Refractory Pneumothorax Secondary to Lung Cancer in a Patient with Idiopathic Pulmonary Fibrosis

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Abstract

An unusual case of refractory pneumothorax secondary to lung cancer in a 69-year-old man patient with idiopathic pulmonary fibrosis (IPF) is described. High-pressure suction applied through chest tube did not resolve the large right pneumothorax. Acute exacerbation of IPF has also appeared. Respiratory state worsened acutely, and the patient died on the fifth hospital day. In the present case, the large right pneumothorax was initially thought to be associated with IPF because pneumothorax is common in patients with IPF. However, postmortem microscopic examination revealed that the refractory pneumothorax was secondary to perforation of the pleura due to a necrotic peripheral lung cancer.

Key words: refractory pneumothorax, lung cancer, idiopathic pulmonary fibrosis, acute exacerbation

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Introduction

Idiopathic pulmonary fibrosis (IPF) is associated with an increased risk of lung cancer (1-6), and primary lung cancer can cause secondary pneumothorax (7-9). To the best of our knowledge, however, no case of pneumothorax secondary to primary lung cancer on a background of IPF has been reported.

Case Report

A 69-year-old man was admitted to Ehime University Hospital in mid-July, 2003 for sudden onset of right-sided chest pain and dyspnea. IPF had been diagnosed in 2001, and long-term oxygen therapy was started on May 24, 2003. The patient suffered fever and dyspnea for 3 days before admission. Upon admission, he showed mild high blood pressure (156/84 mmHg), tachypnea (30 breaths/min), and sinus tachycardia (104 beats per minute). Chest X-ray revealed a large right pneumothorax and a leftward mediastinal shift, suggesting tension pneumothorax (Fig. 1). There was also a new consolidation in the left middle lung field. Chest computed tomography (CT) revealed a right pneumothorax and multiple subpleural bullae secondary to usual interstitial pneumonia (Fig. 2). In addition, an area of ground-glass attenuation was evident in the lower left lung. Laboratory tests revealed that the white blood cell count, C-reactive protein concentration, and lactate dehydrogenase level were elevated to 12,200/μL; 32.34 mg/dL; and 338 IU/L, respectively. The serum KL-6 concentration was 447 U/mL. Arterial blood gas values, obtained with the patient breathing oxygen at 2 L/minute through a face mask, were as follows: pH 7.385, PaO₂ 26.6 mmHg, and PaCO₂ 37.4 mmHg. Acute respiratory failure due to right tension pneumothorax on a background of IPF and community-acquired pneumonia in the left lung were tentatively diagnosed. A thoracotomy tube was placed in the right thorax, and low-pressure suction (10 cmH₂O) was applied through the chest tube. Antibiotic therapy with meropenem and minocycline was also started. The next day, the right lung collapse did not improve despite high-pressure suction (20 cmH₂O) through the chest tube; neither did the hypoxia improve. Chest CT showed expansion of the area of ground-glass opacity, leading to a diagnosis of acute exacerbation of IPF. Methylprednisolone pulse therapy (1 g/day for 3 days) and sivelestat sodium hy-
Figure 1. Chest X-ray film obtained 2 months before admission (A) and upon admission (B). A: Chest X-ray obtained 2 months before admission revealed volume loss of both lungs and a reticular shadow in the lower lung field that was compatible with IPF. B: Chest X-ray upon admission revealed large right pneumothorax and a shift of the mediastinum to the left.

Figure 2. Chest computed tomography scan 2 months before admission (A) and upon admission (B). A: Chest computed tomography (CT) CT obtained 2 months before admission revealed that reticulation and honeycombing were predominantly evident at the subpleural space, compatible with the IPF. B: Chest CT revealed right pneumothorax and multiple subpleural bullae secondary to typical interstitial pneumonia.

drinate (200 mg/day) were started. On the third hospital day, a second thoracotomy tube was used due to a persistent air leak. Because the respiratory failure progressed despite therapy, we planned to initiate mechanical ventilation; however, the patient and his family refused intratracheal intubation. His condition continued to worsen, and he died on the fifth hospital day.

Autopsy specimens revealed diffuse fibrotic changes in both lungs and honeycombing of the lower lungs. Microscopic examination showed a large perforation defect in the pleura of the right lower lobe due to a necrotic lung tumor, diagnosed as moderately differentiated squamous cell carcinoma (Figs. 3A, 3B). Elastica Van Gieson stain of the specimen showed the torn elastic laminae in part of the defect (Fig. 3C). There was no evidence of perforation by subpleural bullae due to IPF. Moreover, diffuse alveolar damage (DAD) was evident in both lungs. Exudate of proteinous material in alveolar spaces and prominent hyaline membranes lining alveolar ducts were found. The alveolar interstitium was mildly to moderately thickened by mature fibrous tissue and occasional lymphocytes (Fig. 4). We reviewed a chest CT film obtained on May 26, 2003 and found a 3 cm-sized tumor shadow in the right lung base (Fig. 5). We concluded that primary lung cancer had perforated the right lower lobe, leading to secondary pneumothorax and acute exacerbation of the IPF.

Discussion

The refractory pneumothorax we encountered was rare in that it resulted from a perforation defect in the pleura caused by a necrotic malignant tumor associated with IPF. Acute exacerbation of the IPF was also noted. To the best of our knowledge, this is the first such case to be reported.

We should be aware that IPF can be complicated by lung cancer; the risk of lung cancer is increased in patients with
Figure 3. Microscopic findings of the right lower lobe obtained at autopsy. (A: Hematoxylin and Eosin staining, loupe, B: Hematoxylin and Eosin staining, ×40, C: Elastica Van Gieson. ×40). A: Microscopic examination revealed a large defective perforation (arrow heads). B: Microscopic examination revealed a large defective perforation of the pleura due to tumor necrosis and moderately differentiated squamous cell carcinoma proximal to the perforation (Hematoxylin and Eosin staining, ×40). C: Elastica Van Gieson stain of the specimen showed the torn elastic laminae in part of the defect (×40).

Figure 4. Microscopic findings showing diffuse alveolar damage. A: Left lower lobe (Hematoxylin and Eosin staining ×40), B: Right lower lobe (Hematoxylin and Eosin staining ×40). There were exudate of proteinous material in alveolar spaces and prominent hyaline membranes lining alveolar ducts. The alveolar interstitium is mildly to moderately thickened by mature fibrous tissue and occasional lymphocytes. These findings were compatible with diffuse alveolar damage.

Figure 5. Chest CT scan obtained 2 months before admission. Upon review, a tumor shadow was seen in the right lung base with cavity formation.

IPF (1-4, 10). In the majority of studies of lung cancer associated with IPF, lung carcinomas were peripheral (1, 2, 5, 6), located in the lower lobes (1, 2), and 65% were topographically associated with honeycombed areas or in the border between honeycombed and non-fibrotic areas (2). These findings are in accordance with the distribution of the severe fibrotic lesions in patients with IPF, implicating the inflammatory process and bronchiolar squamous metaplasia in the pathogenesis of lung cancer. Squamous cell carcinoma was found to be the most common histologic type (35-47%) (1, 4-6). In the present case, the perforating tumor was squamous cell carcinoma of the lung, and it was located in the area of fibrotic change in the right lung base. Review of a previously obtained chest CT film showed a tumor in the right lung base corresponding to microscopic findings.

Pneumothorax is a rare manifestation of lung cancer, although it can be the initial sign (11-13). According to previous reports, 0.03-0.85% of lung cancers cause pneumothorax (11-14). Three mechanisms have been suggested to explain how pneumothorax occurs secondary to malignant tumor (8, 9, 11). First, spontaneous rupture of a necrotic tumor or rupture as a result of oncological treatment causes communication between the bronchus and the pleural cavity; second, tumor nodules in the periphery of the lung cause a ball-valve action, which overdistends the lung to form sub-
pleural bullae, leading to rupture; and third, in rare cases, the tumor spreads to the pleura itself. In the present case, the large right pneumothorax was initially thought to be associated with IPF because pneumothorax is common in patients with IPF (15). However, autopsy proved that the right pneumothorax resulted from perforation of the pleura caused by a necrotic squamous cell carcinoma. Steinhäuslin and Cuttat reviewed 46 cases of spontaneous pneumothorax due to primary lung cancer and found a predominance of squamous cell carcinomas (50%) (11). Squamous cell carcinoma, which has a necrotic tendency, is the histopathological type of lung cancer typically associated with secondary pneumothorax (11, 16).

As previously reported, some patients with IPF experience rapid deterioration secondary to infection, pneumothorax, pulmonary embolism, or heart failure (17). In the present case, although community-acquired pneumonia was tentatively diagnosed on admission, postmortem examination showed DAD pattern without evidence of bacterial pneumonia. However, we thought that there was at least acute airway infection at the time of the admission because he suffered from dyspnea and fever for 3 days prior to admission. In addition, pneumothorax can cause acute exacerbation of IPF. Airway infection and pneumothorax could have caused an exacerbation of IPF.

Pneumothorax is common in patients with IPF. Once pneumothorax has occurred in such patients, it can be refractory and cause acute exacerbation of the IPF, resulting in a downward clinical course. Lung cancer is a possible cause of pneumothorax. In view of the relatively high incidence (10-15%) of lung cancer associated with IPF (10), the possibility of lung cancer as the cause of pneumothorax should be considered in patients with IPF.

References