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CASE REPORT

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A case of Sjögren's syndrome in which diffuse cystic lung lesions led to an accurate diagnosis

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Key Clinical Message

Even in the absence of other symptoms or other pulmonary manifestations suggesting Sjögren's syndrome (SS), it is necessary to include SS in the differential diagnosis of diffuse cystic lung disease (CLD).

Abstract

A case of SS that presented initially with diffuse CLD is reported. This case is considered rare because diffuse pulmonary cysts were observed in the early stage with few symptoms, only cysts were observed without other lung lesions on imaging, cyst formation was histologically considered to be alveolar loss, and airway lesions not observed on imaging were suspected based on lung function testing. The details of this case provide extremely important information to consider for the diagnosis and management of CLD and SS.

KEYWORDS

bronchioloalveolitis, cystic lung disease, hyperproteinemia, Sjögren's syndrome, small airway obstruction

1 | INTRODUCTION

Cystic lung disease (CLD) has been reported as a pulmonary manifestation of Sjögren's syndrome (SS), which has been associated with pulmonary amyloidosis, lymphocytic interstitial pneumonia, and hematological malignancies.[1,2] A case of SS with minor symptoms that presented as CLD, including histological and physiological considerations, is described.

2 | CASE HISTORY/EXAMINATION

A woman in her mid-20s with no smoking history was aware of insidious, recurrent breathlessness at night and visited our hospital. She had a history of recurrent subauricular adenitis. She was not taking any medications. Her mother had myasthenia gravis, and her aunt had rheumatoid arthritis. Her consciousness was clear, temperature

36.3°C, blood pressure 123/88 mmHg, pulse 84 beats/min, and oxygen saturation 98% (room air). On physical examination, there were no abnormal findings.

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS, AND TREATMENT)

A screening blood test showed increased serum total protein (9.0 g/dL). There were no other abnormalities. The frontal chest X-ray (Figure 1A) was normal, but in the lateral projection (Figure 1B), a cyst-like shadow was observed superimposed on the heart shadow. Computed tomography (Figure 1C–E) demonstrated multiple bilateral thin-walled cysts distributed throughout the pulmonary parenchyma. Vessels were seen within some cysts. There were no other findings, including centrilobular nodules, bronchial wall thickening, interstitial changes, or lymphadenopathy.

Further evaluation was initiated to determine the etiology of the hyperproteinemia. Serum immunofixation electrophoresis showed a polyclonal gammopathy, with the following autoimmune profile: antinuclear antibody 1:320 with a homogeneous nuclear pattern; anti-Sjögren's syndrome-related antigen A (anti-SSA) 1: ≥256; anti-Sjögren's syndrome-related antigen B (anti-SSB) 1:32; rheumatoid factor 47.7 IU/mL; and negative anti-cyclic citrullinated peptide (<0.5 U/mL). Her eyes were dry, with an abnormal Schirmer's test (right eye 2 mm, left eye 2 mm) and positive fluorescein-staining test. There was no tooth decay, but her mouth was dry with reduced secretion of saliva (gum test, 2.4 mL/10 min). The diagnosis of primary SS was made.

In addition, her pulmonary manifestations, including diffuse lung cysts, were further evaluated. Pulmonary function testing was almost normal (VC 3.27 L [96.4% predicted], FEV1 2.67 L [92.7% predicted], and FEV1/FVC 79.7). However, V50 was 2.95 L/s (67.8% predicted), V25 was 0.97 L/s (49.4% predicted), and forced expiratory flow between 25% and 75% (FEF25-75%) was 2.44 L/s (62.0% predicted). These findings suggested small airway obstruction.

Surgical biopsy by video-assisted thoracoscopy was then performed. A cavity adjacent to the pleura (Figure 2A) and another cavity adjacent to the interlobular septa (Figure 2B) were found. There were no findings of suspected amyloid deposition. On elastica-Masson staining, collapsed alveolar walls inside and outside the cyst-like structure were not observed (Figure 2C); therefore, it

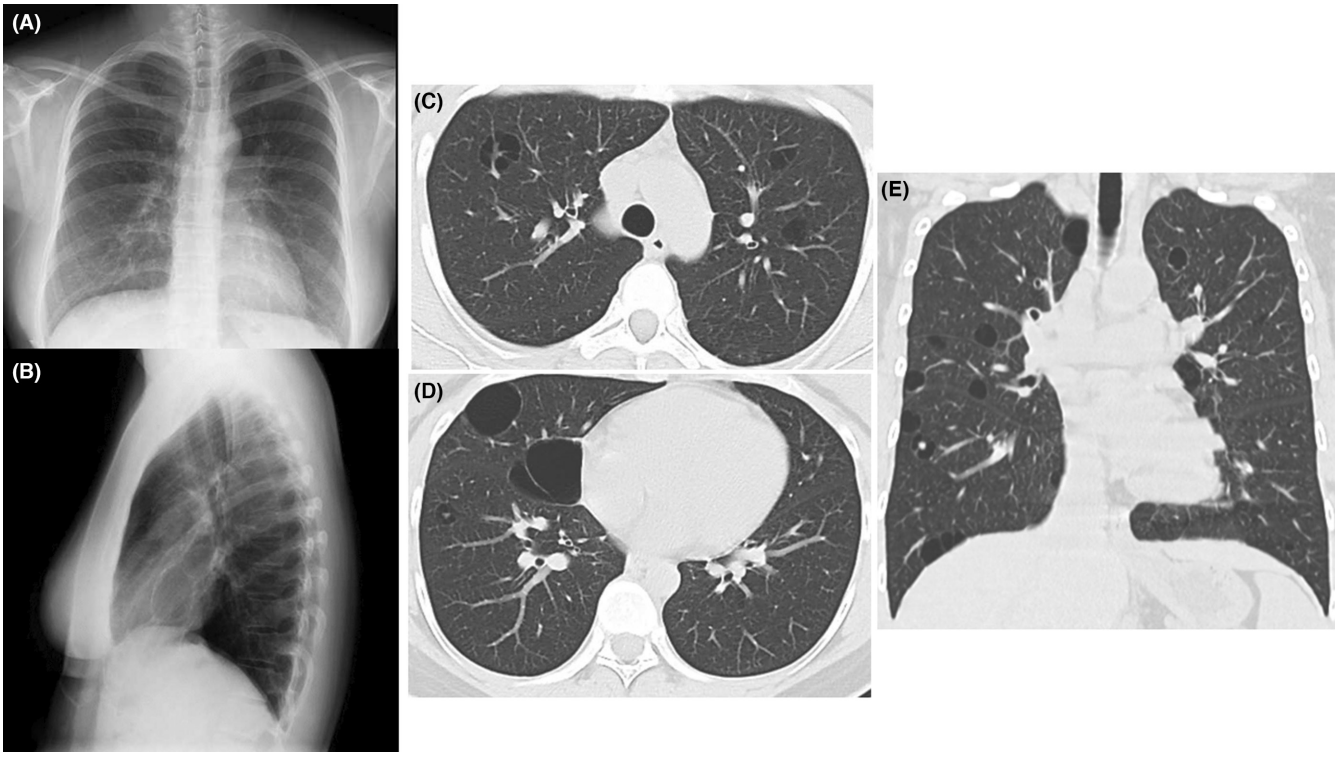

FIGURE 1 Radiological examination. The frontal chest X-ray (A) is normal, but in the lateral projection (B), a cyst-like shadow is observed superimposed on the heart shadow. Computed tomography (C–E) demonstrates multiple, bilateral, and thin-walled cysts that are distributed throughout the pulmonary parenchyma. Vessels can be seen within some cysts (C, D). There are no other findings, including centrilobular nodules, bronchial wall thickening, interstitial changes, or lymphadenopathy.

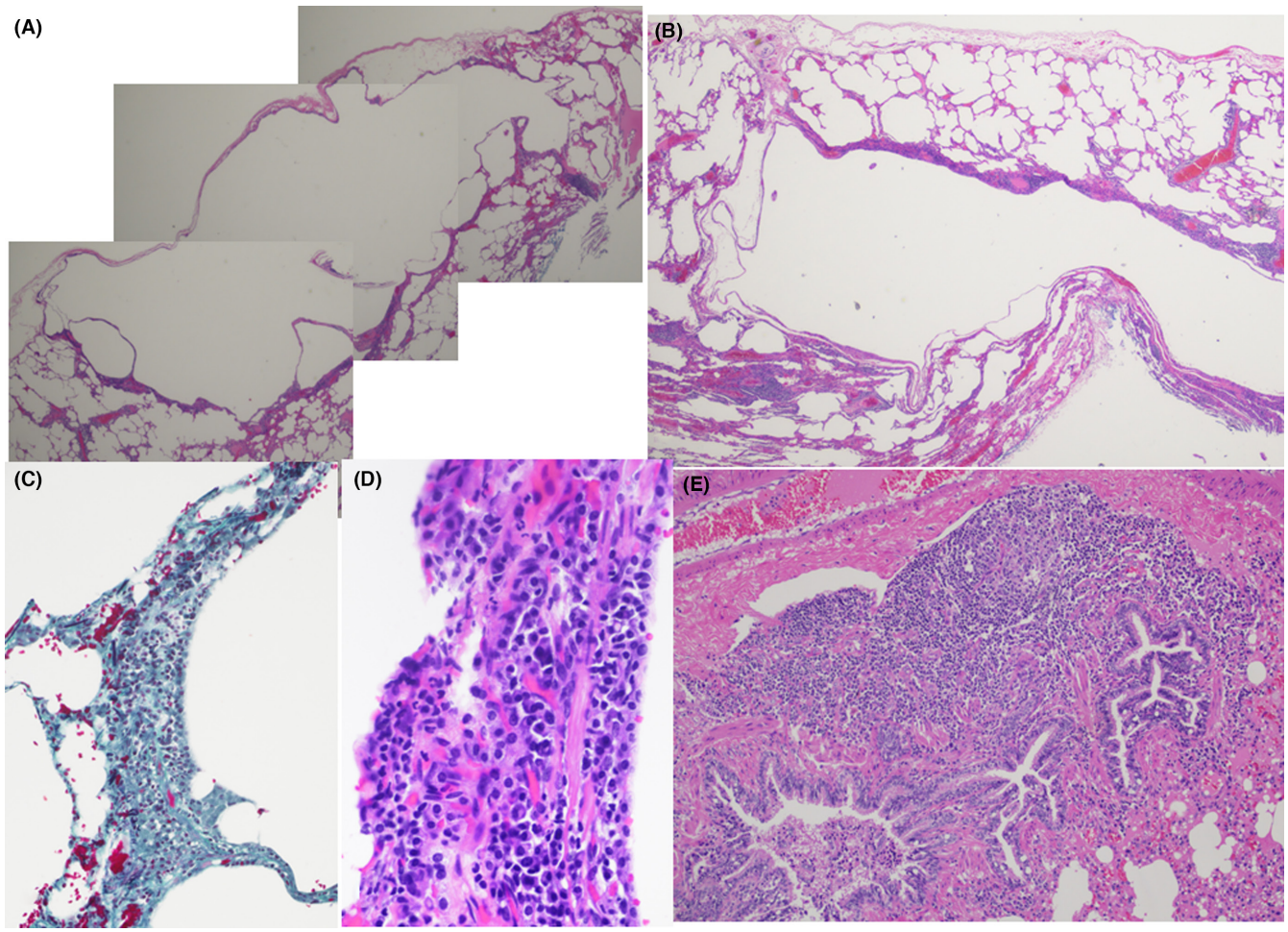

FIGURE 2 Histological examination. A cavity adjacent to the pleura (A, hematoxylin and eosin [H&E] staining, original magnification ×2), and another cavity adjacent to the interlobular septa (B, H&E staining, original magnification ×2) are found. Inside and outside the cyst-like structure, collapsed alveolar walls are not observed (C, elastica-Masson staining, original magnification ×20). In the cavity wall, infiltration of lymphocytes and plasma cells is also observed (D, H&E staining, original magnification ×40). Mixed lymphocyte and plasma cell infiltrates with formation of germinal centers are also observed in part of the bronchioles (E, H&E staining, original magnification ×10).

was a cavity, not a cyst, due to alveolar loss, to be precise. Infiltration of lymphocytes and plasma cells in the cavity wall was also observed (Figure 2D). Lymphoid plasma cell infiltrates with a germinal center were also observed in part of the bronchioles (Figure 2E), reminiscent of follicular bronchiolitis. From the above, the pulmonary lesions were cavities with lymphoplasmacytic bronchioloalveolitis, consistent with SS.

4 | CONCLUSION AND RESULTS (OUTCOME AND FOLLOW-UP)

We diagnosed her as SS with diffuse cystic lung lesions. Based on assessments using the EULAR SS disease activity index, the patient's disease activity was considered to be low. However, as she had a desire to have children, we informed her of the possibility of her infant developing neonatal lupus erythematosus, and that, although there is no established evidence, prophylactic treatment for the mother should be considered.

We managed her without systemic medication and by general condition check every 3–6 months, and chest imaging evaluation one to two times a year. No major changes have been observed at this time.

5 | DISCUSSION

Initially, the diagnosis of the present case was considered to be diffuse CLD, which occurs in young women and has few symptoms and other findings, with lymphangioleiomyomatosis, Birt–Hogg–Dubé syndrome, and pulmonary Langerhans cell histiocytosis as differential diagnoses. The pulmonary manifestations of SS include airway abnormalities, interstitial lung disease, and lymphoproliferative

disorders.[1] These lesions are recognized on imaging as nodules, septal thickening, opacities, honeycomb, ground-glass opacity, bronchiectasis, pleural abnormalities, airway thickening, and CLD. Pulmonary cysts have been reported to occur in 7.4%–46.2% of patients with SS.[2] CLD in SS has been associated with pulmonary amyloidosis, lymphocytic interstitial pneumonia, and hematological malignancies.[2] In the present case, multiple lung cysts were found at an early, near-asymptomatic stage, and no similar cases were found in our review of the literature.

In addition, no findings other than cysts, including centrilobular nodules, bronchial wall thickening, interstitial changes, or lymphadenopathy, were found. Cyst-only disease is less common (2.5%–9%), and the pathological processes leading to its development are unclear.[2] The diffuse CLDs have a broad differential diagnosis. Proposed mechanisms include check-valve obstruction with distal overinflation, and ischemia and remodeling induced by matrix metalloproteinase (MMPs) or other matrix-degrading enzymes.[3,4] CT of the present case showed vessels in some cavities. This may suggest that the mechanism of cavity formation was a check valve. However, on pathological examination, collapsed alveolar walls inside and outside the cyst-like structures were not observed, which means the loss or disappearance of alveolar structure and may suggest that the mechanism of cavity formation was ischemia or remodeling.

Lung function in the present case suggested peripheral airflow limitation. Histologically, lymphoplasmacytic bronchioloalveolitis was seen, which suggests that lung function tests may be able to detect airway lesions earlier than imaging.

Early diagnosis of SS in young women, even in cases that only require follow-up, is very important because it can provide lifestyle guidance. For instance, in pregnant women with primary SS, the presence of anti-SSA and anti-SSB, as in the present case, is responsible for congenital heart block, a severe complication in offspring.[5] If SS is diagnosed early, its complications may be prevented.[6]

The clinical course of this case provides important information to consider for the diagnosis and management of SS and CLD.

AUTHOR CONTRIBUTIONS

Satomi Mizutani: Writing – original draft. **Hidehiko Kuribayashi:** Investigation. **Noriyuki Saeki:** Investigation. **Hideki Ito:** Investigation. **Yasutaka Nakamura:** Visualization. **Makoto Masuda:** Visualization. **Yoshito Kamio:** Visualization. **Masashi Kawamoto:** Writing – review and editing. **Tatsuji Enomoto:** Writing – review and editing.

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None.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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