Idiopathic Pulmonary Fibrosis vs. Pulmonary involvement of Collagen Vascular Disease: HRCT findings

The purpose of this study is to assess the differences of high-resolution CT (HRCT) findings in patients with idiopathic pulmonary fibrosis (IPF) and pulmonary involvement of collagen vascular disease (CVD). We analyzed the HRCT findings of 33 patients with IPF and 23 patients with CVD in terms of predominant pattern, site of involvement, mediastinal lymph node enlargement, pleural change, and pulmonary volume loss. The predominant HRCT pattern was honeycombing for IPF (58%), and ground-glass opacity for CVD (57%). Predominantly subpleural involvement was seen in 90% of IPF and 83% of CVD patients. Mediastinal lymph node enlargement was seen in 61% of the patients with IPF and 13% with CVD (p=0.0004). Pleural thickening was seen in 97% of the patients with IPF and 35% with CVD and the severity of pleural thickening is statistically significant (p=0.00001). Pleural effusion was seen in 6% of the patients with IPF and 26% with CVD (p=0.0351). The hilar height ratio was more than 1.5 in 52% of the patients with IPF and 30% with CVD (p=0.2620). Although HRCT findings of IPF and pulmonary involvement of CVD are similar and overlap considerably, but patients with IPF showed a tendency to more progressed fibrosis than patients with CVD. *(JKMS 1997; 12: 492~8)*

Key Words : *Pulmonary fibrosis; Lung; Lung disease; Collagen diseases; Computed tomography*

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INTRODUCTION

Both idiopathic pulmonary fibrosis (IPF) and pulmonary involvement of collagen vascular disease (CVD) are well known causes of diffuse interstitial lung disease which lead to fibrosis and honeycombing (1, 2). The peripheral portion of the lung is more severely involved with a patchy distribution in the initial stage of the IPF, which then progresses to a uniform rim of fibrosis, cystic spaces and parenchymal distortion. The pattern of pulmonary fibrosis in IPF is identical, both pathologically and radiologically to that seen in some forms of CVD and asbestosis. Thus, these diseases can be distinguished only by their clinical presentations (3). But pathologically, IPF always shows features of usual interstitial pneumonia (UIP) which ultimately leads to honeycombing, in contrast to CVD which encompasses not only features of UIP but also those of bronchiolitis obliterans organizing pnemonia (BOOP), diffuse alveolar damage (DAD), cellular interstitial infilteration, and lymphoid hyperplasia (4-7). The HRCT findings of IPF (8, 9) and CVD (10, 11) have been described in detail, respectively. The purpose of this study is to compare and to assess the differences in HRCT findings between these two group of patients.

MATERIALS AND METHODS

A search of the medical and radiological records, compiled at Seoul National University Hospital from 1985 to 1993, was performed to identify all patients with IPF and CVD who had undergone HRCT scans and chest radiographs. The study included 33 patients with IPF and 23 patients with CVD associated with diffuse pulmonary lesion. The age distribution of the patients with IPF was between 41 and 80 years (mean age, 61), and that of the patients with CVD was between 27 and 83 years (mean age, 47). There were 27 male and six female patients with IPF, six male and 17 female patients with CVD.

Among the patients with IPF, pathologic proof was obtained in eight patients by open lung biopsy (n=4) or transbronchial lung biopsy (n=4). In the remaining 25 patients, the diagnosis was made on the basis of the clinical, functional, and radiological (chest radiograph and CT scan) criteria. In all IPF patients, there was no history of drug ingestion or specific environmental exposure and no clinical stigmata of CVD. The diagnosis of CVD with diffuse lung disease was made on the basis of clinical and radiological criteria, that is, diffuse pulmonary infiltration in chest radiographs and CT scans with specific clinical

criteria of the CVD. In cases of the CVD, pulmonary edema by renal failure, infection, and pulmonary hemorrhage were excluded by its rapid resolution and rapid response to treatment in serial follow up study.

The CVDs that were included in this study were dermatomyositis (n=6), progressive systemic sclerosis (n=5), polymyositis (n=4), systemic lupus erythematosus (n=4), rheumatoid lung (n=3), and mixed connective tissue disease (n=1).

HRCT scans were obtained using a CT/T 9800 scanner (General Electric Medical Systems, Milwaukee) without administration of contrast material. All images were obtained at a maximal inspiration by using a 1.5-mm collimation at 140 kVp and 170 mAs with a 2-3 second exposure time and were reconstructed with a bone algorithm (12).

HRCT findings were analyzed by two chest radiologists independently without information of clinical diagnosis and finally consensus was made in cases of disagreement.

Predominant pattern of HRCT findings was classified into four types with a reasonably objective manner : 1) honeycomb appearance, 2) ground-glass opacity, 3) consolidation, and 4) mixed pattern. The "honeycomb appearance" was defined as a presence of variable sized air cysts with relatively thick wall and distortion of bronchovascular arrangement. The "ground-glass opacity" was used to refer to an increase in the pulmonary opacity, that was not associated with an obscuration of underlying vessels. The "consolidation" was defined as an increase in the pulmonary opacity in which underlying pulmonary vessels were obscured (13). The mixed pattern was used when the predominant lesion could not be classified as one pattern.

HRCT scans were obtained at a 10-15mm interval from the apex of the lung to the diaphragm contiguously, or at six levels; 1) 2cm above the aortic arch, 2) the level of the right upper bronchus, 3) the level of the right middle bronchus, 4) a center of the left atrium, 5) the level of the right diaphragm, 6) the level of the left diaphragm. The levels 1), 3), and 5) were regarded arbitrarily as representative for the upper, middle, and lower lung zones.

HRCT findings were assessed for predominant distribution of the disease divided into three compartments, that is, axial, middle, and peripheral (14). The axial compartment is contiguous with the mediastinum; it extends as a sheath around bronchovascular structures. The middle compartment is formed by alveolar wall. The peripheral compartment includes the pleura, subpleural connective tissue, interlobular septa enclosing pulmonary veins and lymphatics, and the walls of cortical alveoli. Mediastinal lymph nodes larger than 1.5cm in long

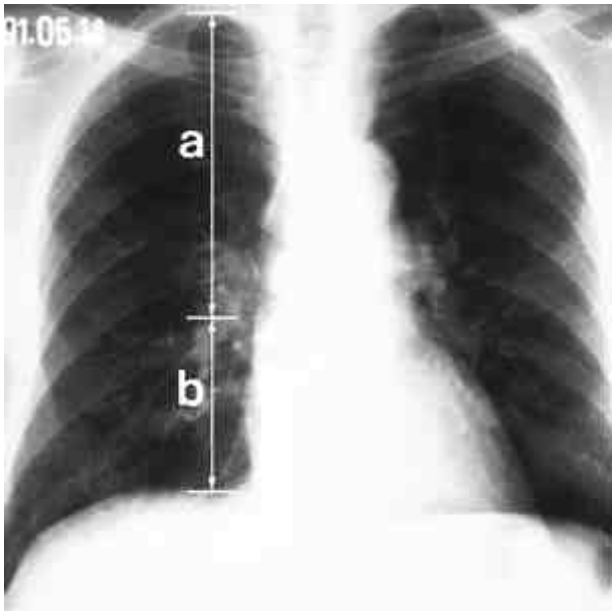

Fig. 1. Hilar height ratio (HHR) is distance between apex and hilum (a) divided by distance between hilum and diaphragm (b) (HHR=a/b).

diameter was considered to be enlarged. Pleural thickening was graded as mild degree if it was visible but less than 2mm, moderate degree when the thickness was between 2 and 3 mm, and severe degree when the thickness was more than 3 mm.

Loss of pulmonary volume was determined by using a hilar-height ratio (HHR) that is calculated by dividing the distance from the hilus to the apex of the lung by the distance from the hilus to the diaphragm in chest radiographs (15, Fig. 1). Chest radiographs were obtained at almost the same time as HRCTs and were taken with maximum inspiratory efforts. Absence or mild degree of pulmonary volume loss was regarded if the HHR of the right lung was less than 1.5, moderate degree if the HHR ranged between 1.5 and 2.0, and severe degree if the HHR was more than 2.0. Statistically significant differences of HRCT findings between the two diseases were assessed with Mantel-Haenszel Chi-Square method and Pearson Chi-Square method.

RESULTS

The predominant pattern of pulmonary lesions in patients with IPF was a honeycombed appearance in 19 (58%) (Fig. 2), ground-glass opacities in eight, mixed pattern in six patients. None of the patients with IPF had a predominant consolidation pattern. Of the 19 patients with IPF who had a predominantly honeycombed appearance, the pattern of the lesion was purely cystic

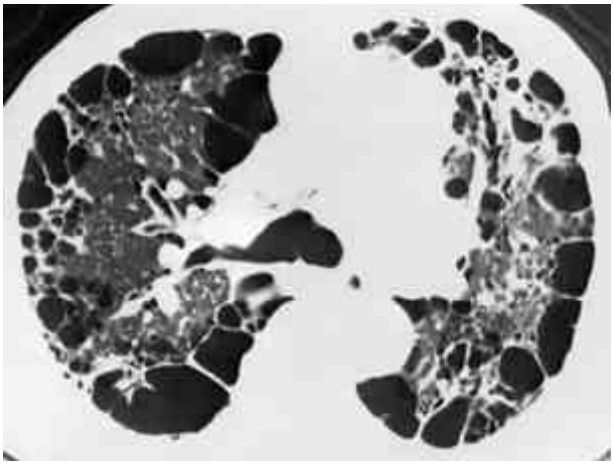

Fig. 2. High-resolution CT of a 66-year-old man with idiopathic pulmonary fibrosis shows typical honeycomb pattern distributing mainly at subpleural area.

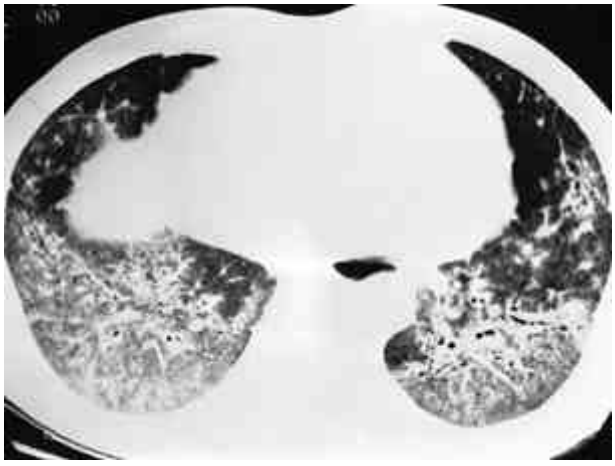

Fig. 3. High-resolution CT of a 51-year-old man with progressive systemic sclerosis shows predominantly ground-glass opacity which is located mainly peripherally.

in 42%, and mixed with ground-glass opacities and consolidations in the remaining 58%. On the contrary, of the 23 patients with CVD, ground-glass opacities were the predominant pattern in 13 (57%) (Fig. 3). Consolidation (n=4) (Fig. 4, 5), honeycombed appearance (n=4) (Fig. 6), and mixed type (n=1) appeared as a predominant lesion in the remaining patients. The differences between IPF and CVD in terms of predominant pattern, honeycombed appearance, ground-glass opacity and consolidation were all statistically significant (p=0.003, 0.014, 0.012, respectively).

Predominantly peripheral distribution of the lesions was noted in the upper lung zones in 88%, middle lung zones in 100%, and lower lung zones in 82% of patients with IPF. Even distribution of the lesions were seen in 12%, 0%, 12% of the patients in each lung zone. On the other hand, in patients with CVD, peripheral predominance was seen in 83%, 87%, 78%, and even distribution was seen in 17%, 13%, 22% in each lung zone. Therefore, predominantly subpleural involvement was

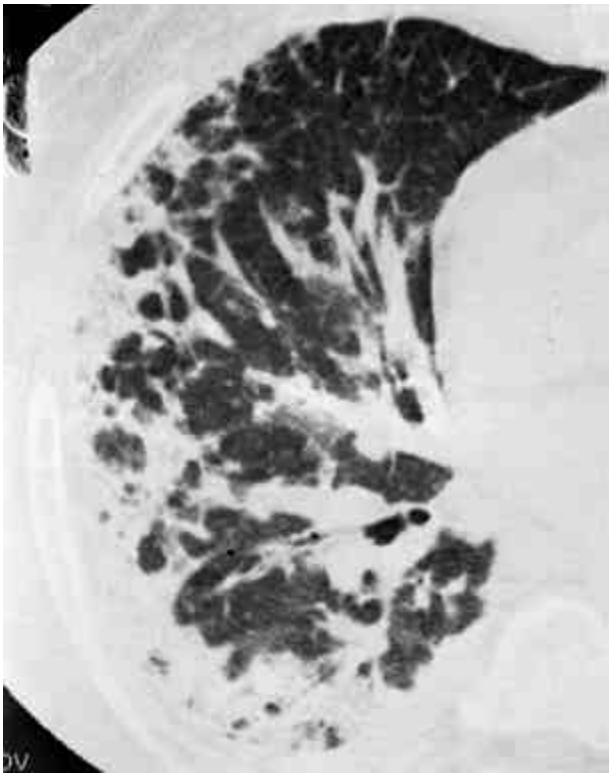

Fig. 4. High-resolution CT of a 62-year-old woman with polymyositis shows predominantly consolidation which is located mainly peripherally.

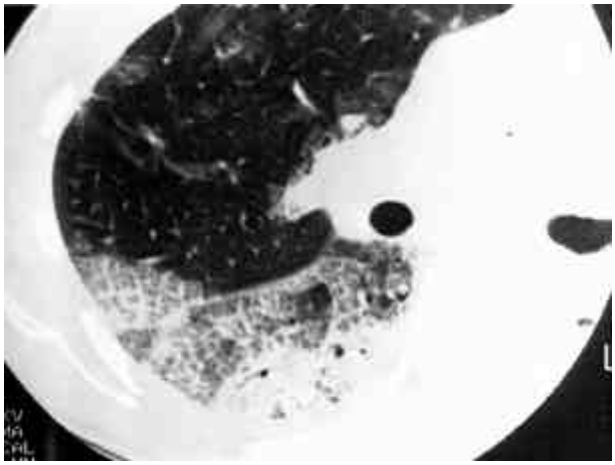

Fig. 5. High-resolution CT of a 34-year-old woman with dermatomyositis shows predominantly ground-glass opacity and also consolidation at dependent portion.

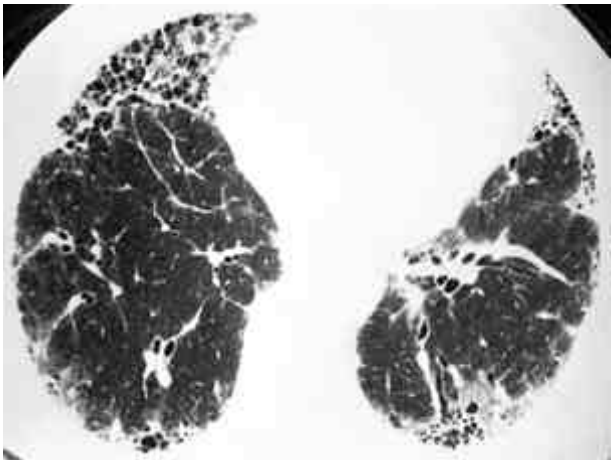

Fig. 6. High-resolution CT of a 83-year-old man with rheumatoid arthritis shows microcystic pattern mainly at subpleural area.

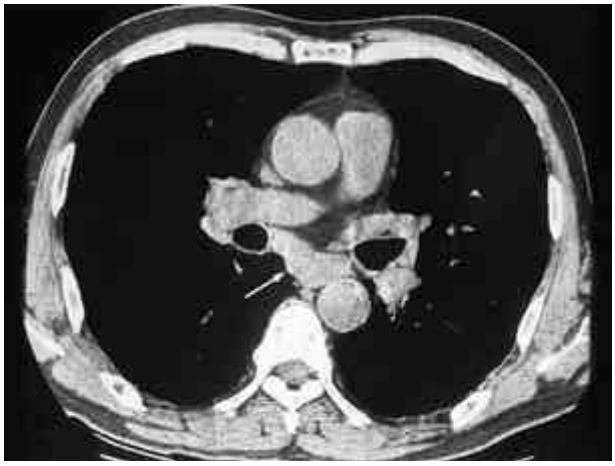

Fig. 7. High-resolution CT of 57-year-old man with idiopathic pulmonary fibrosis shows enlarged subcarinal (arrow) and right intrapulmonary lymph node (long arrow).

seen in 90% of IPF and 83% of CVD patients.

Mediastinal lymph node enlargement was seen in 20 (61%) of the 33 patients with IPF. The common locations of the enlarged lymph nodes were subcarinal (n=8) and right tracheobronchial area (n=6) (Fig. 7). Mediastinal lymph node enlargement was noted only in three (13%) of the 23 patients with CVD. There was a significant statistical difference in the mediastinal lymph node enlargement between the two diseases (p=0.0004).

Pleural thickening was seen in 32 (97%) of the 33 patients with IPF (Fig 8); mild degree in 18, moderate degree in 10, and severe degree in 4 patients. On the

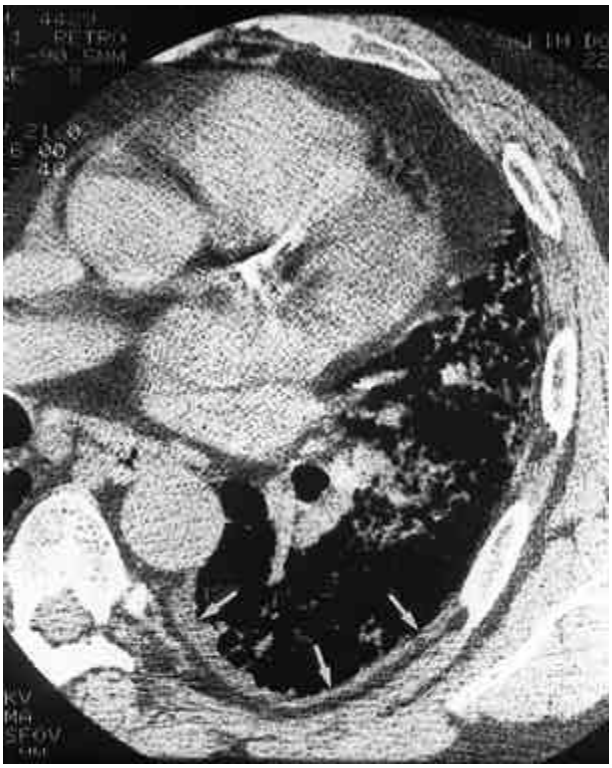

Fig. 8. High-resolution CT of 57-year-old man with idiopathic pulmonary fibrosis shows thickening of the pleura more than 3 mm (arrows).

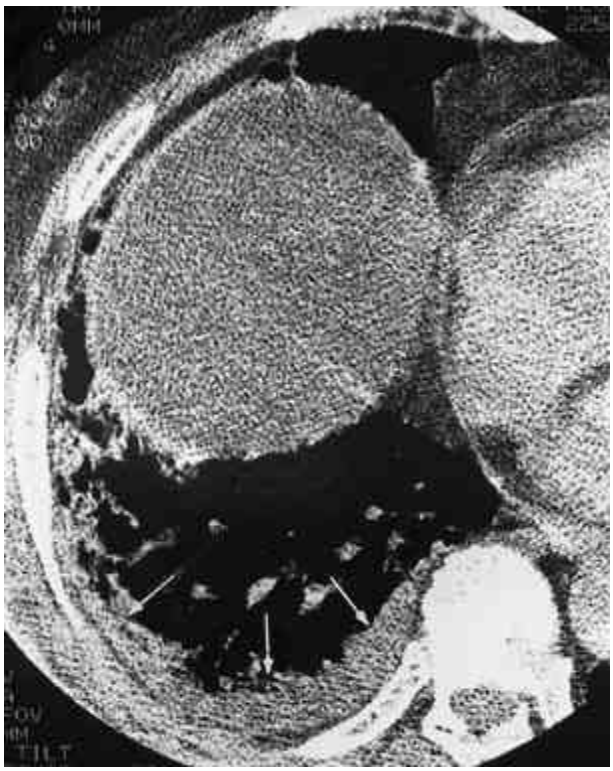

Fig. 9. High-resolution CT of a 62-year-old woman with polymyositis shows right pleural effusion (arrows).

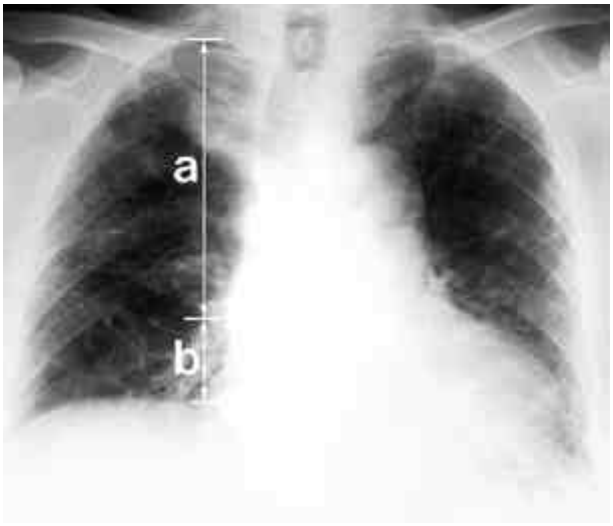

Fig. 10. Hilar height ratio (HHR) of a 80-year-old male with idiopathic pulmonary fibrosis is "3" and was categorized as severe lung volume loss.

contrary, pleural thickening was observed in 8 (35%) of the 23 patients with CVD; mild degree in 5 and moderate degree in 3 patients. There were no patients with a severe degree of pleural thickening . The severity of pleural thickening was significantly different between the two groups ($p=0.00001$), but the difference of the prevalence of pleural thickening was not statistically significant.

Pleural effusion was seen in two (6%) of the 33 patients with IPF and six (26%) of the 23 patients with CVD (Fig. 9). The presence of pleural effusion was statistically significant ($p=0.035$).

Normal pulmonary volume or mild degree of the pulmonary volume loss was noted in 16 (48%) of the 33 patients with IPF. The degree of volume loss was moderate in 13 (39%), and severe in four (12%) patients. On the other hand, the degree of pulmonary volume loss was less than mild in 16 (70%) of the 23 patients with CVD, moderate degree in six (26%) and severe degree in one (4%) patient (Fig. 10). The differences of the presence and severity of the pulmonary volume loss were statistically insignificant.

DISCUSSION

IPF is a progressive, generally fatal disease characterized by an interstitial and intraalveolar inflammatory process with eventual interstitial fibrosis leading to restrictive lung disease, decreased diffusing capacity, shortness of breath, and ultimately, cor pulmonale (1, 8, 9). CVD is a heterogeneous group of chronic inflammatory and immunologically mediated disorders that share certain clinical characteristics, including inflammation of joints, serosal membranes, connective tissue, and blood vessels of various organs. Each of these disorders will first be included under one of three general categories of CVD, that is, classic collagen vascular diseases, other collagen vascular diseases and, the systemic vasculitides (2, 16). In this study, only classic collagen vascular diseases were included because classic collagen vascular diseases have tendency to diffuse pulmonary infiltration than other collagen vascular disease and systemic vasculitides.

In our study, IPF was prevalent in the older age (mean age, 61 years) group and CVD was prevalent in younger patients (mean age, 47 years). It is postulated that the diagnosis of IPF is usually delayed because patients had only non-specific respiratory symptom such as dyspnea. On the other hand, patients with CVD had earlier development of general symptoms such as arthritides or connective tissue inflammation rather than dyspnea, for which reason hospitalization may occur earlier than IPF.

Pathologically, IPF always shows features of usual interstitial pneumonia (UIP) which ultimately leads to honeycombing, but CVD shows not only features of UIP but also those of bronchiolitis obliterans organizing pnemonia (BOOP), diffuse alveolar damage (DAD), cellular interstitial infiltration, and lymphoid hyperplasia (4-7). It was suggested that some cases of BOOP might progress to UIP (17), but it is still unclear whether or not all patients of CVD with the features of BOOP or lymphiod hyperplasia progress to honeycombing. But in some reports (4, 5), the patients with UIP appeared to have the worst prognosis and the patients with cellular interstitial infiltration and lymphoid hyperplasia seemed to have a favorable prognosis. Therefore, it is considered that UIP is a late stage of BOOP and lymphoid hyperplasia, or at least, BOOP or lymphoid hyperplasia is a medically treatable state of the diseases.

The HRCT findings in patients with CVD with BOOP or cellular interstitial infiltration would show ground-glass opacities or consolidation (18), and HRCT findings of CVD with advanced stage of UIP would show honeycombing which is identical to those of advanced stage of IPF. But in early UIP, either in IPF or CVD, the HRCT findings may show ground-glass opacity or consolidation, which are the same as the findings with BOOP or cellular interstitial infiltration in patients with CVD. Ground-glass opacities are the results of morphologic abnormalities below the resolution of HRCT. Thus, this finding can reflect minimal thickening of the septal or alveolar interstitium, alveolar wall thickening, or the presence of cells or a small amount of fluid filling the alveoli (13, 19). Especially in CVD, interstitial infiltration

of reticulin fiber as in polymyositis or dermatomyositis and capillary dilatation and congestion in alveoli as well as inflammatory cells or edema in alveolar ducts and alveolar wall as in IPF, were all thought to contribute to these ground-glass opacities (20). Regardless of pathophysiologic findings, the ground-glass opacity often indicates the presence of an ongoing and potentially treatable process (2, 8, 19).

Our study, the predominant pattern on HRCT was honeycombing in 58% of the patients with IPF, and mostly were mixed with ground-glass opacities and air-space consolidation, which suggested mixed stage of the disease process of UIP. In early state of IPF, ground-glass opacities were also high proportion (24%). On the other hand, in patients with CVD, HRCT findings were mostly ground-glass opacities and consolidation (74%) which may represent BOOP, cellular infiltration or early stage of UIP. Also, pure honeycombed appearance was seen in 17% of the patients.

In UIP with both IPF and CVD, the peripheral lung is abnormal first with a patchy distribution, which then progress to a uniform rim of fibrosis and lung distortion. This pattern of lung fibrosis is identical, both pathologically and radiologically both in IPF and some of CVD; thus these diseases can be distinguished only by their clinical presentations (3). In our study, the subpleural location of the lesion was identical in both diseases.

The mediastinal lymph node enlargement was seen in 61% of the patients with IPF, and 13% with CVD patients in our study. According to other reports (7, 21), the prevalence of mediastinal lymphadenopathy in IPF may represent that the patients with IPF have been in more chronic and advanced state of the disease process because the presence of mediastinal lymphadenopathy suggests a more advanced state of UIP.

Pleural effusion is known to be frequent in rheumatoid lung, systemic lupus erythematosus, and Sjögren syndrome (2, 10, 11). In our study, pleural effusion was relatively frequent in CVD (26%), somewhat more than expected, and it seems to be a helpful finding in differentiation with IPF (6%).

The hilar height ratio can be an objective criteria of the pulmonary volume loss (15). IPF had severer volume loss (moderate to severe volume loss in 51%) than CVD (moderate to severe volume loss in 30%) in our results. The pulmonary volume loss is caused by destruction of the pulmonary parenchyma and associated fibrosis. Therefore, honeycombed lung is generally associated with more severe volume loss than that of the ground-glass opacity or consolidation. That is why the pulmonary volume loss is severer in patients with IPF, which is associated with more advanced fibrosis and honeycombing.

The diagnoses of IPF and CVD were made by clinically and radiologically in almost all the IPF and CVD patients and pathologic confirmations were made in only 8 patients of the IPF, this is the limitation of our study.

In conclusion, although HRCT findings of IPF and pulmonary involvement of CVD are similar and overlap considerably, patients with IPF show a tendency to more progressed fibrosis and chronic and advanced state of disease process than CVD patients.

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