Nonspecific Interstitial Pneumonia Associated with Collagen Vascular Disease: Analysis of CT Features to Distinguish the Various Types

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Abstract

Objective  The purpose of this study was to analyze the CT findings of interstitial lung diseases that are associated with collagen vascular disease (CVD), with particular attention to nonspecific interstitial pneumonia (NSIP), and to examine whether it is possible to predict the clinical diagnosis of CVDs based on the CT findings alone.

Methods  CT scans of 49 patients with NSIP associated with CVD (15 males, 34 females; mean age, 55±10 years; age range, 25-76 years) were included in this retrospective study. All patients underwent a surgical biopsy. The clinical diagnosis comprised rheumatoid arthritis (RA) (n=15), systemic sclerosis (SSc) (n=8), polymyositis and dermatomyositis (PM/DM) (n=18), Sjögren’s syndrome (SjS) (n=4), and mixed connective tissue disease (MCTD) (n=4). Each CT was reviewed by two independent observers who made a clinical diagnosis based on the CT findings alone.

Results  The observers made a correct diagnosis for 22 (45%) of the 49 patients. A correct diagnosis was made for: RA in 7 (47%) of 15 patients; SSc in 3 (38%) of 8 patients; PM/DM in 11 (61%) of 18 patients; SjS in 1 (25%) of 4 patients. None of the 4 MCTD cases was diagnosed.

Conclusion  It is difficult to make a correct clinical diagnosis of the various types of CVDs based solely on CT findings. However, it is probable to make a reasonably accurate clinical diagnosis in cases that show the typical CT findings, especially for PM/DM patients.

Key words: collagen vascular diseases, interstitial lung disease, computed tomography

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Introduction

Collagen vascular diseases (CVDs) constitute a group of autoimmune disorders that can involve the respiratory system and cause focal or diffuse pulmonary disease. CVDs that show radiologic features of interstitial lung disease include rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), polymyositis and dermatomyositis (PM/DM), Sjögren’s syndrome (SjS), and mixed connective tissue disease (MCTD). The American Thoracic Society and European Respiratory Society defined the following seven distinct types of idiopathic interstitial pneumonia (IIP): idiopathic pulmonary fibrosis (IPF) or...
usual interstitial pneumonia (UIP), nonspecific interstitial pneumonia (NSIP), cryptogenic organizing pneumonia (COP) or bronchiolitis obliterans organizing pneumonia (BOOP), acute interstitial pneumonia, respiratory bronchiolitis-associated interstitial lung disease (RB-ILD), desquamative interstitial pneumonia (DIP), and lymphoid interstitial pneumonia (LIP) (1). At pathologic examination, interstitial lung diseases associated with CVD are diverse and include UIP, NSIP, COP (or BOOP), diffuse alveolar damage (DAD), and LIP (2).

Computed tomography (CT) is the most widely available, important, and standardized modality for the evaluation of interstitial lung diseases. The abnormal CT findings seen with IIPs and interstitial lung diseases associated with CVD have been extensively investigated.

Pathologic findings from patients with rheumatoid lung disease have revealed five different groups based on the specimens obtained at open lung biopsy: pulmonary rheumatoid nodules, UIP, BOOP, lymphoid hyperplasia, and NSIP (3). The CT findings reported in patients who have RA include bronchiectasis, bronchiolitis obliterans (i.e., airtrapping, mosaic perfusion), pleural effusions or pleural thickening, and enlarged lymph nodes (4).

Interstitial lung diseases associated with SLE are uncommon; in one series of 120 patients, only five (4%) had findings of interstitial lung diseases (5). The CT findings of interstitial fibrosis with SSc are similar to those of idiopathic NSIP and less extensive, less coarse, and characterized by a greater proportion of ground-glass attenuation than seen in patients with IPF (6). The types of interstitial lung diseases associated with PM/DM were identified, as follows, based on pathologic patterns: NSIP, UIP or BOOP, and DAD (7).

A relatively high prevalence of consolidation (52%) and a low prevalence of honeycombing (16%) which is lower than in patients with SSc (8), were observed on high-resolution CT (HRCT) findings (9).

The common CT findings in SjS consisted of bronchiectasis and poorly defined centrilobular nodular or branching linear opacities, areas with ground-glass attenuation, and honeycombing (10). LIP frequently occurs in association with SjS, a characteristic pattern of extensive areas with ground-glass attenuation with scattered thin-walled cysts is seen in approximately 50% of LIP patients (11). The predominant abnormalities in MCTD included ground-glass attenuation, subpleural micronodules, and nonseptal linear opacities (12). The frequency of honeycombing in MCTD was lower than in SSc and higher than in PM/DM (8).

The most common type of interstitial lung disease associated with CVD is NSIP (2), followed by UIP (2). The purpose of this study was to analyze the CT findings of interstitial lung diseases associated with CVD, with particular attention to NSIP, and to examine whether it is possible to determine the clinical diagnosis of CVDs based on the CT findings alone, with particular attention to the five common CVDs, namely RA, SSc, PM/DM, SjS, and MCTD.

### Methods

#### Study population

CT scans of 66 patients with interstitial lung diseases associated with CVD, taken between January 1995 and December 2006 at four institutions, were collected for this retrospective study. Ultimately, 49 patients with NSIP associated with CVD were enrolled. Demographic data of patients with NSIP associated with CVD are summarized in Table 1. The patients included 15 males and 34 females, aged 55±10 years (mean ± SD) (range: 25-76 years). The institutional review board gave full approval and waived informed consent for this retrospective study.

All patients underwent open lung biopsy or video-assisted thoracoscopic surgery (VATS) and all interstitial lung diseases were histologically proved at each participating institution. Biopsy specimens were obtained from 2 to 3 different lobes in each patient. The diagnosis of interstitial lung disease was based on the current histologic criteria for the diagnosis of the relevant disease by at least two experienced chest pathologists (with more than 15 years experience) (1). The clinical findings of all cases, including those from the CT, were subsequently reviewed by chest physicians. Thus, patients with infectious diseases or other types of interstitial pneumonia associated with pneumococci, eosinophilic lung diseases or hypersensitivity pneumonitis were excluded. The pathological diagnoses of interstitial lung disease comprised UIP (n=12), NSIP (n=49), OP (n=1), DAD (n=2), and LIP (n=2). The clinical diagnoses of CVD with NSIP comprised RA (n=15), SSc (n=8), PM/DM (n=18), SjS (n=4), and MCTD (n=4). All four patients with SjS had primary Sjögren’s syndrome.

### Table 1. Demographic Data of Patients with NSIP Associated with CVD

<table>
<thead>
<tr>
<th></th>
<th>RA (n=15)</th>
<th>SSc (n=8)</th>
<th>PM/DM (n=18)</th>
<th>SjS (n=4)</th>
<th>MCTD (n=4)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>7/8</td>
<td>3/7</td>
<td>3/15</td>
<td>1/3</td>
<td>1/3</td>
<td>0.450</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>53.5 ± 7.7</td>
<td>56.6 ± 12.3</td>
<td>54.0 ± 11.6</td>
<td>54.8 ± 8.2</td>
<td>54.5 ± 7.8</td>
<td>0.999</td>
</tr>
<tr>
<td>Smoking index (pack-years)</td>
<td>15.5 ± 12.7</td>
<td>24.0 ± 15.0</td>
<td>10.2 ± 25.8</td>
<td>0</td>
<td>0</td>
<td>0.102</td>
</tr>
<tr>
<td>VC (L)</td>
<td>2 ± 0.6</td>
<td>2 ± 1.0</td>
<td>1.7 ± 0.4</td>
<td>2.0 ± 0.5</td>
<td>1.9 ± 0.2</td>
<td>0.315</td>
</tr>
<tr>
<td>VC (% predicted)</td>
<td>71 ± 14</td>
<td>71 ± 9.3</td>
<td>68.4 ± 14.3</td>
<td>75.5 ± 21.2</td>
<td>76.8 ± 3.1</td>
<td>0.750</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>1.9 ± 0.5</td>
<td>1.9 ± 0.8</td>
<td>1.5 ± 0.4</td>
<td>1.7 ± 0.3</td>
<td>1.7 ± 0.3</td>
<td>0.490</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>86.7 ± 7.8</td>
<td>88.3 ± 2.5</td>
<td>86.2 ± 7.3</td>
<td>92.2 ± 6.4</td>
<td>89.8 ± 9.5</td>
<td>0.807</td>
</tr>
</tbody>
</table>

Note.-Data are shown as means ± SD. The data was assessed with the Kruskal-Wallis H-test.


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Thin-section CT techniques

Sequential CT scans were obtained using a variety of scanners. All CT scans were performed at the end of inspiration with the patient in the supine position, and no intravenous contrast material was used. Each patient had a single chest CT examination. The CT scans consisted of 1- to 2-mm collimation sections reconstructed using a high-spatial-frequency algorithm. Images were photographed at window settings appropriate for viewing both the lung (window level from -600 to -800 HU; window width from 1,200 to 2,000 HU) and the mediastinal (window level from 20 to 80 HU; window width from 300 to 400 HU) windows. The protocols consisted of thin-sections obtained at 1-cm intervals (40 patients), 2-cm intervals (7 patients), or 3-cm intervals (2 patients).

Evaluation of thin-section CT findings

The CT scans were assessed for the presence and extent of abnormalities. The observers knew that they were all NSIP cases associated with CVD; they were also aware of the patient’s age and gender, but were unaware of any other clinical findings. The CT scans were assessed for the presence and extent of areas with ground-glass attenuation, areas of air-space consolidation, honeycombing, cysts, intralobular reticular opacity, nonseptal linear or platelike opacity, subpleural lines, thickening of bronchovascular bundles, interlobular septal thickening, centrilobular nodules, traction bronchiectasis, pleural thickening, pleural effusion, pericardial effusion, and lymph node enlargement.

Ground-glass attenuation was defined as hazy increased attenuation of the lung that did not obscure the underlying vessels (13, 14). Air-space consolidation was defined as a homogeneous increase in pulmonary parenchymal attenuation that obscured the underlying vessels (13, 14). Honeycombing was considered present when clustered cystic airspaces that ranged in size from 2 mm to 1 cm with well-defined thick walls were seen in the subpleural regions (13, 14). Cysts were defined as round airspaces with a well-defined wall (13, 14). Intralobular reticular opacity was considered present when interlacing line shadows were separated by a few millimeters (13, 14). Nonseptal linear or platelike opacity was defined as an elongated line of soft-tissue attenuation that was distinct from interlobular septa and bronchovascular bundles (13, 14). Subpleural lines were defined as a curvilinear opacity a few millimeters or less in thickness, less than 1 cm from the pleural surface and parallel pleura (13, 14). Thickening of bronchovascular bundles was defined as an increase in bronchial wall thickness and an increase in the diameter of pulmonary artery branches caused by thickened peribranchovascular interstitium (13). Interlobular septal thickening was defined as abnormal widening of interlobular septa (13, 14). A nodule was defined as a focal, rounded opacity of less than 3 cm in diameter, which could be either well or poorly defined.

When a nodule was located in the center of the lobule or lobular core, it was defined as a centrilobular nodule (13). Traction bronchiectasis was defined as irregular bronchial dilatation within or around areas with a parenchymal abnormality. Architectural distortion was considered present when bronchi, pulmonary vessels, or interlobar fissures or septa were abnormally displaced (14). Lymph nodes were considered to be enlarged if their short-axis diameter on CT exceeded 10 mm.

The lungs were divided into six zones (upper, middle, and lower zones in both lungs), and each zone was evaluated separately. The upper zone was defined as the part of the lung above the level of the tracheal carina; the lower zone, as the part of the lung below the level of the inferior pulmonary vein; and the middle zone, as the portion of the lung between the upper and lower zones. Each CT finding was assessed and considered present, and the extent of involvement of the findings was evaluated visually and independently for each lung zone. A score was assigned on the basis of the percentage of lung parenchyma that showed evidence of an abnormality and was estimated to the nearest 10% of parenchymal involvement. The overall percentage of involvement was calculated by averaging the scores of the six lung zones.

The extent of traction bronchiectasis was evaluated by counting the number of segments that showed evidence of traction bronchiectasis. The following 18 segments or subsegments were evaluated: right apical upper, right anterior upper, right posterior upper, right lateral middle, right medial middle, right superior upper, right medial basal, right anterior basal, right lateral basal, right posterior basal, left apicoposterior upper, left anterior upper, left superior lingular, left inferior lingular, left superior lower, left anteromedial basal, left lateral basal, and left posterior basal. The extent of traction bronchiectasis was also quantified by assessing the generations of the most proximal bronchial branches involved. Traction bronchiectasis was scored as follows: 0, no bronchial dilatation; 1, bronchial dilatation involving bronchi distal to the fourth-generation bronchi; 2, bronchial dilatation involving from the second- and third-generation bronchi; 3, bronchial dilatation involving the trachea and/or the main bronchus.

After assessing the presence and extent of findings, the observers evaluated their predominant distribution. Zonal predominance was assessed as being upper or lower. Upper lung zone predominance was present when most of the abnormalities were above the level of the tracheal carina; and lower zone predominance was present when most of the abnormalities were below this level. The anatomic distribution was noted to be central if the abnormalities were primarily located in the inner third of the lung, and peripheral if the abnormalities were primarily present in the outer third of the lung. Peribronchovascular predominance was defined as findings located mainly around the bronchus and artery.

After reviewing the thin-section CT findings, the observers recorded the clinical diagnosis of CVDs, as suggested by
the CT findings according to previously published data of each interstitial lung diseases associated with CVD (Table 2). Differential diagnosis was limited to the five types (RA, SSc, PM/DM, SjS, and MCTD).

**Statistical analysis**

All statistical analyses were performed using statistical software (SPSS, version 12.0J; SPSS, Tokyo, Japan). The inter-observer variation for the extent of various abnormalities was analyzed using the Bland-Altman plot. The inter-observer variation for the clinical diagnosis of CVDs based on CT findings was analyzed with the κ statistic. Inter-observer agreement was classified as poor (κ=0.00-0.20), fair (κ=0.21-0.40), moderate (κ=0.41-0.60), good (κ=0.61-0.80), or excellent (κ=0.81-1.00). Statistical significance was defined as p<0.05.

The readings of the two observers pertaining to the extent of various abnormal findings were combined by calculating the average. Disagreement regarding the existence of pleural thickening, pleural effusion, pericardial effusion, lymph node enlargement, the anatomic distribution, the zonal predominance, and the clinical diagnosis of CVDs based on the CT findings was resolved by the consensus of the two observers.

The Kruskal-Wallis H-test was used to evaluate differences in the demographic data of patients, the extent of various abnormalities, pleural thickening, pleural effusion, pericardial effusion, lymph node enlargement, the anatomic distribution, and the zonal predominance between each NSIP associated with CVD. A post-hoc test (Tukey’s HSD procedure) was used to evaluate differences between each set of two groups.

**Results**

**Observer agreement**

Inter-observer agreement for the clinical diagnosis of CVDs based on CT findings was fair (κ=0.28).

The result of the Bland-Altman plot between the two observers is shown in Fig. 1. The x-axis of this graph is the average of two results for the extent of various abnormalities. The y-axis represents the difference between two results for the extent of various abnormalities. This assay indicates the inter-observer agreement of the extent of various abnormalities, if each plot existed within the bound of the average ±2 × SD of difference of two results. The SD was 2.6 (2 SD=5.2), and the average was 0.3 (%) (Fig. 1).

**Diagnosis**

The observers made a correct diagnosis for 22 (45%) of the 49 patients, as summarized in Table 3. A correct diagnosis of RA was made for 7 (47%) of 15 patients (Figs. 2-4); of the 8 RA cases misdiagnosed by the observer, 3 were incorrectly recorded as SSc and 5 as PM/DM. A correct diagnosis of SSc was made for 3 (38%) of 8 patients (Figs. 5-7); of the 5 misdiagnosed SSc cases, the observer recorded 4 as RA and 1 as PM/DM. A correct diagnosis of PM/DM was made for 11 (61%) of 18 patients (Figs. 8, 9); of the 7 misdiagnosed PM/DM cases, the observer recorded 5 as RA and 2 as SSc. A correct diagnosis of SjS was made

### Table 2. Summary of CT Findings of Each Interstitial Lung Diseases Associated with CVD

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>CT findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>Intralobular reticular opacity, honeycombing, lower lung zone and posterior predominance. Bronchiectasis, centrilobular nodules, Pleural effusions or pleural thickening, and enlarged lymph nodes.</td>
</tr>
<tr>
<td>SSc</td>
<td>Intralobular reticular opacity similar to those of idiopathic NSIP and less extensive, less coarse. Ground-glass attenuation, air-space consolidation, lower lung zone and posterior predominance. Nonseptal linear or pleatlike, subpleural lines.</td>
</tr>
<tr>
<td>PM/DM</td>
<td>Air-space consolidation, a low prevalence of honeycombing (lower than SSc), lower lung zone and posterior predominance. Nonseptal linear or platelike, subpleural lines.</td>
</tr>
<tr>
<td>SjS</td>
<td>Bronchiectasis, centrilobular nodules, thickening of bronchovascular bundles. Ground-glass attenuation with scattered thin-walled cysts.</td>
</tr>
<tr>
<td>MCTD</td>
<td>A combination of those seen in SLE, SSc, and PM/DM. Ground-glass attenuation, air-space consolidation, honeycombing (lower than SSc and higher than PM/DM). Pleural effusions or pleural thickening.</td>
</tr>
</tbody>
</table>

Note: The descriptions of CT findings are based on information from references 3-15.

Figure 2. Nonspecific interstitial pneumonia (NSIP) associated with RA in a 63-year-old man. Transverse thin-section CT (2-mm collimation) at the level of tracheal carina demonstrates areas of air-space consolidation with traction bronchiectasis (large arrows) in a predominantly peribronchovascular distribution, and extensive diffusely distributed centrilobular nodules (small arrows).

Figure 3. Nonspecific interstitial pneumonia (NSIP) associated with RA in a 54-year-old man. Transverse thin-section CT (1-mm collimation) at the level of the right inferior pulmonary vein demonstrates intralobular reticular opacity (arrows) with a predominantly peripheral distribution.

Figure 4. Nonspecific interstitial pneumonia (NSIP) associated with RA in a 55-year-old woman. Transverse thin-section CT (2-mm collimation) through the left lower lobe demonstrates areas of air-space consolidation (arrows) with a predominantly peribronchovascular distribution.

Figure 5. Nonspecific interstitial pneumonia (NSIP) associated with SSc in a 42-year-old man. Transverse thin-section CT (1-mm collimation) through the lower lobes demonstrates intralobular reticular opacity (arrows) with a predominantly peripheral distribution.

Figure 6. Nonspecific interstitial pneumonia (NSIP) associated with SSc in a 52-year-old woman. Transverse thin-section CT (2-mm collimation) at the level of the right superior pulmonary vein demonstrates areas of air-space consolidation (arrows) with a predominantly peripheral distribution.

for 1 (25%) of 4 patients (Fig. 10). None of the 4 MCTD cases was diagnosed based on CT findings alone (Fig. 11).

Extent and distribution of CT findings

Significant differences in the extent of various abnormalities between each patient with NSIP associated with CVD were found with honeycombing (p=0.014), cysts (p=0.030), intralobular reticular opacity (p=0.007), subpleural lines (p=0.002), and interlobular septal thickening (p=0.042) (Table 4).

Among patients with NSIP associated with CVD, areas with ground-glass attenuation were present in all types of
Figure 7. Nonspecific interstitial pneumonia (NSIP) associated with SSc in a 67-year-old woman. Transverse thin-section CT (1-mm collimation) at the level of the right inferior pulmonary vein demonstrates intralobular reticular opacity (large arrows) with a predominantly peribronchovascular distribution and extensive diffusely distributed centrilobular nodules (small arrows).

Figure 8. Nonspecific interstitial pneumonia (NSIP) associated with polymyositis and dermatomyositis (PM/DM) in a 51-year-old woman. Transverse thin-section CT (2-mm collimation) at the level of the inferior pulmonary vein demonstrates subpleural lines (arrows).

Figure 9. Nonspecific interstitial pneumonia (NSIP) associated with PM/DM in a 51-year-old woman. Transverse thin-section CT (2-mm collimation) through the left lower lobe demonstrates intralobular reticular opacity (large arrows) with a predominantly peripheral distribution and platelike opacity (small arrow).

Figure 10. Nonspecific interstitial pneumonia (NSIP) associated with SjS in a 62-year-old woman. Transverse thin-section CT (1-mm collimation) at the level of the inferior pulmonary vein demonstrates intralobular reticular opacity with traction bronchiectasis (arrows) with a predominantly peribronchovascular distribution.

CVDs and showed the greater extent in SSc, although the differences were not significant (p=0.369). Areas of airspace consolidation were found in all types of CVDs with similar extent, except for MCTD in which this finding showed the lowest extent. Honeycombing was present in four types of CVDs, except for SjS. The extent of honeycombing in MCTD was significantly greater than those in SSc (p=0.050). The extent of honeycombing in SSc was less than in RA and PM/DM, but there were no significant differences (p=0.853, 0.895). Cysts were present in PM/DM, SjS, and MCTD with similar extent. Intralobular reticular opacity was present in all types of CVDs. The extent of intralobular reticular opacity in SSc was significantly greater than in RA (p=0.007) and PM/DM (p=0.029) (Fig. 5). Non-septal linear or platelike opacity was present in all types of CVDs, but with no significant differences (p=0.701). Subpleural lines were found in all types. The extent of subpleural lines in PM/DM was significantly greater than those in RA (p=0.024) and SSc (p=0.017) (Fig. 8). The extent of subpleural lines in MCTD was also greater than others, but there were no significant differences (Fig. 11). Interlobular
septal thickening was found in all types. The extent of interlobular septal thickening in SjS was significantly greater than in RA (p=0.050). Centrilobular nodules were present in RA, SSc, and PM/DM, and showed a greater extent in RA (Fig. 2), although the differences were not significant. Traction bronchiectasis was present in all types, but with no significant difference.

Pleural thickening and lymph node enlargement were present in all types, and the differences were not significant. Pleural effusion was present in SSc, PM/DM, and SjS, with no significant differences. Pericardial effusion was absent in all types (Table 4).

The incidence of patients with RA and SjS with a lower zonal predominance was less than for the other 3 types (p=0.001) (Table 4). There were no significant differences in anatomic distribution among patients with NSIP associated with CVD.

**Discussion**

The observers made a correct diagnosis for 22 (45%) of the 49 patients. A correct diagnosis was made for: RA in 7 (47%) of 15 patients; SSc in 3 (38%) of 8 patients; PM/DM in 11 (61%) of 18 patients; and SjS in 1 (25%) of 4 patients. None of the 4 MCTD cases was diagnosed based on CT findings alone.

The types of interstitial lung diseases associated with PM/DM were identified on the basis of pathologic patterns: NSIP, UIP or BOOP, and DAD (7). The frequency of honeycombing was 16% of patients who had abnormal HRCT findings (9), which is lower than in patients with SSc (8). In the present study, the extent of honeycombing in patients with NSIP with PM/DM was not significantly different from each other (Table 4). The extent of intralobular reticular opacity was less than in patients with NSIP with SSc, while it was also almost the same as in patients with NSIP with RA (Table 4). Nonseptal linear or plate-like opacity has been reported as one of the most common CT findings in interstitial lung diseases associated with PM/DM (9, 15). In the present study, in patients with NSIP with PM/DM, nonseptal linear or plate-like opacity was present in 7 (39%) of 18 patients (Fig. 9).

Subpleural lines were defined as a curvilinear opacity, which was also termed a subpleural curvilinear shadow, a few millimeters or less in thickness, less than 1 cm from the pleural surface and paralleling pleura (13, 14). It was first described in patients with asbestosis. This occurs as a result of atelectasis, fibrosis, or inflammation, and can be seen in a variety of lung diseases including IPF or UIP (16), as well as in normal patients as a result of atelectasis. Schurawitzki et al reported that 17 (74%) of 23 patients with SSc showed subpleural lines on HRCT (17). Mino et al reported that 7 (38%) of 19 patients with PM/DM showed subpleural lines on HRCT (18). In the present study, subpleural lines were present in: 12 (67%) of 18 NSIP cases with PM/DM; 4 (27%) of 15 NSIP cases with RA; 2 (15%) of 8 NSIP cases with SSc; 1 (25%) of 4 NSIP cases with SjS; and 2 (50%) of 4 NSIP cases with MCTD. Subpleural lines were therefore most commonly found in patients with NSIP with PM/DM (Fig. 8). This information may be useful in the diagnosis of interstitial lung diseases associated with PM/DM.

Pulmonary parenchymal abnormalities are more common and more severe in SSc than in the other types of CVD. The pathologic features are of NSIP or UIP, the former being more common (7). The CT findings of interstitial fibrosis with SSc are similar to those of idiopathic NSIP and less extensive, less coarse, and characterized by a greater proportion of ground-glass attenuation than seen in patients with IPF (6). In the present study, in NSIP patients with SSc, the extent of intralobular reticular opacity was significantly greater than those in RA (p=0.007) and PM/DM (p=0.029) (Table 4). The abnormalities showed lower lung zone and posterior predominance, which is the same as in a previous report (6) (Figs. 5, 6). This might be useful information for

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**Table 3. Clinical Diagnosis of NSIP Associated with CVD Based on CT Findings**

<table>
<thead>
<tr>
<th></th>
<th>RA (n=15)</th>
<th>SSc (n=8)</th>
<th>PM/DM (n=18)</th>
<th>SjS (n=4)</th>
<th>MCTD (n=4)</th>
<th>Total (n=49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td>7 (47%)</td>
<td>3 (38%)</td>
<td>11 (61%)</td>
<td>1 (25%)</td>
<td>0 (0)</td>
<td>22 (45%)</td>
</tr>
</tbody>
</table>

Note: *Data in parentheses are percentages.

identifying interstitial lung diseases associated with SSC. However, there were some SSC cases with combined centrilobular nodules that the observers incorrectly recorded as RA (Fig. 7). It is difficult to clearly distinguish the clinical diagnosis of SSC from the other types based solely on CT findings.

In NSIP patients with RA, the extent of honeycombing was not significantly different from each other (Table 4). The extent of intralobular reticular opacity in RA was significantly less than those in SSC (p=0.007). The extent of centrilobular nodules in RA was not significantly different from each other (Table 4). In the present study, pleural effusion was not present in patients with NSIP with RA. Pleural thickening was present in 3 (20%) of 15 RA patients with NSIP. Lymph node enlargement was present in 4 patients (27%). Patterns of CT findings from NSIP cases with RA were diverse (Figs. 2-4) and there were no characteristic CT findings of NSIP with RA to allow differentiation from the other 4 types with NSIP.

Sjögren’s syndrome can occur as a primary disease, without features of other CVD, or as a secondary disease in association with other CVDs, most commonly RA. LIP frequently occurs in association with SjS, followed in frequency by airway abnormalities such as follicular bronchitis, bronchiectasis, and bronchiolitis (7). A characteristic pattern of extensive areas with ground-glass attenuation with scattered thin-walled cysts is seen in approximately 50% of patients with LIP (19). Poorly defined centrilobular nodules and thickening of the bronchovascular bundles, also seen in LIP, represent expansion of the interstitial tissue by lymphoplasma cell infiltration (19). In the present study, cysts were seen in NSIP patients with SjS, but the extent of cysts was not significantly different from each other (Table 4). Honeycombing, thickening of bronchovascular bundles and centrilobular nodules were not seen in NSIP patients with SjS (Table 4).

Based on the findings of this study and previous reports (8, 12), CT findings of NSIP associated with MCTD resemble NSIP with PM/DM (Fig. 11). Saito et al (8) also concluded that CT findings in MCTD were a combination of those seen in other patients (SLE, SSC, and PM/DM). In the present study, 4 MCTD cases were recorded incorrectly as RA (n=2), SSC (n=1), and PM/DM (n=1). Indeed, it is difficult to define the clinical diagnosis of MCTD based on the CT findings alone.

The present study has several limitations. First, the number of patients with NSIP associated with SjS and MCTD was relatively small. Second, patients with interstitial lung diseases associated with SLE were not included. Interstitial lung diseases associated with SLE are rare, and this limitation must be reflected in clinical practice. Third, this was a retrospective study and thus a prospective study is required to confirm the results. Finally, the CT images used in this study were obtained using different CT scanners and proto-

Table 4. Extent and Distribution of Thin-section CT Findings of Each NSIP Associated with CVD

<table>
<thead>
<tr>
<th>CT finding</th>
<th>RA (n=15)</th>
<th>SSC (n=8)</th>
<th>PM/DM (n=18)</th>
<th>SjS (n=4)</th>
<th>MCTD (n=4)</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground-glass attenuation*</td>
<td>1.4 ± 3.1</td>
<td>0.2 ± 0.8</td>
<td>1.3 ± 4.7</td>
<td>0</td>
<td>4.8 ± 1.1</td>
<td>0.014†</td>
</tr>
<tr>
<td>Air-space consolidation†</td>
<td>0.007</td>
<td>6.2 ± 2.1</td>
<td>0.4 ± 1.2</td>
<td>0.4 ± 0.7</td>
<td>0.4 ± 0.7</td>
<td>0.156†</td>
</tr>
<tr>
<td>Honeycombing‡</td>
<td>9.8 ± 5.4</td>
<td>0.007</td>
<td>9.8 ± 5.4</td>
<td>0.014</td>
<td>9.8 ± 5.4</td>
<td>0.007‡</td>
</tr>
<tr>
<td>Cysts§</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NA</td>
</tr>
<tr>
<td>Intralobular reticular opacity†</td>
<td>3.3 ± 6.0</td>
<td>4.4 ± 3.9</td>
<td>4.4 ± 3.9</td>
<td>4.4 ± 3.9</td>
<td>4.4 ± 3.9</td>
<td>0.007‡</td>
</tr>
<tr>
<td>Subpleural lines‡</td>
<td>0.9 ± 2.3</td>
<td>1.2 ± 2.1</td>
<td>2.7 ± 2.1</td>
<td>1.4 ± 2.4</td>
<td>2.9 ± 2.5</td>
<td>0.002‡</td>
</tr>
<tr>
<td>Thickening of bronchovascular bundle‡</td>
<td>0.2 ± 0.8</td>
<td>0.2 ± 0.8</td>
<td>0.2 ± 0.8</td>
<td>0.2 ± 0.8</td>
<td>0.2 ± 0.8</td>
<td>0.222</td>
</tr>
<tr>
<td>Interlobular septal thickening‡</td>
<td>0.2 ± 0.7</td>
<td>1.5 ± 3.2</td>
<td>0.6 ± 1.4</td>
<td>2.3 ± 2.0</td>
<td>1.0 ± 1.7</td>
<td>0.042†</td>
</tr>
<tr>
<td>Centrilobular nodules§</td>
<td>1.4 ± 3.1</td>
<td>0.6 ± 1.4</td>
<td>0.1 ± 0.4</td>
<td>0</td>
<td>0.007</td>
<td>0.189</td>
</tr>
<tr>
<td>Generations of traction bronchiectasis‡</td>
<td>1.4 ± 0.5</td>
<td>1.3 ± 0.5</td>
<td>1.3 ± 0.5</td>
<td>1.3 ± 0.5</td>
<td>1.3 ± 0.5</td>
<td>0.007†</td>
</tr>
<tr>
<td>No of segments with traction bronchiectasis</td>
<td>10.8 ± 3.8</td>
<td>11.4 ± 3.2</td>
<td>9.9 ± 3.0</td>
<td>8.8 ± 4.5</td>
<td>11.0 ± 4.8</td>
<td>0.206</td>
</tr>
<tr>
<td>No of patients with pleural thickening‡</td>
<td>3 (20)</td>
<td>4 (50)</td>
<td>9 (50)</td>
<td>1 (25)</td>
<td>2 (50)</td>
<td>0.181</td>
</tr>
<tr>
<td>No of patients with pleural effusion‡</td>
<td>0 (0)</td>
<td>2 (25)</td>
<td>3 (17)</td>
<td>1 (25)</td>
<td>0 (0)</td>
<td>0.159</td>
</tr>
<tr>
<td>No of patients with peribronchial effusion‡</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NA</td>
</tr>
<tr>
<td>No of patients with lymph node enlargement‡</td>
<td>4 (27)</td>
<td>2 (25)</td>
<td>2 (11)</td>
<td>1 (25)</td>
<td>1 (25)</td>
<td>0.508</td>
</tr>
<tr>
<td>Zonal predominance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of patients with upper predominance‡</td>
<td>3 (20)</td>
<td>1 (13)</td>
<td>0 (0)</td>
<td>1 (25)</td>
<td>0 (0)</td>
<td>0.062</td>
</tr>
<tr>
<td>No of patients with lower predominance‡</td>
<td>10 (67)</td>
<td>7 (88)</td>
<td>17 (94)</td>
<td>2 (50)</td>
<td>4 (100)</td>
<td>0.001†</td>
</tr>
<tr>
<td>Anatomic distribution</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of patients with central predominance‡</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NA</td>
</tr>
<tr>
<td>No of patients with peripheral predominance‡</td>
<td>8 (53)</td>
<td>3 (38)</td>
<td>9 (50)</td>
<td>2 (50)</td>
<td>3 (75)</td>
<td>0.850</td>
</tr>
<tr>
<td>No of patients with peribronchovascular predominance‡</td>
<td>13 (87)</td>
<td>7 (88)</td>
<td>17 (94)</td>
<td>3 (75)</td>
<td>4 (100)</td>
<td>0.230</td>
</tr>
</tbody>
</table>

Note. *Unless otherwise indicated, data are mean ± standard deviation. The data was assessed with the Kruskal–Wallis H-test. NA = not available

1 Data are percentage of lung parenchyma.
2 Data are scores.
3 Data are percentage of lung parenchyma.
4 Data in parentheses are percentages.
cols, and thus the details of each finding could be evaluated only to a limited degree.

In conclusion, generally speaking, it is difficult to arrive at a correct clinical diagnosis of CVDs based on CT findings alone. However, it is probable to make a reasonably accurate clinical diagnosis in cases that show the typical CT findings, especially for PM/DM patients. Using the detailed findings on HRCT, a feasible method to predict the diagnosis of NSIP-associated CVD.

Acknowledgement

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References