

[CASE REPORT]

Lupus Pleuritis with Silicotic Nodules in the Parietal Pleura

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Abstract:

A 63-year-old man with occupational exposure to silica presented with cutaneous ulcer, pleuritic pain, and a fever. Laboratory data showed lymphopenia and positive serum antinuclear and anti-DNA antibodies. Computed tomography of the chest showed egg shell-like calcification of the hilar and mediastinal lymph nodes without pulmonary parenchymal involvement of silicosis. A surgical biopsy showed silicotic nodules with surrounding infiltration of lymphocytes and plasma cells in the parietal pleura. With a diagnosis of systemic lupus erythematosus (SLE), systemic corticosteroid therapy was given, which led to the resolution of symptoms and laboratory abnormalities. We discuss the relationship between silica exposure and the development of SLE.

Key words: systemic lupus erythematosus, silicosis, silicotic nodule, parietal pleura, lupus pleuritis

(Intern Med 57: 1277-1280, 2018)

(DOI: 10.2169/internalmedicine.9193-17)

Introduction

Previous studies have demonstrated that silica exposure is a risk factor for the development of systemic lupus erythematosus (SLE) (1). Experimental studies also support the hypothesis that silica exposure is associated with the development of SLE (2, 3). In addition, there have been several case reports of patients with silicosis who developed SLE (4-9). In this study, we describe a case of lupus pleuritis with silicotic nodules in the parietal pleura but without radiologic findings of silicosis in the pulmonary parenchyma. The relationship between silica exposure and SLE is also discussed.

Case Report

A 63-year-old man presented with a 2-month history of cutaneous ulcer, followed by symptoms of right pleuritic pain and a low-grade fever after 1 month. His occupational history included welding of automobile parts for 22 years and cutting of cylinder heads for 4 years without the use of any respiratory protection. He had a 63-pack-year history of smoking. There was no intake of drugs except for alprosta-

dil alfadex ointment for cutaneous ulcer prescribed by a plastic surgeon. On admission, his temperature was 37.2°C, and his respiratory rate was 16 breaths per minute. His oxygen saturation was 96% by pulse oximetry. No findings of arthritis or photosensitivity were evident. Visual inspection revealed a cutaneous ulcer on the left hip. Pleural friction rub on the right was noted on chest auscultation. Laboratory tests showed leukopenia (leukocyte 2,700/ μ L); lymphopenia (lymphocyte 386/ μ L); normocytic anemia (hemoglobin 8.4 \times 10³/ μ L, mean corpuscular volume 99.0 fl.); hypergammaglobulinemia (IgG 4,340 mg/dL); and elevated serum levels of C-reactive protein (1.3 mg/dL), lactate dehydrogenase (402 IU/L), anti-nuclear antibody (2,560 \times , homogenous pattern), anti-DNA antibody (13 IU/mL), anti-SS-A antibody (1,200 U/mL), and anti-SS-B antibody (10.6 U/mL). Although a direct Coombs test was positive, the serum level of haptoglobin was normal (168 mg/dL), and a decrease in the serum level of Fe (26 μ g/dL) and an increase in the serum level of ferritin (2,161 ng/mL) were seen, suggesting anemia of chronic disorder. The serum anti-Smith, anti-ribonucleoprotein, myeloperoxidase- and proteinase 3-anti-neutrophil cytoplasmic antibodies, anti-cardiolipin antibody, and lupus anticoagulant were negative. The serum cryoglobulin was also negative, and the serum levels of comple-

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Received: March 21, 2017; Accepted: September 5, 2017; Advance Publication by J-STAGE: December 27, 2017

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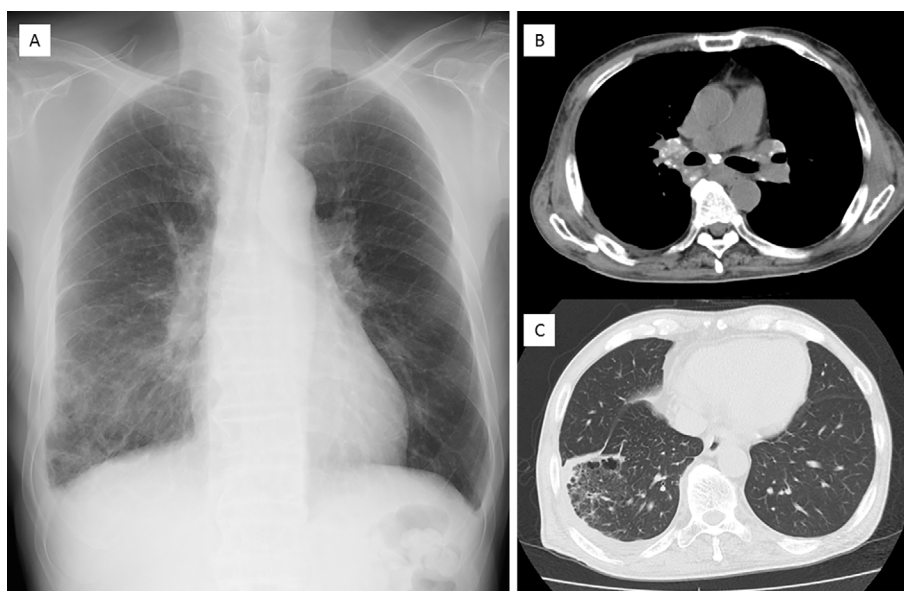


Figure 1. Chest radiography shows pleural thickening on the right (A). Computed tomography of the chest reveals pleural thickening, ground-glass opacity in the right lower lobe, and egg shell-like calcification of the bilateral hilar and mediastinal lymph nodes (B, C).

ment were normal. A biopsy specimen from the cutaneous ulcer demonstrated the findings of vasculitis with lymphoplasmacytic infiltration. Urinalysis did not show any abnormalities. On an ophthalmologic examination, Schirmer's test showed decreased lacrimal production, and fluorescein staining revealed keratoconjunctivitis sicca.

Chest radiography showed pleural thickening on the right. Computed tomography (CT) of the chest revealed pleural thickening, ground-glass opacity in the right lower lobe, and egg shell-like calcification of the bilateral hilar and mediastinal lymph nodes. Findings of silicosis in both lungs and pleural effusion were not evident (Fig. 1). The results of a pulmonary function test were as follows: vital capacity of 3.47 L (98.6% predicted), forced expiratory volume in 1 second of 3.14 L (90.5% predicted), and diffusion capacity of the lung for carbon monoxide of 20.79 mL/min/mmHg (100.0% predicted). A bronchoalveolar lavage fluid (BALF) analysis revealed cell count of $1.81 \times 10^5/\mu\text{L}$, with a cell differential of 81.0% macrophages; 15.0% lymphocytes; 1.5% neutrophils, and a CD4/CD8 ratio of 2.3. No microorganisms were detected on BALF culture. A transbronchial lung biopsy (TBLB) specimen obtained from the right lower lobe showed alveolar septal thickening, inflammatory cell infiltration, and fibrosis (Fig. 2A).

To exclude tuberculosis, a surgical parietal pleural biopsy was performed. The parietal pleural biopsy specimen showed infiltration of lymphocytes and plasma cells around silicotic nodules (Fig. 2B and C) and vasculitis (Fig. 3). Polarized light microscopy revealed multiple refractile white particles of varying size and shape around silicotic nodules, consistent with silica (Fig. 2D). Based on the American College of Rheumatology criteria (i.e. presence of anti-nuclear antibody, anti-DNA antibody, hematologic disorder, and pathologically confirmed pleuritis), a diagnosis of

SLE with secondary Sjögren's syndrome was made. In this case, the presence of serositis, leukopenia, an elevated level of anti-nuclear antibody, and a positive result for the direct Coombs test also met the 2012 systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. Based on the BAL and TBLB findings, the patient was thought to have SLE-associated interstitial lung disease.

The patient's pleuritic pain persisted despite the administration of loxoprofen. However, systemic corticosteroid therapy with prednisolone 30 mg per day resolved the pleuritic pain, as well as the cutaneous ulcer and low-grade fever. Four months later, prednisolone was tapered to 10 mg daily. The patient remains asymptomatic with maintenance therapy of prednisolone. The laboratory findings of leukopenia, lymphopenia, anemia, and elevated serum levels of C-reactive protein and lactate dehydrogenase also improved.

Discussion

SLE is a relatively uncommon, complex, and multisystem autoimmune disease that is thought to result from the interaction between genetic and environmental risk factors. Epidemiologic studies have shown that silica exposure is a risk factor for the development of SLE. Other risk factors include cigarette smoking, oral contraceptive use, and postmenopausal hormone replacement therapy (1). In addition, experimental studies on silica-exposed individuals using human cells *in vitro* have suggested that the development of autoimmune diseases might be associated with silica-induced alterations in Fas and Fas-related molecules and the attenuated function of regulatory T cells (2). The ingestion of silica particles by alveolar macrophages initiates an inflammatory response via cytokine production. In studies us-

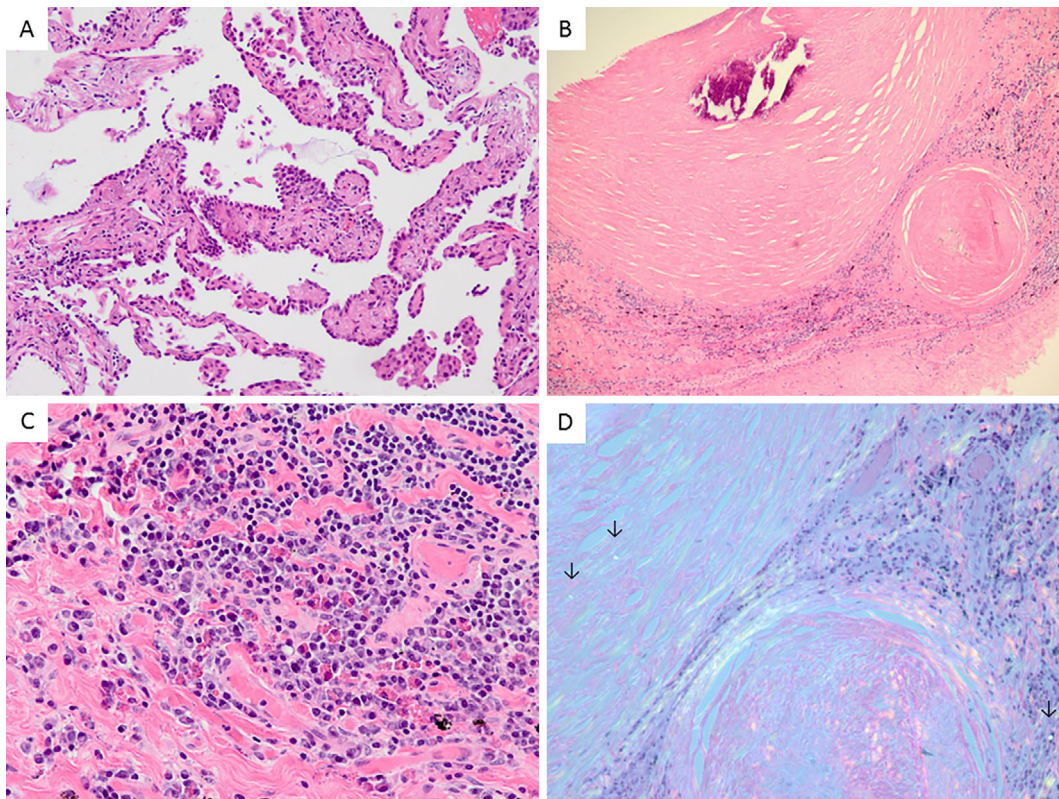


Figure 2. A transbronchial lung biopsy specimen from the right lower lobe shows alveolar septal thickening and infiltration of inflammatory cells (A, Hematoxylin and Eosin staining, $\times 200$). A surgical parietal pleural biopsy shows silicotic nodules (B, $\times 40$) and surrounding infiltration of lymphocytes and plasma cells (C, $\times 200$). Polarized light microscopy demonstrates multiple refractile white particles of varying size and shape around the silicotic nodules (D, $\times 100$).

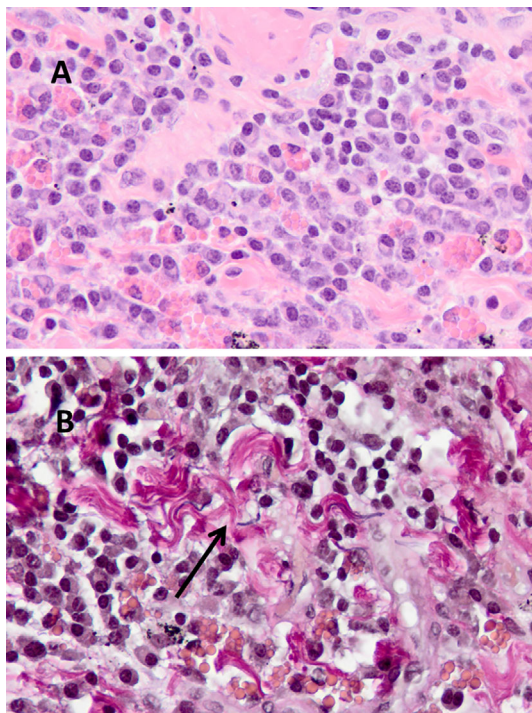


Figure 3. Higher magnification of the surgical parietal pleural biopsy specimen shows lymphoplasmacytic infiltration around vessels (A, Hematoxylin and Eosin staining, $\times 400$) and elastic fiber fragmentation (arrow) by inflammatory cell infiltration (B, Elastic van Gieson, $\times 400$).

ing animal models, silica exposure was shown to induce autoimmunity and can lead to the development of SLE-like disease (3). There have also been several case reports on silicosis associated with SLE (4, 5).

In the present case, the patient had been engaged in jobs that exposed him to silica. Although radiologic findings of silicosis in the bilateral pulmonary parenchyma were not evident, egg shell-like calcification of the bilateral hilar and mediastinal lymph nodes were seen on chest CT. In addition, the parietal pleura contained silicotic nodules, which have been reported to spread to extrapulmonary organs, such as the liver, spleen, bone marrow, and peritoneum, via the lymphohematogenous route (6, 7). These observations confirmed his exposure to silica, even if there was no radiologic evidence of pulmonary parenchymal involvement.

The reported pathological findings of silica-induced pleuritis are fibrous thickening of the pleura and macrophage infiltration (8), which are different from lymphoplasmacytic pleuritis in this case. In addition, findings suggestive of vasculitis were seen. Although lupus pleuritis is usually bilateral, two cases of unilateral lupus pleuritis have been reported (9, 10). We therefore consider that the present patient had lupus pleuritis. The pathologic findings of lupus pleuritis, such as parietal pleural infiltration of lymphocytes and plasma cells around silicotic nodules, might have been coincidental and could have been manifestations of silica-

induced autoimmune inflammatory processes at the sites involved. One case report described similar pathological findings around silicotic nodules in the pulmonary parenchyma (4). To our knowledge, this was the first case report of SLE in a patient who had been exposed to silica in which the pathologic findings of lupus pleuritis were demonstrated around silicotic nodules in the parietal pleura. Based on these observations, we speculated that autoimmune inflammatory processes might have occurred in the silica-laden sites surrounding the silicotic nodules; however, the precise pathophysiology of SLE related to silica exposure remains to be clarified. Furthermore, the number of patients with SLE related to silica exposure might be greater than previously believed, even in the absence of obvious radiologic findings of silicosis.

In conclusion, we reported a case of lupus pleuritis in a patient who was exposed to silica, wherein the pathologic findings of lymphocytic and plasma cell infiltration around silicotic nodules in the parietal pleura were seen. The autoimmune inflammatory processes might have started around the silica-laden sites. Further investigations will be needed to clarify the pathophysiology of SLE related to silica exposure.

The authors state that they have no Conflict of Interest (COI).

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