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Distinct Characteristics of Pleuroparenchymal Fibroelastosis With Usual Interstitial Pneumonia Compared With Idiopathic Pulmonary Fibrosis

Tsuneyuki Oda, MD; Takashi Ogura, MD; Hideya Kitamura, MD, PhD; Eri Hagiwara, MD, PhD; Tomohisa Baba, MD; Yasunori Enomoto, MD; Tae Iwasawa, MD, PhD; Koji Okudela, MD, PhD; Tamiko Takemura, MD, PhD; Fumikazu Sakai, MD, PhD; and Yoshinori Hasegawa, MD, PhD, FCCP

BACKGROUND: Pleuroparenchymal fibroelastosis (PPFE) is a rare form of interstitial pneumonia and sometimes coexists with a histologic usual interstitial pneumonia (UIP) pattern. This study aimed to describe the distinct clinical features of PPFE with UIP pattern compared with idiopathic pulmonary fibrosis (IPF).

METHODS: We conducted a retrospective review of the medical records of 110 consecutive patients with IPF with a histologic UIP pattern on surgical lung biopsy specimen. Patients meeting radiologic criteria for the diagnosis of PPFE based on high-resolution CT scan and with a histologic UIP pattern were included.

RESULTS: Nine of eleven patients meeting radiologic criteria for the diagnosis of PPFE were histologically confirmed as having PPFE with UIP pattern. The PPFE with UIP pattern group showed a significantly higher residual volume (1.8 L vs 1.3 L, $P < .01$), higher $Paco_2$ (44.6 mm Hg vs 41.7 mm Hg, $P = .04$), and higher complication rate of pneumothorax and pneumomediastinum than the 99 patients with IPF/UIP. The ratio of anteroposterior to transthoracic diameter in patients with PPFE with UIP pattern was significantly lower than that in patients with IPF/UIP ($P = .04$). Survival time tended to be shorter in patients with PPFE with UIP pattern.

CONCLUSIONS: The results support the view that PPFE with UIP pattern is a disease entity distinct from IPF/UIP and may well be classified as PPFE. CHEST 2014; 146(5):1248-1255

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ABBREVIATIONS: APDT = anteroposterior diameter of the thorax; ATS = American Thoracic Society; ERS = European Respiratory Society; HRCT = high-resolution CT; IPF = idiopathic pulmonary fibrosis; PPFE = pleuroparenchymal fibroelastosis; RV = residual volume; TDT = transthoracic diameter of the thorax; TLC = total lung capacity; UIP = usual interstitial pneumonia

AFFILIATIONS: From the Department of Respiratory Medicine (Drs Oda, Ogura, Kitamura, Hagiwara, Baba, and Enomoto) and Department of Radiology (Dr Iwasawa), Kanagawa Cardiovascular and Respiratory Center, Yokohama; Department of Pathobiology (Dr Okudela), Yokohama City University Graduate School of Medicine, Yokohama; Department of Pathology (Dr Takemura), Japan Red Cross Medical Center, Tokyo; Department of Diagnostic Radiology (Dr Sakai), International Medical Center of Saitama Medical University, Saitama; and Department of Respiratory Medicine (Drs Oda and Hasegawa), Nagoya University Graduate School of Medicine, Nagoya, Japan.

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CORRESPONDENCE TO: Takashi Ogura, MD, Department of Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Center, 6-16-1 Tomioka-higashi, Kanazawa-ku, Yokohama 236-0051, Japan; e-mail: ogura@kanagawa-junko.jp

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Idiopathic pleuroparenchymal fibroelastosis (PPFE) is a rare form of interstitial pneumonia. In 2004, five cases were reported of a unique idiopathic pleuroparenchymal lung disease characterized by a chronic idiopathic interstitial pneumonia with upper lobe-predominant marked pleural and parenchymal involvement.[1] The disease shares common features with idiopathic pulmonary upper lobe fibrosis proposed by Amitani et al.[2] Since, several case reports of PPFE have been published,[3-13] but no consensus has been reached regarding disease entity, characteristics, and diagnostic criteria.

Lobar histologic variability is frequent in patients with idiopathic interstitial pneumonia, and multiple histologic and high-resolution CT (HRCT) image patterns may coexist in the same patient. Cases with coexisting usual interstitial pneumonia (UIP) pattern and fibrotic nonspecific interstitial pneumonia pattern named as discordant UIP appear to behave similarly to those of concordant UIP.[14,15] One study on PPFE reported that HRCT imaging could show other interstitial lung disease patterns in other locations in some patients.[16] Indeed, specimens from patients with PPFE occasionally show a UIP pattern in the lower lobe (ie, PPFE with UIP pattern). Because PPFE with UIP pattern is regarded as inconsistent with UIP on HRCT scan and as UIP by histopathologic analysis, it is considered possible idiopathic pulmonary fibrosis (IPF) in accordance with the 2011 American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society/Latin American Thoracic Association official statement on IPF.[17] However, whether this diagnosis is appropriate when PPFE coexists with UIP pattern is not clear. This retrospective study has two objectives: to define the clinical and radiologic features of PPFE with UIP pattern compared with IPF/UIP by identifying PPFE with UIP pattern from surgically proven IPF/UIP and to determine whether PPFE with UIP pattern is a disease entity distinct from IPF/UIP.

Materials and Methods

Study Population

We retrospectively reviewed medical records of 291 consecutive patients with idiopathic interstitial pneumonia who underwent surgical lung biopsy between January 2001 and December 2011 at Kanagawa Cardiovascular and Respiratory Center. Included were 110 consecutive patients with IPF diagnosed according to the 2002 ATS/ERS statement,[18] with histologic UIP pattern shown in the biopsy specimen from the lower lobe. This study was approved by an institutional review board of Kanagawa Cardiovascular and Respiratory Center (approval number 24-14).

Radiologic Criteria for PPFE

Two expert pulmonary radiologists (T. I. and F. S.) identified patients according to the following radiologic criteria for the diagnosis of PPFE as previously reported in the literature[16] and without knowledge of their clinical background or histologic findings:

- Definite PPFE: demonstrating pleural thickening with associated subpleural fibrosis concentrated in the upper lobes, with involvement of lower lobes being less marked or absent.
- Consistent with PPFE: upper lobe pleural thickening with associated subpleural fibrosis present, but (1) distribution of these changes not concentrated in the upper lobes or (2) features of coexistent disease present elsewhere.
- Inconsistent with PPFE: lacking the requisite features just described.

In this study, only patients with definite or consistent with PPFE by radiologic criteria were included. If the two radiologists disagreed, the final diagnosis was reached by consensus. HRCT scan had been performed within 2 months before surgical lung biopsy.

Histologic Criteria for PPFE

Surgical biopsies of multiple lobes were performed in all patients. All available slides were reviewed independently by two expert pulmonary pathologists (K. O. and T. T.) who were not aware of the clinical and radiologic findings for the patients. Patients with a possibility of chronic hypersensitivity pneumonitis, pneumoconiosis, fungal or mycobacterial infection, and connective tissue disease-related lung disease on biopsy specimens were excluded. Histologic UIP pattern was diagnosed according to the 2002 ATS/ERS consensus classification of idiopathic interstitial pneumonias.[18] Histologic criteria for the diagnosis of PPFE were previously described in the literature as follows[16]:

- Definite PPFE: upper zone pleural fibrosis with subjacent intraalveolar fibrosis accompanied by alveolar septal elastosis.
- Consistent with PPFE: intraalveolar fibrosis present but (1) not associated with pleural fibrosis, (2) not predominantly beneath the pleura, or (3) not observed in an upper lobe biopsy specimen.
- Inconsistent with PPFE: lacking the requisite features just described.

If the two pathologists disagreed, the final diagnosis was reached by consensus. In this study, only patients with definite or consistent with PPFE by histologic criteria were included.

Clinical and Radiologic Review

The pulmonologists reviewed the medical records, pulmonary function data, and laboratory data, analyzing pulmonary function data obtained within 6 months before surgical lung biopsy. Radiologic features such as dense subpleural consolidation, honeycombing, and degree of flattened thoracic cage were also analyzed. The anteroposterior diameter of the thorax (APDT) was measured on HRCT scan as the longest distance of the anterior-posterior dimension of the thoracic cage at the level of the sixth thoracic vertebra.[19] The transthoracic diameter of the thorax (TDT) was measured as the longest transverse diameter of the thoracic cage at the level of the sixth thoracic vertebra.[19] The ratio of anteroposterior to transthoracic diameter was then derived. Survival analysis was performed from the time of initial consultation. Patients with clinical connective tissue disease, autoimmune disease, or hypersensitivity pneumonitis were excluded.

Statistical Analysis

Data are presented as mean ± SD unless otherwise stated. Fisher exact test or Mann-Whitney *U* test was used for between-group comparisons as appropriate. Survival time from initial consultation was analyzed by the Kaplan-Meier method and log-rank test, with the end points being death or last contact. $P < .05$ was considered significant.