A Rapidly Progressive Case of Interstitial Pneumonia

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We treated a 51-year-old woman who had rapidly progressive respiratory distress with an interstitial shadow on chest roentgenogram. Pathologically, open lung biopsy specimens showed an acutely changed lesion such as interstitial inflammatory thickening, polypoid intraluminal organizing exudates, and also honeycombing which was not recognized on chest computed tomogram. These findings were considered unconformable to acute interstitial pneumonia (AIP), bronchiolitis obliterans organizing pneumonia (BOOP), and also usual interstitial pneumonia, although the clinical diagnosis was AIP or BOOP. We diagnosed a rapidly progressive interstitial pneumonia showing an acute lung injury pattern like AIP and BOOP. She showed significant recovery with corticosteroid and cyclophosphamide.

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Key words: idiopathic pulmonary fibrosis, bronchiolitis obliterans organizing pneumonia, acute interstitial pneumonia, usual interstitial pneumonia

Introduction

Clinically, diffuse infiltrative lung diseases are sometimes encountered with acute or subacute progressive courses, and complaints of dyspnea, however the etiology is unknown. These disorders include, for example, acute interstitial pneumonia (AIP) (1) and bronchiolitis obliterans organizing pneumonia (BOOP) (2). Epler et al stated that 86% of BOOP patients improved by steroid therapy and that the prognosis was excellent (2). But AIP is a grave disease because most patients die within two months of onset and there is no known definite effective therapy (3). Here, we present a case of interstitial pneumonia with a rapid course which pathologically showed the findings of acute lung injury pattern (AIP and/or BOOP) (3) and usual interstitial pneumonia (UIP) (4, 5), which responded to corticosteroid and immunosuppressant therapies.

Case Report

A 51-year-old female was admitted to our hospital on July 27, 1992 because of fever, cough, and exertional dyspnea (Hugh-Jones II) for about a one-month duration. She was a non-smoker and had neither a past history of pulmonary diseases nor exposure episodes to dust or fumes. She had had no previous respiratory symptoms.

Physical examination on admission showed height of 152 cm, body weight of 74 kg, blood pressure of 142/102 mmHg, and body temperature of 37.5°C. There was no evidence of clubbed fingers, peripheral cyanosis, heart murmur or lymphadenopathy, but fine crackles were heard over the bilateral lower chest. Laboratory investigations revealed the following abnormal results; white blood cell of 11,400/mm³ with 6% band forms, 65% polymorphonuclear leukocytes, 7% eosinophils, 9% monocytes, 13% lymphocytes, increased level of lactic acid dehydrogenase (LDH) 288 IU/L (normal range: 100–250 IU/L), and C-reactive protein 4.4 mg/dl. There was no elevation of viral titer serologically. Pulmonary function test showed restrictive ventilatory disorder and impairment of diffusing capacity [FVC 1,220 ml (%VC 47.7%); DLCO 10.0 ml/min/mmHg (%DLCO 47.8%)]. Arterial blood gas analysis revealed PaO₂ 67.4 Torr, PaCO₂ 40.9 Torr, and pH 7.44 on room air. The chest roentgenogram (Fig. 1) demonstrated linear-reticular shadow in the bilateral lower lung fields with shrinkage. And chest computed tomogram (CT) (Fig. 2) showed a bilateral patchy density elevated area and partial pleural thickening, but no obvious honeycombing. On bronchofiberscopy, there was no abnormality in visual findings. But bronchoalveolar lavage fluid (BALF) study performed from right B₂ demonstrated total cell count of 1.35×10⁶/ml, cell population of 60% lymphocytes, 8% neutrophils, and 32% alveolar macrophages.

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The percentages of lymphocytes and neutrophils were elevated. Transbronchial lung biopsy specimens from right S3 and S8 revealed fibrosis and infiltration of lymphocytes and plasma cells to the interstitium. In the bacterial culture only normal flora was detected in sputum and BALF. In spite of administration of antibiotics after admission, her clinical symptoms did not improve; hypoxemia worsened to PaO2 50.4 Torr on room air. We thus suspected AIP or BOOP because of her acute clinical course, no obvious infectious evidence and the inefficacy of antibiotic therapy. On August 7, open lung biopsy was performed to diagnose and to determine a therapeutic plan. Pleural effusion and pleural adhesion were not present in the right thorax. Visceral pleura of the lower lobe was edematous and lung parenchyma was elastic firm in consistency. The upper lobe seemed normal. Specimens were taken from S9 and S3. Pathological findings in S9 (Fig. 3A, B) showed edematous swelling of pleura and structural alteration of the lung parenchyma. The alteration was characterized as peripheral acinar fibrosis with muscle tissue proliferation, central microscopic honeycombing, cellular infiltration, and mild fibrous thickening of the interstitium with intraluminal organizing lesions. Many of the intraluminal organizing lesions were fibroblastic foci and some were polypoid lesions. Normal appearing lung tissue was seen in the region adjacent to the fibrous areas. These spatial and temporal variegations of the lesion seemed to be of UIP. In S3, polypoid and obliterative type intraluminal organizing exudate were found with infiltration of inflammatory cells and mild fibrous thickening of the corresponding alveolar wall (Fig. 3C). In other areas edematous swelling and inflammatory cell infiltration to the alveolar wall with epithelial metaplasia were observed together. Organizing intraalveolar exudate was slight in degree (Fig. 3D). There was no hyaline membrane in S9 or S3. The S3 lesion resembled that of BOOP or AIP but did not fulfill all criteria. These findings were interpreted as acute lung injury pattern. Since in S9 the findings were nearly the same as S3, pathologically it was interpreted that acute lung injury pattern overlapped the UIP lesion.
Steroid pulse therapy was administered twice (from August 7 and from August 15), and maintenance therapy was started with methylprednisolone at 40 mg/day on August 20. Interstitial shadow on chest roentgenogram was improved with corticosteroid, but the lymphocyte percentage was 67% in cell population of BALF performed on October 13. We interpreted this to mean that the inflammatory state of the lung lesion had not stabilized yet, so cyclophosphamide of 50 mg/day was added. However, the LDH level in serum exceeded 300 IU/L, therefore we increased the cyclophosphamide dose to 100 mg/day and 50 mg/day alternating every other day from November 19. Her symptoms and clinical data improved with these therapies. In April 1993, the abnormal shadow on chest roentgenogram disappeared (Fig. 4) and only irregularity in pleura without obvious honeycombing remained on chest CT (Fig. 5). %VC improved to 71.1% on pulmonary function test, and lymphocyte percentage in BALF cell population decreased to 6.2%. Cyclophosphamide was tapered to 50 mg/day five months later, because petechia and conjunctiva bleeding which would be caused by cyclophosphamide were observed. Methylprednisolone was also tapered gradually in the course. She was...
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**Fig. 5.** Only slight irregularity on pleura without obvious honeycombing was found; with therapy, the density elevated lesion disappeared on chest computed tomogram eight months after open lung biopsy.

...discharged on May 6, 1993 and visited our hospital as an outpatient without trouble or symptoms after that.

**Discussion**

The condition of this patient worsened in a few weeks, and the clinical course was characterized as a rapid progression of respiratory distress. Although the diagnosis of AIP or BOOP could be given clinically, the pathological findings such as acute lung injury patterns in the open lung biopsy specimens were not typical for AIP or BOOP, but a mixture of both AIP and BOOP were observed. The findings were too mild for AIP and were also against BOOP even if with the presence of intraluminal organization. Katzenstein and Askin stated that some cases show overlapping features of both DAD/AIP and BOOP (3). Clinically the present case could be termed rapidly progressive interstitial pneumonia or simply interstitial pneumonia.

Pathologically, UIP lesion was observed in S9. We consider the following two possible explanations concerning the existence of this UIP lesion: 1) acute exacerbation of idiopathic pulmonary fibrosis (IPF) (4), superimposition of acute lung injury pattern on UIP, 2) only incidental findings. Typical IPF progresses in a chronic course that spans over many years with cough and dyspnea, and honeycombing areas are usually seen on CT (5–7). But our patient had no chronic respiratory symptoms before June 1992 and had no honeycombing or consolidation on chest CT before and after improvement. Therefore it may be difficult to term this case acute exacerbation of IPF, clinically. However, we have had many autopsy cases of AIP/DAD with subpleural and localized UIP. We also have reported early IPF cases which complicated acute exacerbation that responded to steroid pulse therapy (4). There was no hyaline membrane in the acutely worsened area. It might be suspected that this case was acute worsening of subclinical stage IPF as shown in Fig. 6. To date there are no reports of early or subclinical stage IPF, and there is no proof that localized UIP which cannot be detected by CT, progresses to IPF. Now we simply term this case rapidly progressive interstitial pneumonia clinically.

This patient responded very well to corticosteroid and im-

![Fig. 6. Natural course of idiopathic pulmonary fibrosis (thick line) is divided into three stages; 1) subclinical stage (lack of symptoms and computed tomogram (CT) abnormalities), 2) asymptomatic stage (only CT abnormalities), 3) symptomatic stage. Acute exacerbation can be recognized in any points and some cases of them respond corticosteroid therapy (thin line).](image-url)
munosuppressant therapies. Previously we reported three cases of acute exacerbation of IPF which responded to steroid pulse therapy (4). The histological findings of those cases of acutely worsened areas resembled the present case. As corticosteroid therapy is generally effective in BOOP (2), the BOOP-like lesion might respond to steroid therapy in the present case. And Olson et al (8) revealed that 12 of 29 Hamman-Rich syndrome cases survived after a long and complicated hospitalization. This means that AIP cases might not be always fatal, and that corticosteroid and immunosuppressant therapies are effective in some cases. That is, AIP-like changed regions also might respond to corticosteroid therapy in the present case. Considering those facts, it is suggested that the combination of corticosteroids and immunosuppressants might be effective in some cases of rapidly progressive interstitial pneumonia.

We sometimes encounter acute or subacute diffuse infiltrative lung disease cases of which the etiology is unknown. These cases include AIP and BOOP. Moreover more atypical unclassified cases such as this case might exist. Further study is needed to clarify those rapidly progressive cases.

References