Primary Sjögren’s Syndrome Complicated by Sarcoidosis

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Abstract

A 51-year-old woman suffered from xerophthalmia and xerostomia for 3 years without being medically examined. In July 2006, she was referred to our hospital for the evaluation of chest roentgenogram showing slight pleural effusion in the right lung. A chest CT scan revealed multiple nodules, enlarged mediastinal and hilar lymph nodes, and bilateral slight pleural effusions. A diagnosis of Sjögren’s syndrome was made on the basis of the results of sialography, lip biopsy, Schirmer’s test, and elevated titer of antibody to SS-A antigen. Histological examination of the specimen from the nodular lesion by video-assisted thoracoscopic biopsy revealed noncaseating epithelioid cell granuloma containing giant cells, which confirmed the diagnosis of sarcoidosis. Although the coexistence of Sjögren’s syndrome and sarcoidosis has been reported occasionally, cases with histological evidence of sarcoidosis have been rare. Pulmonary sarcoidosis should be considered in the differential diagnosis of pulmonary multiple nodules in patients with Sjögren’s syndrome.

Key words: Sjögren’s Syndrome, sarcoidosis, pulmonary multiple nodules

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Introduction

Sarcoidosis and Sjögren’s syndrome are chronic multisystem diseases of obscure etiology. The coexistence of Sjögren’s syndrome and sarcoidosis has been reported in only 1% of patients with Sjögren’s syndrome (1). Pulmonary involvement of Sjögren’s syndrome and sarcoidosis may have similar clinical and radiographic manifestations (2). Here, we report a rare case of a patient with Sjögren’s syndrome who presented with multiple 1- to 10-mm diameter pulmonary nodules and was subsequently histologically diagnosed to have pulmonary involvement of sarcoidosis.

Case Report

In July 2006, a 51-year-old Japanese woman was referred to our hospital for the evaluation of chest roentgenogram showing slight pleural effusion in the right lung. She was a nonsmoker and had no history of occupational exposure. She had suffered from xerophthalmia and xerostomia from 2003. Physical examination revealed that she had no skin lesions or neurological abnormalities. There was no peripheral lymphadenopathy in the cervical, axillary, or inguinal region. Chest auscultation showed no abnormal findings.

The white blood cell count was 4.4×10⁹/L with 78.5% neutrophils, 11% lymphocytes, 7.5% monocytes, and 1.0% eosinophils. The total protein level was 8.2 g/dL with 23.6% gamma globulin. The serum level of IgG and IgA was elevated to 2,177 mg/dL (normal, 837-1,825 mg/dL) and 814 mg/dL (normal, 113-463 mg/dL), respectively, and the serum IgM level was within the normal range. The antinuclear antibody titer was 1:1,280 (homogenous pattern). The titer of antibody to SS-A antigen was >1:256, whereas no antibody to SS-B antigen was detected. The soluble interleukin-2 receptor (sIL-2R) level increased to 1,335 U/mL (normal, 127-582 U/mL). The serum angiotensin-converting enzyme level was normal. Vital capacity, forced expiratory volume (1s, FEV₁) and lung diffusion for carbon monoxide (DLCO) were 2.06 L (78.0% of predicted), 1.85 L (79.4% of predicted), and 79.7% of predicted, respec-
Figure 1. A. Histological examination of a minor salivary gland in the lower lip. Focal lymphocytic sialadenitis which is compatible with the histology of Sjögren’s syndrome was found (Hematoxylin and Eosin staining, original magnification ×400). B. Histology of a lung biopsy specimen by video-assisted thoracoscopy. Non-caseating epithelioid cell granulomas containing giant cells without any necrotic lesions are evident (Hematoxylin and Eosin staining, original magnification ×200).

Keratoconjunctivitis sicca was confirmed by Schirmer’s test, with test values of 2 mm in the right eye and 5 mm in the left eye, and by a positive reaction in the Rose-Bengal test. Xerostomia was confirmed by an apple tree-like pattern observed by sialography. There was no evidence of uveitis. Histological analysis of a minor salivary gland in the lower lip revealed lymphocytic infiltrate; this finding is consistent with Sjögren’s syndrome (Fig. 1A). Sjögren’s syndrome was diagnosed on the basis of clinical and histological findings.

A chest roentgenogram showed bilateral hilar lymphadenopathy and right pleural effusion (Fig. 2A). Chest CT scan revealed bilateral multiple nodular lesions along the broncho-vascular bundle, enlarged mediastinal and hilar lymph nodes, and bilateral slight pleural effusions (Fig. 2B, C, D). The sizes of nodular lesions were varied, measuring up to 10 mm in diameter. Histological examination of the specimen from the nodular lesion and macroscopically normal regions of the right lung by video-assisted thoracoscopic biopsy revealed noncaseating epithelioid cell granuloma containing giant cells (Fig. 1B). Intraoperative examination revealed a small amount of pleural effusion and no pleural thickening. The patient was classified to have stage II pulmonary sarcoidosis. To date, there has been no evidence of multiorgan involvement of sarcoidosis in this patient.

Discussion

Sjögren’s syndrome is a chronic inflammatory disease characterized by lymphocytic infiltration of the exocrine glands, mainly the salivary and lachrymal glands; it usually manifests with xerostomia and xerophthalmia, but it may also have systemic manifestations, with lymphoma being the most feared of these manifestations. Among 50 patients with Sjögren’s syndrome and associated lymphoma, 10 had pulmonary involvement of lymphoma (3). Strimlan et al reported that among 343 patients with Sjögren’s syndrome, a histologic diagnosis of pleuropulmonary manifestations was established in 13 patients, with malignant lymphoma and amyloidosis observed in 3 and 2 patients, respectively (4). Bilateral hilar lymphadenopathy, which is more common in sarcoidosis, could be interpreted as a sign indicating lymphoma associated with Sjögren’s syndrome (5). Lohrmann et al reported small pulmonary nodules, large nodules (10-30 mm), and masses (>30 mm) in 46.2%, 4.2%, and 4.2% patients with primary Sjögren’s syndrome, respectively (6). These findings prompted us to determine whether the nodular lesions were associated with Sjögren’s syndrome or caused by lymphoma or other causes.

Sarcoidosis is a chronic granulomatous disease that mainly affects the lungs, but it may also have systemic manifestations. Ninety-five percent of patients with sarcoidosis have granulomas in the lung (7). Gal et al reported 5 patients with sarcoidosis among 464 patients with Sjögren’s syndrome (1). Lung involvement of Sjögren’s syndrome has been reported to be similar to that of sarcoidosis (2). Although Sjögren’s syndrome sometimes accompanies sarcoidosis (8), pulmonary multiple nodular lesions are rarely pathologically diagnosed to be sarcoidosis in patients with Sjögren’s syndrome. Fuke et al reviewed 28 cases of histologically diagnosed sarcoidosis complicated by primary Sjögren’s syndrome; the chest roentgenologic types of sarcoidosis were stage 0, 4 cases; stage I, 10 cases; stage II, 3 cases; stage III, 7 cases; and unknown, 3 cases (9). In this report, in 3 cases of stage II sarcoidosis, pulmonary involvement was confirmed by observation of bilateral fine nodular shadows in chest radiographs.

Huggins et al reported that the frequency of pleural effusions caused by sarcoid pleural involvement was 1.1%, and concluded that pleural effusion in patients with sarcoidosis should not be assumed to be related to sarcoidosis (10). On the other hand, Lohrmann et al performed high-resolution CT imaging and reported bilateral pleural effusion in 8.4% of patients with primary Sjögren’s syndrome (6). In the present case, the disease that caused pleural effusions is unknown. Since pleural effusions of the other side of the lung that was operated on disappeared without treatment with
systemic corticosteroids, it is easy to assume that pleural effusions are related to sarcoidosis with a high remission rate. Minshall et al reported a high level expression level of interleukin (IL)-2 and interferon-gamma (IFN-gamma) mRNAs in bronchoalveolar lavage cells in sarcoidosis patients compared to that in normal patients, but no significant differences were observed in the percentages of IL-4 and IL-5 mRNA-positive cells between sarcoidosis patients and normal controls (11). These results showed that there is a preferential expression of T-helper type 1 (Th 1) cytokines in pulmonary sarcoidosis. On the other hand, Fox et al found that salivary gland cluster of differentiation 4-positive (CD 4+) T cells produce over 40-fold more IL-2 and IFN-gamma than peripheral blood CD4+ T cells in patients with Sjögren’s syndrome compared to that in normal controls (12). Their results showed activation of Th 1 lymphocytes at the site of organ-specific immune damage. Thus, the predominance of Th 1 lymphocytes may be associated with the coexistence of Sjögren’s syndrome and sarcoidosis.

In summary, we describe a case of Sjögren’s syndrome accompanied with pulmonary sarcoidosis. Although the coexistence of Sjögren’s syndrome and sarcoidosis has been reported occasionally, cases with histological evidence of sarcoidosis have been rare. Pulmonary sarcoidosis should be considered in the differential diagnosis of pulmonary multiple nodules in patients with Sjögren’s syndrome.

**References**