



Case report

Acute onset systemic lupus erythematosus interstitial lung disease: A case report

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ABSTRACT

A 40-year-old Japanese man was diagnosed with systemic lupus erythematosus. Chest computed tomography showed patchy consolidation in both lungs. A cryobiopsy and bronchoalveolar lavage showed organizing pneumonia, not acute lupus pneumonia or diffuse alveolar hemorrhage. This case demonstrates the usefulness of cryobiopsy for the management of systemic lupus erythematosus interstitial lung disease.

1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by a wide spectrum of clinical manifestations, including cardiac, vascular, renal, mucocutaneous, and pulmonary involvement [1]. Pulmonary involvement includes acute lupus pneumonitis (ALP) and diffuse alveolar hemorrhage (DAH), which are the most severe conditions [2,3].

Accurate diagnosis is important for treatment planning and prolonging survival. However, due to the poor general condition of patients at onset, it is not always possible to perform sufficient investigations. A case of acute onset SLE interstitial lung disease (SLE-ILD), which was diagnosed as organizing pneumonia (OP), not ALP or DAH, by cryobiopsy and bronchoalveolar lavage fluid (BALF) examinations and started on appropriate treatment, is presented.

This case demonstrates the usefulness of cryobiopsy to determine appropriate treatment for acute onset SLE-ILD in a low invasive way.

2. Case report

A 40-year-old Japanese man visited the emergency department with

a two-week history of fever, cough, shortness of breath, and chest pain. He had a more than a one-and-a-half-year history of skin ulcers (Fig. 1a and b) on both forearms and photosensitivity and erythema on the cheek and neck (Fig. 1c and d) since the previous summer. On physical examination, fine crackles were heard in both lungs.

The chest X-ray (Fig. 2a) showed bilateral diffuse infiltrates and cardiomegaly. On chest computed tomography (CT) (Fig. 2b and c) many spots or nodular ground glass shadows were evident in both lungs, and a pleural effusion was seen on the right side. Laboratory tests showed (Table 1) lymphopenia, anti-double-stranded DNA-positive, and anti-nuclear antibody-positive. SLE was diagnosed based on the above results. A skin biopsy showed the findings of discoid lupus, with shedding of epidermal cells and neutrophilic infiltration, and the subcutaneous fatty tissue was lost and fibrotic.

A cryobiopsy and BAL were performed to rule out ALP and DAH because of the acute clinical course of the SLE-associated pulmonary disease. Based on the gross findings of the BALF and no findings of hemosiderin-laden macrophages on histopathology and cytology, DAH was ruled out (Fig. 3a). The cell fraction of BALF was lymphocyte-dominant (Table 1).

A histological analysis of the lung tissues obtained by cryobiopsy

Abbreviations: ALP, acute lupus pneumonitis; BALF, bronchoalveolar lavage fluid; CT, computed tomography; DAD, diffuse alveolar damage; DAH, diffuse alveolar hemorrhage; OP, organizing pneumonia; SLB, surgical lung biopsy; SLE, systemic lupus erythematosus; SLE-ILD, systemic lupus erythematosus interstitial lung disease.

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Fig. 1. Discoid lupus erythematosus on both forearms (a, b). Photosensitivity and erythema on the cheek and neck (c, d).

(Fig. 3b) showed OP pattern, with excessive proliferation of granulation tissue with bronchiolar intraluminal polyps, and fibrin deposition in the alveolar space showed severe alveolar damage. There were no findings of organizing diffuse alveolar damage (DAD) or acute fibrinous OP.

The patient was referred to the Department of Rheumatology, and he was started on high-dose methylprednisolone and intermittent intravenous cyclophosphamide therapy. Three months later, the bilateral diffuse infiltrates had decreased on chest X-ray and chest CT (Fig. 4), and the pulmonary function tests were improved (Table 2).

3. Discussion

A case of acute onset SLE-ILD that was histopathologically diagnosed as OP by cryobiopsy was reported. DAH was suspected radiologically, and ALP was suspected clinically, but both were ruled out by the cryobiopsy and BALF examinations, and appropriate intensity treatments were performed.

Enomoto et al. reported that the most frequent onset of SLE-ILD at diagnosis was chronic onset (63.6%), followed by subacute (20.0%) and

acute (12.7%) [4]. The frequent patterns on high-resolution CT were NSIP + OP pattern (25%), OP pattern (22%), NSIP pattern (13%), and DAD pattern (2%). In the present case, ALP was suspected based on the acute onset, and DAH was suspected based on the chest CT findings.

ALP and DAH have been described as the major forms of severe pulmonary involvement in SLE. They are characterized by the sudden onset of non-specific symptoms including dyspnea, cough, fever, pleuritic chest pain, and, occasionally, hemoptysis [5].

DAH is usually diagnosed by BALF examination when an increasingly or persistently bloody BALF return is noted. ALP is generally a histological diagnosis that has been described as DAD with or without alveolar hemorrhage and capillaritis.

In the present patient, ALP and DAH were suspected due to the clinical symptoms and radiological findings, but they were ruled out by BALF and cryobiopsy examinations. Treatment with high-dose methylprednisolone and intermittent intravenous cyclophosphamide was started.

In SLE-ILD, surgical lung biopsies have generally not been performed because of the patients' poor respiratory status. Enomoto et al. reported

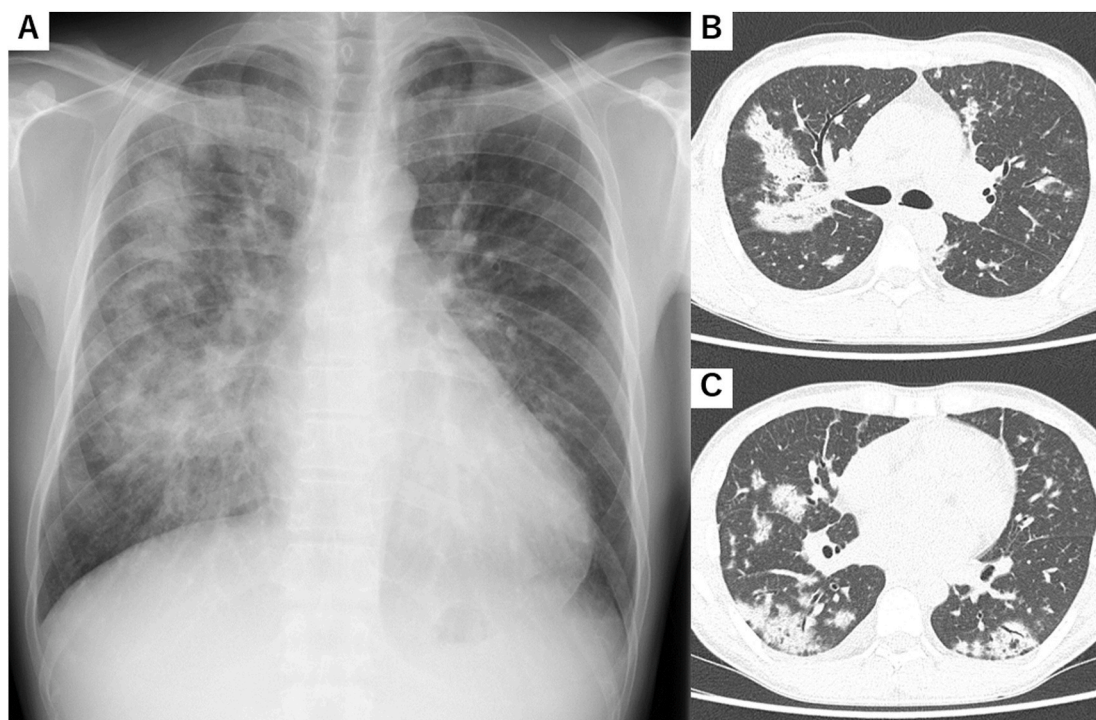


Fig. 2. Chest X-ray on admission shows consolidation mainly of the left lung (a). Chest CT shows consolidation of the left lung (b,c).

that, of 55 SLE-ILD patients, only 9 underwent lung biopsy [4].

Although cryobiopsy is a technique similar to forceps biopsy, cryobiopsy could obtain sufficient specimens to contribute to a definitive diagnosis, better than forceps biopsy. Some reports showed that cryobiopsy has a higher diagnostic yield than conventional forceps biopsy [6], with high levels of agreement between cryobiopsy and surgical lung biopsy (SLB) for both histopathological interpretation and multidisciplinary discussion [7]. Moreover, cryobiopsy may enable histopathological assessment even in patients with more advanced disease unsuitable for SLB [8]. In the present case, the degree of alveolar damage could be assessed by histological examination, and adequate treatment was provided. We hope that further knowledge of the relationship between the histological diagnosis of SLE-ILD and its treatment

outcomes will be obtained.

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Author contributions (Credit roles)

Machiko Arita: conceptualization, Keiichiro Kadoba: supervision, Takashi Niwa: writing-review and editing, Fumiaki Tokioka: writing-review and editing, Tadashi Ishida: writing-review and editing.

Table 1

Laboratory findings on admission and bronchoalveolar lavage fluid (BALF) and pulmonary function test (PFT) findings.

Laboratory findings		BALF			
WBC(μ L)	4200	CRP(mg/dL)	1.55	Total cell count(/mL)	1.1×10^6
Neutro(%)	68.0	C3(mg/dL)	81.8	Macrophages(%)	56.0
Eos(%)	3.0	C4(mg/dL)	22.2	lymphocytes(%)	42.0
Lymph(%)	18.0	CH50(U/mL)	48.0	Neutrophil(%)	2.0
Mono(%)	11.0	KL-6(U/mL)	250	Cytology	negative
Hb(g/dL)	12.2	ANA	80	Culture	normal flora
PLT(μ L)	24.9×10^4	Homo	\pm	Pneumocystis PCR	negative
Alb(g/dL)	3.0	Nucleola	+	Cytomegalovirus PCR	negative
AST(U/L)	28	Cyto	+		
ALT(U/L)	22	ds-DNA ELISA(IU/mL)	23.0		
LDH(U/L)	282	ds-DNA RIA(IU/mL)	7.8		
BUN(mg/dL)	12	SS-A antibody	negative		
CRE(mg/dL)	0.68	SS-B antibody	negative		
eGFR(mL/min/1.73m ²)	102.6	ANCA	negative		
Na(mmol/L)	135	Urinary protein	-		
K(mmol/L)	4.1	Urinary occult blood	-		
Ca(mg/dL)	8.8	Urinary sugar	-		

Alb: Albumin, **ANA:** Anti-nuclear antibody, **AST:** Aspartate aminotransferase, **ALT:** Alanine aminotransferase, **BUN:** Blood urea nitrogen, **Ca:** Calcium, **CH50:** 50% Hemolytic unit of complement, **CRE:** Creatinine, **CRP:** C-reactive protein, **Cyto:** Cytoplasmic, **C3:** Complement 3, **C4:** Complement 4, **ds-DNA:** Anti-double-stranded DNA, **eGFR:** Estimated glomerular filtration rate, **Eos:** Eosinophil, **Hb:** Hemoglobin, **Homo:** Homogeneous, **LDH:** Lactate dehydrogenase, **Lymph:** Lymphocyte, **K:** Potassium, **Mono:** Monocyte, **Na:** Sodium **Neutro:** Neutrophil, **PCR:** Polymerase chain reaction, **PLT:** Platelets, **WBC:** White blood cell.

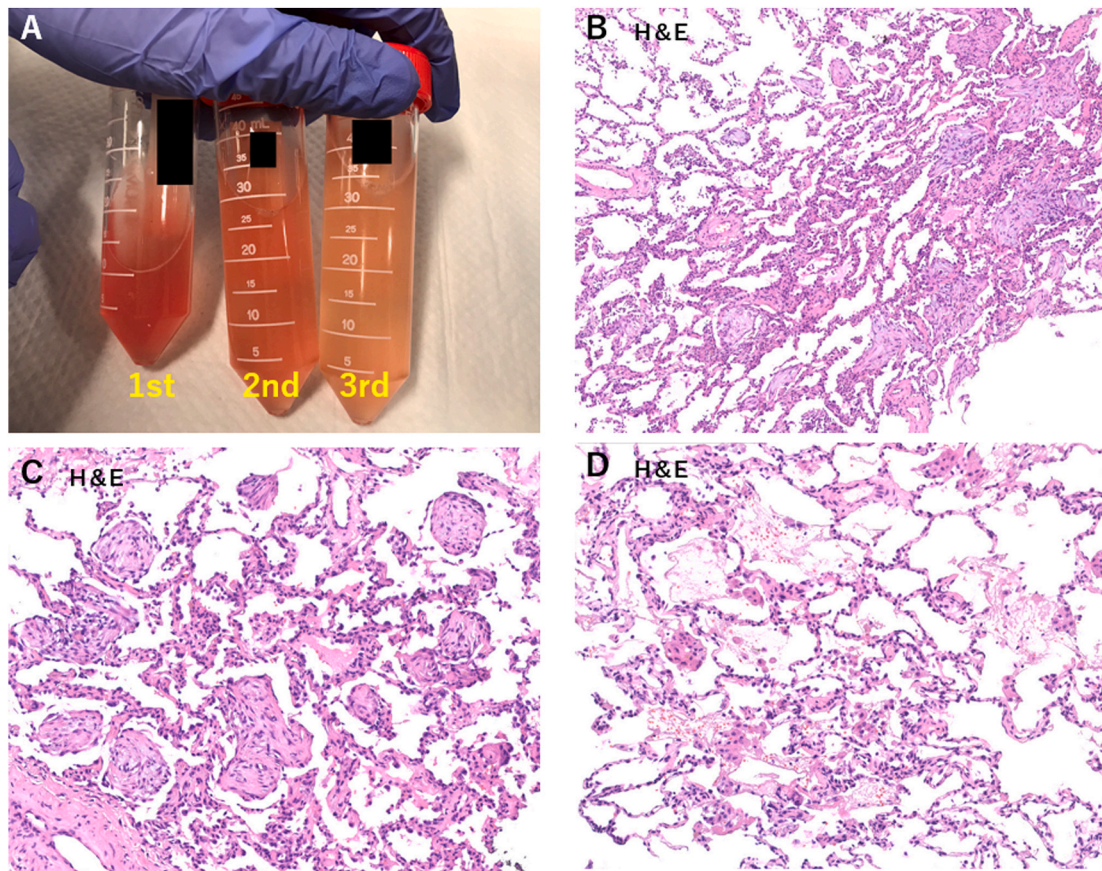


Fig. 3. Appearance of bronchoalveolar lavage fluid (A). There is no alveolar hemorrhage, since there is no sign of a gradual increase in bloodiness. Pulmonary histopathological findings of the tissues obtained by cryobiopsy (hematoxylin and eosin stain; H&E) (B–D). An excessive proliferation of granulation tissue with bronchiolar intraluminal polyps, which suggests organizing pneumonia (OP) pattern (B, C). Fibrin precipitation into the alveolar space is present, suggesting severe alveolar epithelial damage (D).

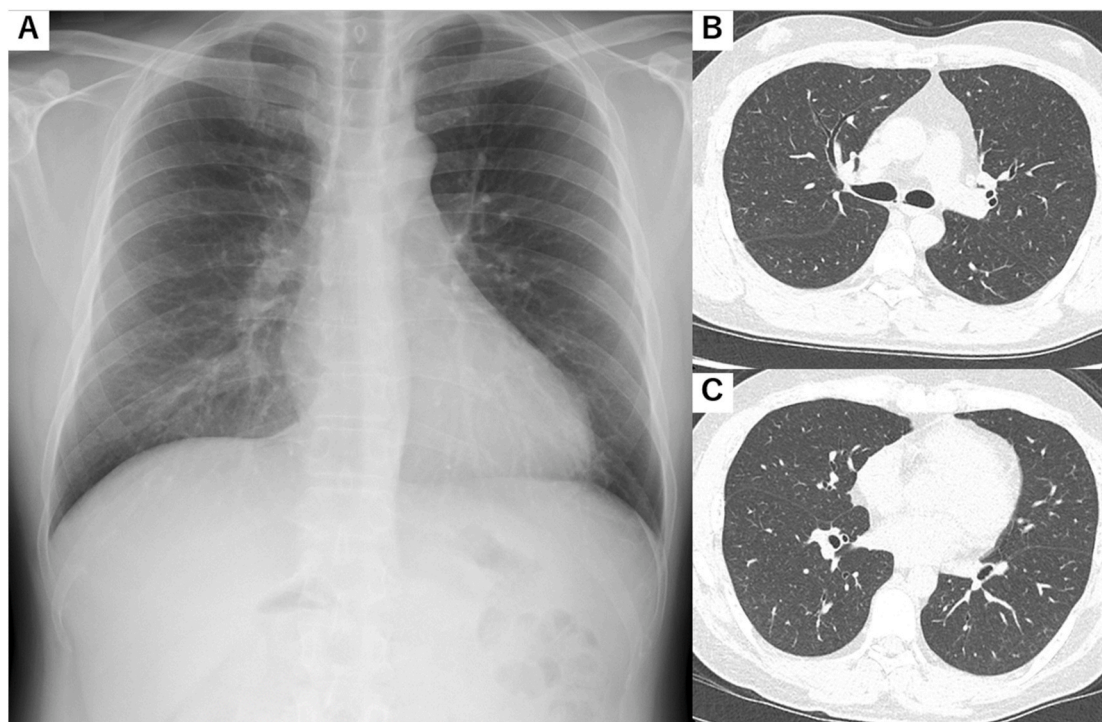


Fig. 4. Chest X-ray 3 months after admission shows that consolidation has improved (a). Chest CT 3 months after admission shows that consolidation has improved (b, c).

Table 2
Pulmonary function test results.

PFT	On admission	3 months later
VC(L)	3.02	4.19
%VC(%)	69.1	95.2
FEV ₁ (L)	2.40	3.22
%FEV ₁ (%)	64.2	85.6
FEV ₁ % (%)	79.5	76.8
%DL _{CO} (%)	80.9	73.0

DL_{CO}: Diffusing capacity for carbon monoxide, FEV₁: Forced expiratory volume in one second, PFT: Pulmonary function test, VC: Vital capacity.

Declaration of competing interest

None.

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