Nonspecific Interstitial Pneumonia Associated With Polymyositis and Dermatomyositis*

Serial High-Resolution CT Findings and Functional Correlation

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Study objectives: We described the features seen on serial high-resolution CT scans of nonspecific interstitial pneumonia (NSIP) that was associated with polymyositis (PM) and dermatomyositis (DM), and we correlated the changes in the CT scan findings with those of pulmonary function test results.

Design, setting and patients: Serial CT scans of 14 patients with histologically proven NSIP and PM/DM from two university hospitals were evaluated retrospectively (follow-up period, 3 to 61 months; mean follow-up period, 27.6 months). Using initial and follow-up CT scan findings, the extent of each type of opacity and the total area of increased opacity were calculated and correlated with the results of pulmonary function tests.

Measurements and results: The predominant findings on the initial CT scans were of reticular and/or ground-glass opacities with or without consolidation. Reticular and ground-glass opacities predominated in the lower zone of each lung, and consolidation predominated at the lung periphery. Thirteen patients showed significant improvement of the total area of increased opacity (p < 0.05), and this decrease in extent inversely correlated with changes in FVC (r = −0.650; p = 0.031). Ground-glass and reticular opacities also were improved significantly in 11 and 13 patients, respectively. The decrease in the extent of ground-glass opacity correlated inversely with the changes in FVC (r = −0.758; p = 0.0119) and diffusion capacity for carbon monoxide (r = −0.669; p = 0.0448). In one patient, ground-glass opacity progressed, and death occurred after 3 months. Traction bronchiectasis was seen in 12 patients, and it improved in four patients after treatment. Honeycomb lung was not noted in any patient during follow-up.

Conclusions: With treatment, serial CT scans of PM/DM patients with NSIP showed significant improvement in the abnormal opacities, and radiographic progression of lung fibrosis was limited. The CT scan features and clinical course of NSIP in PM/DM patients were relatively uniform, and this constitutes a subset of NSIP.

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Key words: CT scanners; interstitial lung diseases; polymyositis-dermatomyositis; x-ray

Abbreviations: BOOP = bronchiolitis obliterans organizing pneumonia; DAD = diffuse alveolar damage; DLCO = diffusing capacity of the lung for carbon monoxide; DM = dermatomyositis; NSIP = nonspecific interstitial pneumonitis; PM = polymyositis; UIP = usual interstitial pneumonia

Interstitial lung disease has been reported1–5 to occur in 5 to 46% of patients with polymyositis (PM) and dermatomyositis (DM), depending on the criteria for diagnosis, and is a common cause of morbidity and mortality in these patients. The prog-

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monia (UIP), diffuse alveolar damage (DAD), bronchiolitis obliterans organizing pneumonia (BOOP), and cellular interstitial pneumonia. Patients with a histologic diagnosis of BOOP have a more favorable prognosis than those with UIP, and patients with DAD generally have a poor prognosis. Furthermore, the response to corticosteroid therapy seems to be influenced by both the cellularity of the chronic interstitial infiltrates and the degree of fibroplasia of the alveolar septae. However, the histologic features of PM/DM have not been clearly specified in most of the previous reports.

In 1994, Katzenstein and Fiorelli introduced a new pathologic entity that could not be classified into any of the known types of idiopathic interstitial pneumonia, and this was termed nonspecific interstitial pneumonia (NSIP). NSIP differs from the other types of interstitial pneumonia with respect to its pathologic and clinical features, and it may be idiopathic or associated with collagen vascular disease, including PM/DM. Many of the previous reports on NSIP included both the idiopathic and secondary diseases. Because NSIP is a pathologic descriptor for histologic findings that cannot be classified into any previously established category of interstitial lung disease, and because various radiographic appearances are reported, we limited our study to NSIP and PM/DM so that there would be a homogeneous group. The purpose of this study was to describe the initial and follow-up features of NSIP that are associated with PM/DM on high-resolution CT scans, as well as any correlations with the results of pulmonary function tests.

Materials and Methods

Patient Selection

Between April 1996 and July 2001, 22 patients with either PM or DM underwent video-assisted thoracoscopic surgery for their pulmonary disease in our two university hospitals. The lung tissue was initially examined by a pathologist at each of our hospitals, and the findings were confirmed by consultation with an experienced pulmonary pathologist. Of the 22 patients, the histologic diagnosis included NSIP in 18 patients, UIP in 2 patients, BOOP with DAD in 1 patient, and unclassifiable diffuse interstitial pneumonia in 1 patient. Of the 18 patients who had a diagnosis of NSIP, 4 patients were excluded from our study because a follow-up CT study was not available at the time of our review. Thus, our study group consisted of 14 patients with either DM (11 patients) or PM (3 patients). There were 3 men and 11 women with an age range of 34 to 70 years (mean age, 53.5 years).

The diagnosis of DM or PM was based on the criteria of Bohan and Peter. No patient had multiple collagen vascular diseases. NSIP was diagnosed and the patients were grouped based on the following criteria of Katzenstein and Fiorelli: group I, inflammation that was predominantly interstitial with little or no fibrosis; group II, showed an equal mixture of inflammation and fibrosis; and group III, showed interstitial collagen deposition with minimal inflammation. Two patients were in group I, 10 patients were in group II, and 2 patients were in group III.

High-Resolution CT Scanning

The initial high-resolution CT scan was performed within 1 month before or after a biopsy had been performed in all but one patient, who had undergone the initial CT scanning 13 months before undergoing a biopsy. In all patients, steroid therapy with or without immunosuppressive therapy was initiated after the initial CT examination was performed. Follow-up CT scans were obtained from 3 to 61 months (average, 27.6 months) after the initiation of therapy. High-resolution CT scanning was performed with one of several different CT scanners (X-Vigor, 900-S, Asteion, or Aquilion; Toshiba; Tokyo, Japan; or Quantec; GE Yokokawa; Tokyo, Japan). The patient was always supine, and scans were obtained from the lung apex to the base using 2-mm collimation and a 10-mm reconstruction interval. The anatomic distribution in the transverse section was described as being peripheral, central, peribronchial, or random. Peripheral predominance was not seen in the central third of the transverse plane, and central predominance was noted if the abnormality was in the central third of the transverse plane. If abnormality was seen along the bronchovascular bundles, the distribution was regarded as peribronchial. If the abnormality had no predilection, it was considered randomly distributed. In the craniocaudal direction, the lung was divided into three parts from the apex to below the right diaphragm, and these parts were denoted as the upper, middle, and lower zones. The extent of involvement of ground-glass opacity, reticular opacity (ie, intralobular reticular opacity and or septal line thickening), consolidation, honeycombing, and traction bronchiectasis was assessed independently for each of the three zones of each lung. The CT scan score in the upper, middle, and lower lung zones was determined for intralobular reticular opacity, septal line thickening, curvilinear subpleural opacity, ground-glass opacity, consolidation, traction bronchiectasis, and honeycombing. Curvilinear subpleural opacity was defined as linear opacity running parallel to the chest wall within 1 cm of the pleural surface. Ground-glass opacity was defined as areas showing a hazy increase of lung attenuation through which vessels could still be seen. Honeycombing was defined as end-stage lung damage, which was manifested as multiple thick-walled cysts. The anatomic distribution in the transverse section was described as being peripheral, central, peribronchial, or random. Peripheral predominance was noted if the abnormality was seen in the outer third of the transverse plane, and central predominance was noted if the abnormality was in the central third of the transverse plane. If abnormality was seen along the bronchovascular bundles, the distribution was regarded as peribronchial. If the abnormality had no predilection, it was regarded as randomly distributed. In the craniocaudal direction, the lung was divided into three parts from the apex to below the right diaphragm, and these parts were denoted as the upper, middle, and lower zones. The extent of involvement of ground-glass opacity, reticular opacity (ie, intralobular reticular opacity and or septal line thickening), consolidation, honeycombing, and traction bronchiectasis was assessed independently for each of the three zones of each lung. The CT scan score in the upper, middle, and lower lung zones was determined by visually estimating the extent of each abnormality in each zone based on the percentage of the lung parenchyma that showed evidence of each abnormality in each zone (estimated to the nearest 5% of parenchymal involvement). The CT scan score was calculated by multiplying the percentage of each abnormality in each zone by a factor that corrected for differences in volume between the zones. The ratio of the volumes of the upper, middle, and lower lung zones was estimated as 1:1:6:1:3, based on previously published data. We also assessed the extent of the lung involved with any increased opacity (ie, reticular opacity, ground-glass opacity, or consolida-
tion) in each zone of each lung and calculated the CT scan score in the same way. CT scan scores were compared between before and after treatments.

**Pulmonary Function**

Pulmonary function tests were performed within 1 month of the CT scans using computerized pulmonary function instruments (FUDAC 50 or 70; Fukuda Denshi; Tokyo, Japan). The FVC was determined by spirometry, while the diffusing capacity of the lung for carbon monoxide (DLCO) was determined by a single-breath method. Each result was expressed as a percentage of the predicted value.

**Statistical Analysis**

Statistical analysis was performed to assess the differences of each CT scan score before and after treatments by Wilcoxon signed rank test. Changes in CT scan scores and pulmonary function parameters also were correlated using the Spearman rank correlation coefficient.

**RESULTS**

The frequency and distribution of each abnormal opacity on the initial and follow-up high-resolution CT scans are indicated in Table 1. On the initial high-resolution CT scans, ground-glass opacity was the most frequent abnormality (15 patients) [Fig 1, top], followed by the presence of intralobular reticular opacity (12 patients) and traction bronchiectasis (12 patients) [Fig 2, top]. Septal line thickening was seen in 11 patients. When septal line thickening and intralobular reticular opacity were combined, they were the most common findings and were seen in all patients. Consolidation was seen in six patients (Fig 3, top), but no patient showed honeycombing. Reticular opacity (ie, intralobular reticular opacities and septal line thickening) predominated in the lower lung zone in 10 patients, but no such predominance was noted in 4 patients. On axial scans, reticular opacity predominated at the lung periphery in seven patients, while the other seven patients showed random distribution. Ground-glass opacity predominated in the lower zones of the lungs in 11 patients but were evenly distributed in all three zones of two patients. Ground-glass opacity predominated at the lung periphery in five patients but was distributed randomly on axial scans in the other eight patients. Consolidation predominated at the lung periphery in six patients, while lower lobe predominance of consolidation was noted in three patients and peribronchial consolidation was seen in one patient. Traction bronchiectasis was associated with ground-glass opacities in 10 patients, but also occurred in 2 patients at sites without other abnormalities. In two patients in group II, subpleural curvilinear opacity was seen in the dorsal part of the lower lobes. In all patients, the abnormalities were regarded as bilateral and symmetrical.

Follow-up high-resolution CT scans showed improvement of the abnormalities in most of the patients. The changes in CT scan scores for each abnormality are indicated in Figures 4-6. The CT

**Table 1—CT Scan Findings in 14 Cases of NSIP and PM/DM**

<table>
<thead>
<tr>
<th>Findings</th>
<th>Cases</th>
<th>Predominant Distribution</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Peripheral</td>
</tr>
<tr>
<td>Reticular opacity</td>
<td>14 (100)</td>
<td>7 (50)</td>
</tr>
<tr>
<td>Ground-glass opacity</td>
<td>13 (92.9)</td>
<td>5 (38.5)</td>
</tr>
<tr>
<td>Consolidation</td>
<td>6 (42.9)</td>
<td>6 (100)</td>
</tr>
<tr>
<td>Traction bronchiectasis</td>
<td>12 (85.7)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Honeycombing</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Values given as No. (%).
scan score for the extent of increased opacities showed improvement in 13 patients, and it only progressed in one patient (Fig 4). This patient was in group II and had NSIP that showed rapid progression, with death occurring 3 months after undergoing the lung biopsy. CT scans obtained during the period of deterioration showed a diffuse increase of ground-glass opacity involving both lungs. The CT scan scores for increased opacities ranged from 8.3 to 60.8% (mean, 23.4%) at the time of the initial CT scanning, and from 5.0 to 41.3% (mean, 15.4%) at the time of the latest scans. The difference was significant (p < .05) by Wilcoxon signed ranks test. No patient had complete resolution of abnormal opacities.

Follow-up high-resolution CT scans showed an improvement of reticular opacity in 11 patients and a progression in 3 patients (group II, 2 patients; and group III, 1 patient) [Fig 5]. The average scores for reticular opacity were 16.2% (SD,11.0%) before treatment and 8.5% (SD, 5.4%) after treatment (p < 0.01). Ground-glass opacity improved in the 12 patients (Fig 1, bottom) but progressed or newly appeared in 2 patients (group II, 1 patient; and group III, 1 patient). The average scores for ground-glass opacity were 18.7% (SD, 16.8%) before treatment and 12.2% (SD, 9.7%) after treatment (p < 0.05) [Fig 6]. Consolidation resolved in five patients but progressed in one patient (group II). The average scores for consolidation were 2.9% (SD, 4.1%) before treatment and 0.7% (SD, 2.8%) after treatment (p > 0.05). When consolidation improved, it evolved into ground-glass opacity mixed with a variable degree of reticulation (Fig 3, bottom). Traction bronchiectasis improved in four patients, was unchanged in six patients, and progressed or newly appeared in each of two patients (group I, one patient; group II, two patients; and group III, one patient). Traction bronchiectasis generally improved along with the reticular and ground-glass opacities (Fig 2, bottom). In two patients in group II, however, traction bronchiectasis progressed despite the improvement of the reticular and ground-glass opacities. The average score for traction bronchiectasis was 6.2% (SD, 4.5%) before treatment and 5.1% (SD, 2.8%) after treatment (p > 0.05). No patient developed honeycomb lung during the follow-up period. Curvilinear subpleural opacities resolved in both patients.

Figure 2. A 66-year-old woman with NSIP and DM in group III. Top: the initial high-resolution CT scan shows diffuse reticular and ground-glass opacities, as well as traction bronchiectasis (arrows). Bottom: follow-up high-resolution CT scan obtained 33 months later shows improvement of the reticular and ground-glass opacities. Traction bronchiectasis also showed significant improvement in this patient.
Paired pulmonary function test results were obtained in 12 patients before and after treatment (Table 2). The difference between the initial and follow-up CT scan scores for increased lung opacity was inversely correlated with the difference between pulmonary function parameters before and after treatment (FVC: $r = -0.650$; $p = 0.031$) [Fig 7]. The difference between the initial and follow-up CT scan scores for ground-glass opacity was inversely correlated with the difference between pulmonary function parameters before and after treatment (FVC: $r = -0.758$; $p = 0.0119$; DLCO: $r = -0.669$; $p = 0.0448$).

**Discussion**

High-resolution CT features of NSIP have been reported previously as patchy ground-glass opacity with or without consolidation. However, in a study of 50 patients with idiopathic NSIP, a wide variety of high-resolution CT scan findings was reported including ground-glass opacity (76% of the cases), reticular opacity (46% of the cases), honeycomb lung (30% of the cases), consolidation (16% of the cases), and nodules (14% of the cases). In our patients with NSIP and PM/DM, the most common high-resolution CT scan feature was reticular opacity (100%), followed by ground-glass opacity (92.9%) and consolidation (42.9%). The lung area involved was 18.7% for ground-glass opacity and 16.2% for reticular opacity, while consolidation involved only 2.9% of the lung fields and was almost always a minor finding. When compared with the series mentioned above, our patients showed relatively uniform CT scan findings, since most of them had reticular and ground-glass opacity as the predominant abnormalities, and there were no cases of nodules or honeycombing of the lungs.

In patients with NSIP and PM/DM, abnormal opacities predominated in lower lung zones, and the peripheral predominance of opacities was not a
striking feature. Reticular opacity, ground-glass opacity, and consolidation predominated in the lower lung zone in 71.4%, 84.6%, and 50.0%, respectively, while axial sections showed peripheral predominance of these opacities in 50.0%, 38.5%, and 100%, respectively. In the study of 50 patients with idiopathic NSIP, lower lobe predominance of reticular opacity, ground-glass opacity, and consolidation was seen in 87%, 59%, and 75%, respectively.13 Also, peripheral predominance of reticular opacity, ground-glass opacity, and consolidation was reported in 96%, 68%, and 86%, respectively. When compared with these findings, the peripheral predominance of abnormal opacities was less common in our series, while lower lobe predominance was comparable.

The clinical course of NSIP has been reported to be relatively more favorable than that of UIP.11,18,19 However, the clinical deterioration of idiopathic NSIP is not uncommon and has been reported to occur between 16.2% and 41.7%.18–20 Because those data previously reported did not clearly describe the follow-up period, we cannot accurately compare our results with those previously reported. However, it seems that our patients with NSIP and PM/DM showed better clinical courses than did those with idiopathic NSIP, since the condition of only one patient (7.1%) deteriorated during the follow-up period.

| Table 2—Serial Pulmonary Function Test Results in Patients With NSIP and PM/DM* |
|---|---|---|---|---|
| Age, yr/Sex | Interval, mo | FVC Initial | FVC Follow-up | DLCO Initial | DLCO Follow-up |
| 58/F | 14 | 71.6 | 76.3 | 59.8 | 56.4 |
| 48/F | 48 | 93.3 | 81 | 51.7 | 44.7 |
| 70/F | 18 | 90.2 | 55.2 | 49.2 |
| 63/F | 14 | 75.8 | 87.6 | 44.9 | 51.4 |
| 34/F | 18 | 95.3 | 102.8 | 62.9 | 53.9 |
| 48/M | 19 | 46.4 | 66.2 | 37 |
| 48/F | 3 | 57.5 | 41.4 | 36.8 | 34.8 |
| 57/M | 40 | 98.3 | 102.8 | 62.4 | 55.8 |
| 63/F | 14 | 78 | 53.3 |
| 45/F | 61 | 84 | 104.8 | 31.6 | 53.8 |
| 55/M | 33 | 56 | 90 | 65.1 | 75.6 |
| 43/F | 21 | 65.1 | 89 | 53.8 | 76.2 |
| 48/F | 25 | 88.8 | 66.1 |
| 66/F | 34 | 63.9 | 82.7 | 51.8 | 62.4 |
| Mean | 25.9 | 75.0 | 82.2 | 52.2 | 55.2 |

*Values given as percent predicted. F = female; M = male.
Serial high-resolution CT scan findings have been reported\textsuperscript{9,10,21} to show a favorable response to treatment in most of the patients with NSIP. Those areas with ground-glass opacity, reticulation, and consolidation usually improve, but complete resolution is rather a rare occasion.\textsuperscript{9} These observations were also true in our series, in which the total area of increased opacities, reticular opacity, and ground-glass opacity decreased significantly. Although occasional case reports of honeycombing were noted in patients with idiopathic NSIP\textsuperscript{10,21} (up to 25% in the series in which it occurred most frequently),\textsuperscript{19} no patient in our series developed honeycomb lung, and thus our series also showed better radiographic courses.

In our series, traction bronchiectasis improved in four patients. The presence of traction bronchiectasis indicates a direct effect of the fibrosis of the lung parenchyma around the bronchi.\textsuperscript{22} It usually occurs in areas of advanced fibrosis and is generally considered to be irreversible.\textsuperscript{22} However, previous reports\textsuperscript{9,21} had indicated that traction bronchiectasis sometimes improved in NSIP patients. Our results also support this observation. This may not be surprising if one considers that the primary cause of traction bronchiectasis is fibrosis of the lung parenchyma surrounding the bronchi. With the improvement of peribronchial fibrosis, the elastic recoil of the lung parenchyma would decrease, in which case traction bronchiectasis may be reversible, especially in patients in whom the fibrosis has not yet advanced.

Because our series included a small number of patients in each NSIP group, we did not evaluate the difference in CT scan findings among them. However, it seemed difficult to find any correlations between the serial CT scan changes and the histologic subtype of NSIP patients with PM/DM. The only patient whose lung disease deteriorated was in group II. The opacities of two patients in group III showed improvement, with one patient showing a decrease from 43.1 to 23.1% over > 34 months and the other patient showing a decrease from 12.1 to 5.4% over > 25 months. On the other hand, the lung opacities of two patients in group I showed only minimal improvement (12.1 to 5.1% over > 48 months and 8.7 to 6.7% over > 14 months). In a series of 29 patients with idiopathic NSIP (fibrosing NSIP, 22 patients; cellular disease, 7 patients), the patients with a cellular pattern showed better 5-year and 10-year survival rates than did those with a fibrosing pattern.\textsuperscript{20} Thus, the pathologic fibrosis score is regarded as an important factor affecting the prognosis of patients with idiopathic NSIP. However, this may not be true in patients with NSIP and PM/DM. Other factors may play important roles in determining the prognosis.

Our study had several limitations. First, the number of patients included was small, and the period of follow-up did not exceed 3 years. Second, it was a retrospective review of patients who underwent surgical lung biopsy, and those who were too ill to undergo surgical biopsy and those who refused to undergo surgical biopsy were excluded. So, our study group had some bias. Third, we did not compare NSIP associated with PM/DM with other histologic diagnoses of interstitial pneumonia, such as UIP associated with PM/DM or idiopathic NSIP. Although our patients showed relatively homogeneous high-resolution CT scan findings and clinical courses, further study comparing patients with NSIP and PM/DM with those having other types of interstitial pneumonia, including NSIP in patients with other collagen vascular diseases, idiopathic NSIP, and UIP in patients with PM/DM, may be necessary for better characterizing NSIP in patients with PM/DM. Fourth, because all patients underwent high-resolution CT scanning in the supine position, there might be some overestimation of the extent of ground-glass opacity in the dependent portions of the lung.

In conclusion, the high-resolution CT scan features of NSIP that are associated with PM/DM can be summarized as bilateral diffuse reticular opacity and ground-glass opacity, with and without consolidation. During follow-up, the extent of the lung opacities improved in most patients, however, no patient showed complete resolution. Honeycomb lung was never observed during a mean follow-up period of 27.6 months. Traction bronchiectasis, which has been regarded as irreversible in patients with lung fibrosis, can improve in selected...
patients with NSIP who also have PM/DM. NSIP associated with PM/DM showed relatively uniform serial CT findings and clinical course and, thus, is considered to form a subset of NSIP.

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