Case Report
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Gradual Progression of Intrapulmonary Lymph Nodes Associated with Usual Interstitial Pneumonia in Progressive Systemic Sclerosis on Chest Radiographs and CT[1]

진행성 전신경화증에서 간질폐렴과 동반하여 점진적 진행을 보이는 폐내 림프절: 증례 보고[1]

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A 40-year-old female visited the clinic for evaluation of Raynaud's phenomenon for a period of four years. The initial chest radiograph showed a fine reticular density and ground glass opacity with lower lobe predominance. These findings are consistent interstitial fibrosis. Additionally, high resolution CT showed multiple, small, coexisting nodular opacities, ranging from 3 to 7 mm in size in both lungs. These nodules grew up to 1.5 cm and showed moderate enhancement. Because of the rareness of intrapulmonary lymph node in patient of progressive systemic sclerosis, we couldn't exclude the possibility of malignancy. These nodules are turned out to be intrapulmonary lymph nodes on video-assisted thoracoscopic lung biopsy.

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INTRODUCTION

Progressive systemic sclerosis (PSS) is a chronic, multisystemic disease, which is characterized by vascular changes, fibrosis, and inflammation of the skin and visceral organs. Pulmonary involvement occurs frequently in patients with PSS and is now considered as the main cause of death among these patients (1). Lung abnormalities are often subtle, most frequently occurring at the lung bases, and progressively expanding to involve the lower two-thirds of the lungs (2). High resolution CT (HRCT) findings of interstitial fibrosis in PSS include fine reticular opacities, ground-glass opacity, consolidation, traction bronchiectasis, honeycombing, and coarse or irregular reticulations.

The presence of faint parenchymal micronodules on CT scans is not unexpected, as focal lymphoid hyperplasia (follicular bronchiolitis) has been reported as a frequent histologic feature. Subpleural micronodules may reflect lung involvement at the pleural parenchymal interface, as small lymphoid aggregates adjacent to the pleura have been observed in lower lobe biopsies of patients with PSS (3). However, the radiologic detection of progressive intrapulmonary lymph nodes (IPLNs) with PSS has not yet been reported.

In this review, we report the serial chest radiologic findings in one case of PSS with multiple growing lung nodules, which turned out to be IPLNs on video-assisted thoracoscopic lung biopsy (VATS).

CASE REPORT

A 40-year-old female visited the internal medicine outpatient department for the evaluation of Raynaud's phenomenon for a

period of four years (from 2004 to 2008). She had symptoms of dry cough, skin pigmentation, skin thinning, scleroderma-like change below both elbows, and gastroesophageal reflux.

Initial chest radiograph showed the pattern of interstitial lung disease in the lung bases (Fig. 1A). These findings were consistent with lung involvement in PSS. HRCT performed one month later showed diffuse ground-glass opacities and fine reticular densities in the posterior portions of both lower lobes (Fig. 1B). In addition, multiple, small, coexisting nodular opacities, ranging from 3 to 7 mm in size, were detected in the both upper, right middle and both lower lobes. The authors thought that HRCT findings were consistent with interstitial lung involvement, as seen in the usual interstitial pneumonia or nonspecific interstitial pneumonia in patients with PSS. However, larger nodules were overlooked during interpretation of the initial HRCT scan. After three months, pulmonary function test showed mild restrictive patterns.

Follow-up chest radiograph showed minimally increased extent of coarse reticulation in both lower lung zones (Fig. 1C). However, she had no respiratory symptoms at the time of follow-up enhanced chest CT and CO diffusion test. HRCT showed interval increase in size of the multiple small nodules (7-11 mm in size) and an aggravation in areas of honeycomb cystic change in the right middle lobe and both lower lobes (Fig. 1D, E). Nodules were found more than 1 cm away from the pleura. Finally, she was admitted for a VATS lung biopsy of small nodules in the right middle lobe. The macroscopic findings revealed that the nodules were 10 × 10 mm in size, round, marginated, white and black in color. Histologic examination (Fig. 1F, G) revealed a lymph node with lymphoid follicles in the lung parenchyma. The lung tissue obtained by wedge resection of the right middle lobe showed organizing pneumonia with lymphocyte aggregation with follicle formation. Lung tissue from the right lower lobe showed the usual interstitial pneumonia pattern (Fig. 1H). The findings were compatible with interstitial pneumonia due to lung involvement in PSS. The activity was of a moderate degree. Two years later, the last follow-up nonenhanced chest CT was performed, and it revealed a slight regression or no definite aggravation of diffuse lung disease, and no overall interval change in the larger pe-

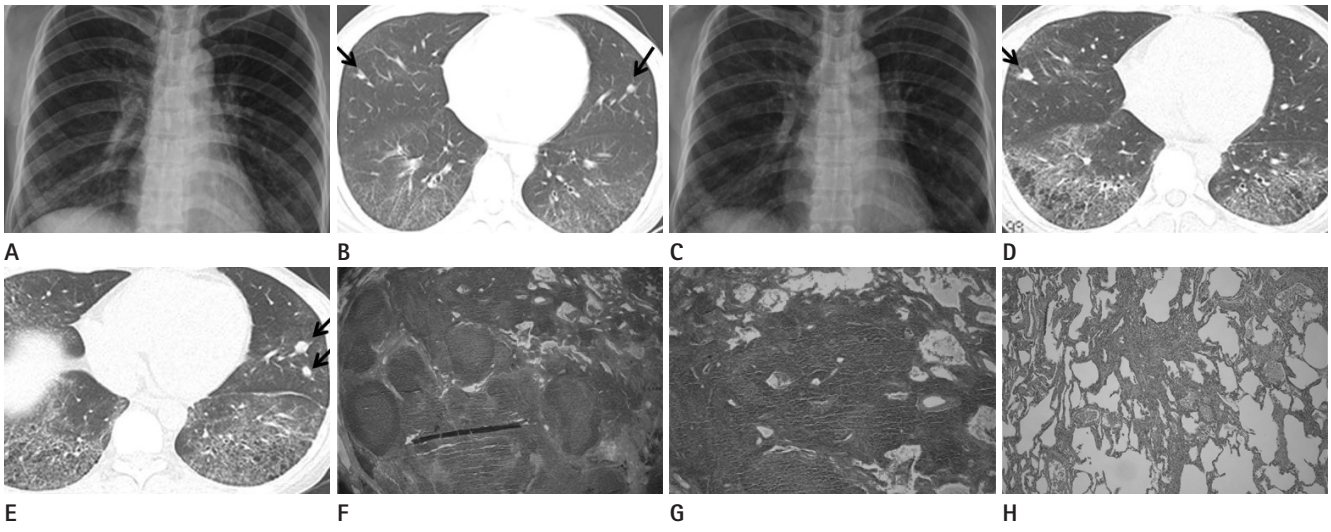

Fig. 1. A 40-year-old female with history of Raynaud's phenomenon.
A. The initial chest radiograph shows diffuse fine reticular densities and ground-glass opacities in both lung fields with basal lung predominance.
B. HRCT shows fine reticulonodular densities and diffuse ground-glass opacities in the right middle lobe, both lower lobes and left lingular segment. Findings are compatible with interstitial lung disease due to PSS. Nodules in the right middle lobe and left lingular segments (arrows) were overlooked at this point of time.
C. Six years later, follow-up chest radiograph shows irregular reticulonodular opacities bilaterally. The lung volume was slightly decreased.
D, E. Follow-up HRCT shows interval increase in size of the nodules in the right middle lobe (arrow) and left lingular segment (arrow). The nodules in the right middle lobe become lobulated. Nodules are found more than 1 cm away from the pleura. There are increased in the honeycomb cysts.
F, G. Histologic examination of the nodules reveals a lymph node with lymphoid follicles in the lung parenchyma (Hematoxylin and Eosin stain, x 100).
H. Lung tissue obtained by wedge resection of the right lower lobe shows interstitial pneumonia compatible with the usual interstitial pneumonia pattern, due to the moderate activity of PSS (Hematoxylin and Eosin stain, x 100).
Note.—HRCT = high resolution CT, PSS = progressive systemic sclerosis

ripheral nodules.

DISCUSSION

Most reports of lung pathology in PSS describe abnormalities, including extensive interstitial fibrosis with cystic changes, bronchiolectasis, and pleural thickening. Focal lymphoid hyperplasia (follicular bronchiolitis) is more common in the PSS patient than in the lone cryptogenic fibrosing alveolitis (3). Focal lymphoid hyperplasia manifest as faint parenchymal micronodules on a CT scan, although, the nodules of focal lymphoid hyperplasia in rheumatoid arthritis patient measured about 3 and 10 mm in diameter (4). Recent results suggest that the B cells may have multiple pathogenic roles in PSS and there may be increased incidence of B cell lymphomas in PSS (5). The association of PSS and non-Hodgkin's lymphoma may be a rather uncommon feature. The other report was about a solitary lung nodule in PSS, which was an IPLN in patients with PSS (6). In each patient, a follow-up chest CT scan showed a pulmonary nodule, which could not be seen on a chest radiograph, as in this case. In these cases, the nodules had an irregular margin and a linear shadow resembling pleural indentation. Histological examination of the open lung biopsy specimens revealed that these nodules were IPLNs surrounded by an interstitial pneumonia and lymphoid hyperplasia. In our case, the nodules were less than 5 mm in diameter, without definite pleural indentation, on an initial CT scan, and were grown up to 1.5 cm for a period of five years. Our patient had longer follow up time and serial CT findings. In general, ill-defined margins, involvement of bronchi or vessels, and nodule enlargement visualized by CT are important signs of malignancy, even for less than 10 mm in size (7). All nodules in our patient grew in size, the largest nodule in the right middle lobe increased in size from 7 mm to 1.5 cm in diameter.

It has been generally believed that IPLNs exist in the vicinity of the hilar region of the lung and the central bronchi, but not after the fourth branching point. Nevertheless, it has been known for a long time that IPLNs sometimes show up on chest radiographs as solitary nodular shadows. The following points of the CT findings in IPLNs were confirmed; 1) the border was sharp in most cases; 2) IPLNs were found within several millimeters from the pleura; 3) sometimes, more than one node were seen; 4) they may cause pleural indentations; and 5) the border may sometimes be rough, like that in lung cancer. These findings are not necessarily specific for IPLNs. Nevertheless, they suggest that when nodular shadows with a sharp border are found just under the pleura, IPLNs should be suspected. Peripheral small lung cancer does not always have specific features, and the CT features of IPLNs and small lung cancer sometimes overlap (8). These IPLNs have been occasionally found to coexist with several diseases, such as silicosis (9) and diseases affecting African miners (10).

In PSS, IPLNs are very rare, and hence, we should be able to differentiate them from cancerous conditions, infected nodules, and nodules of other origin.

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진행성 전신경화증에서 간질폐렴과 동반하여 점진적 진행을 보이는 폐내 림프절: 증례 보고[1]

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40세 여자 환자가 4년 이상의 레이노 증상을 주소로 내원하였다. 내원시 단순흉부촬영 소견에서 망상 음영 소견과 간유리음영이 주로 양 폐하에 있었다. 이는 사이질 섬유화에 합당한 소견이다. 고해상도 흉부전산화단층촬영에서 3~7 mm 크기의 다수의 작은 결정형 음영들이 양 폐에 있었다. 이 결절들은 추적 관찰 중 1.5 cm까지 성장하였고 조영증강이 잘 되었다. 진행성 전신경화증 환자에서의 폐내 림프절은 매운 드문 일이기에 진단시 악성 종양의 가능성을 배제할 수 없었다. 환자는 생검을 통하여 폐내 림프절로 조직학적 확진을 받았다.

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