2A). Chest radiograph on admission showed almost no change except for the appearance of a nodule (1 cm in diameter) in
Figure 1. A: Electrocardiography one year before admission. B: Electrocardiography on admission, showing an appearance of T wave inversion in leads V1-V4 compared with electrocardiography one year before admission.

Figure 2. A: Chest radiograph 3 months before admission. B: Chest radiograph on admission, showing an appearance of a nodule of 1 cm in diameter in the right middle lung field (arrow).

the right middle lung field (Fig. 2B). Contrast-enhanced chest computed tomography (CT) demonstrated filling defects of the right upper and middle lobe branches of the pulmonary artery (Fig. 3A). Chest high-resolution computed tomography (HRCT) showed ground-glass opacities with honeycombing and traction bronchiectasis predominantly in the subpleural region of both lower lobes. Ground glass opacities were almost unchanged in comparison with those 3 months before admission. In addition, a mass lesion of 1 cm in diameter was newly found in the right S2 segment (Fig. 3B). Coronal images revealed a wedge-shaped consolidation originating from pulmonary artery above the horizontal fissure of the right lung (Fig. 3C). Follow-up CT revealed disappearance of this shadow, suggesting a presence of pulmonary infarction. A perfusion lung scintigram on admission showed multiple segmental and subsegmental deficits in both lungs, particularly in most of the right upper lobe (Fig. 4A). On the basis of these findings, she was diagnosed as having pulmonary thromboembolism with pulmonary infarction.

Under oxygen administration, combined therapy using heparin and urokinase was started because of echocardiographic evidence of right ventricular dysfunction and the presence of underlying pulmonary disease. Urokinase (48×10^4 units/day) was administered for 7 days. The dose of heparin was titrated against the measurement of activated partial thromboplastin time (APTT) which is maintained at 1.5 times the control value. Warfarin therapy was initiated at 4 mg/day on the 5th hospital day, and maintained at 2.5 mg/day. After starting heparin, her symptoms were quickly re-
Figure 3. Contrast-enhanced chest computed tomography (CT) on admission (A-C). A: The mediastinal window revealed filling defects in the right upper and middle lobe pulmonary artery (arrow). B: The lung window revealed a mass lesion of 1 cm in diameter in the right S2 segment (arrow). C: Coronal images revealed a wedge-shaped consolidation originating from pulmonary artery above the horizontal fissure of the right lung (arrow). D: Follow-up CT after treatment showed considerable improvement (arrow).

Figure 4. A: A perfusion lung scintigram on admission showed multiple segmental and subsegmental deficits in both lungs, particularly in most of the right upper lobe. B, C: A perfusion lung scintigram after treatment showed an improvement of the right upper lung field. D: A ventilation scan was nearly normal.
lieved. Repeat contrast-enhanced chest CT (Fig. 3D) and a perfusion lung scintigram (Fig. 4B, C) on the 7th hospital day showed considerable improvement. Echocardiography on the 8th hospital day showed improvement of the estimated pulmonary artery systolic pressure from 47 mmHg to 36 mmHg. Arterial blood gas analysis under room air on the 21st hospital day also showed improvement (PaO₂ and PaCO₂ changed from 51 mmHg and 31.9 mmHg to 82 mmHg and 38.9 mmHg, respectively). Deep venous thrombosis was not detected by ultrasonography of lower limbs and pelvis on the 7th hospital day. In addition, there was no persisting underlying risk factors or thrombotic disorder such as deficiency of antithrombin III, protein C, protein S, or the presence of lupus anticoagulant.

**Discussion**

Pulmonary thromboembolism has been reported to be associated with prominent interstitial fibrosis at autopsy (4). King reported that 3-7% of patients with idiopathic pulmonary fibrosis (IPF) died of pulmonary thromboembolism and major risk factors for pulmonary thromboembolism include reduced mobility, heart failure, malignant diseases, and steroid administration (1). But reports of pulmonary thromboembolism associated with IPF are rare in Japan. To our knowledge, only 3 cases have been reported in Japan (5-7). Shishido et al reported a case of IPF associated with bilateral pulmonary arterial thrombosis which was found at autopsy. The patient was treated with steroids because of suspicion of exacerbation of IPF, and she died suddenly after 16 days treatment. An autopsy revealed large thrombi in both pulmonary arteries (5). Thus, if pulmonary thromboembolism goes unrecognized, the outcome can be fatal.

The reason why patients with idiopathic interstitial pneumonias might be more predisposed to pulmonary thromboembolism is uncertain. A possible mechanism is coagulation-fibrinolytic disorder. Nagata has reported that patients with respiratory failure have hypercoagulability and that 27% of patients had associated pulmonary thromboembolism. They also reported that patients with interstitial pneumonia who do not have associated respiratory failure do have decreased levels of antithrombin III and α₂ plasmin inhibitor, leading to hypercoagulability (2). Yanai reported that endothelial damage in pulmonary microvessels and hypoxemia caused increased coagulation and decreased fibrinolysis, resulting in increased thrombus formation in patients with interstitial pneumonia (3). It should be particularly emphasized that pulmonary thromboembolism is important because most cases with APTE are treatable. Therefore, APTE should be considered as a differential diagnosis in patients with interstitial pneumonia who have an acute decrease in PaO₂ and an increase in D-dimer level with unchanged chest radiograph and KL-6 level.

**References**