


Longitudinal lung involvement of systemic lupus erythematosus-related vasculitis and alveolar proteinosis-like reaction

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Keywords

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Abstract

A 44-year-old woman with no symptoms was referred to our hospital for thorough examination of consolidation opacity on her left lung, which was growing for four years. She was diagnosed with systemic lupus erythematosus (SLE) at the age of 35 years and had been treated with prednisolone 10 mg/day. Physical examination and bronchoscopy revealed no abnormality including microbiological tests. She underwent surgical resection of the lung lesion. Lung biopsy specimens showed aggregation of lymphocytes with germinal centres and collagen deposition. Vasculitis and pulmonary alveolar proteinosis (PAP)-like reaction were also found. We diagnosed this lung opacity as an SLE-related lung lesion with vasculitis and PAP-like reaction. Lung involvement of SLE is scarce and long-term lung vasculitis and PAP-like reaction are extremely rare in patients with SLE. Clinicians should be aware of such SLE-related lung consolidation opacity that comprises lung vasculitis and PAP-like reaction.

Introduction

Systemic lupus erythematosus (SLE) is a major connective tissue disease that affects multiple organs, mainly in young women. Predominant manifestations include the involvement of joints, serosal membrane, haematocytes, skin, kidneys, and the central nervous system. Although involvement of lungs is rare in patients with SLE, pleuritis is the most frequently reported thoracic disorder [1,2]. Furthermore, SLE-related vasculitis in the lung is extremely rare while it predominantly occurs in skin of patients with SLE [3]. In addition, pulmonary alveolar proteinosis (PAP) is also scarce in patients with SLE [4]. Here, we present a case of SLE-related lung vasculitis concomitantly with PAP-like reaction.

Case Report

A 44-year-old woman with no symptoms was referred to our hospital for thorough examination of consolidation opacity that was growing for four years on her left lung

(Fig. 1). She had 10 pack-years of ex-smoking history. She was diagnosed with SLE at the age of 35 years and had been treated with prednisolone 10 mg/day. Physical examination revealed no abnormality. Laboratory data showed increased levels of serum anti-double-stranded DNA antibody (19 IU/mL) and anti-single-stranded DNA antibody (514 AU/mL; Table 1). Serum C-reactive protein, Krebs von den Lungen-6, surfactant protein-D, and titres of PR3-antineutrophilic cytoplasmic antibody (ANCA) and MPO-ANCA remained within normal ranges. Pulmonary function was not impaired. Chest radiograph showed a growing consolidation opacity in the left middle to lower lung field over four years (Fig. 1A: at the first diagnosis of the lung lesion, B: four years later). Chest high-resolution computed tomography (HRCT) showed consolidation opacity on her left lingular segment that had been growing for four years (Fig. 1C: at the first diagnosis of the lung lesion, D: four years later). Bronchofibrescopy and microbiological tests revealed no abnormality, although bronchoalveolar lavage was not performed. She underwent

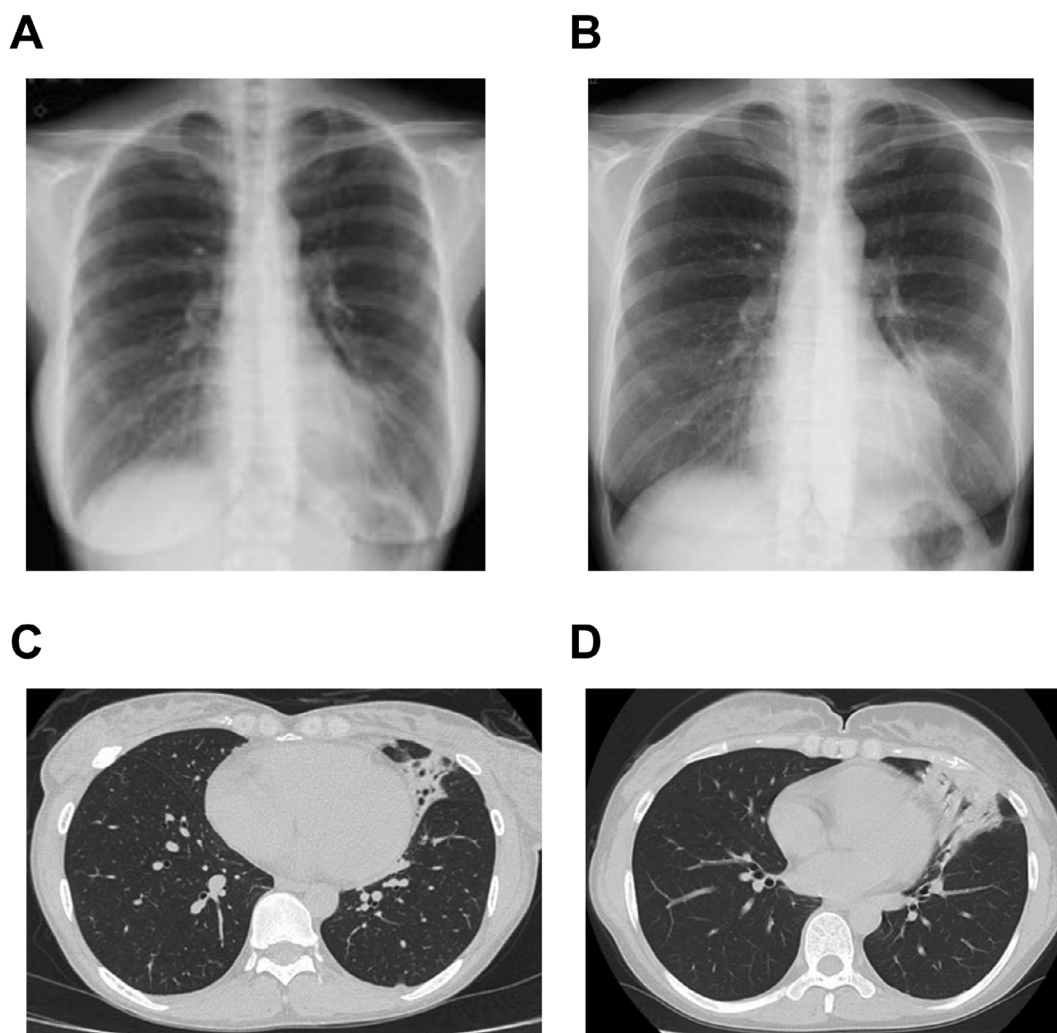


Figure 1. Changes of lung opacity in chest X-ray and high-resolution computed tomography (HRCT). (A) Faint consolidation opacity appears in the left lower lung field at the first diagnosis of lung lesion. (B) Four years later, a growing consolidation opacity is seen in the left middle to lower lung field. (C) Consolidation opacity is newly appearing in the left lingular segment at the first diagnosis of lung lesion. (D) Four years later, gradually growing consolidation opacity with traction bronchiectasis is seen in the left lingular segment. Pleural effusion is not found.

surgical resection of the lung lesion. Lung biopsy specimens showed aggregation of lymphocytes and plasma cells with germinal centres and collagen deposition (Fig. 2A). Vasculitis was also found (Fig. 2B–D). Furthermore, eosinophilic exudate and cholesterol clefts existed in the other lung lesion (Fig. 2E, F). In this area, concentric globules mixed with foamy macrophages were seen in alveolar space (Fig. 2G). These globules were positive for periodic acid-Schiff (PAS) and showed “rose-like appearance” (Fig. 2H). We diagnosed this opacity as SLE-related lung lesion with vasculitis and PAP-like reaction. Several other diseases, which can cause small vessel vasculitides, such as anti-glomerular basement membrane (Goodpasture)

disease, cryoglobulinaemic vasculitis, IgA vasculitis, and hypocomplementaemic urticarial vasculitis, were excluded based on lack of typical eruption, renal dysfunction, and peripheral nerve disorders. There was no recurrence of lung lesion for the three-year period after surgical resection during which she had been receiving corticosteroid therapy.

Discussion

We herein report a case of SLE-related vasculitis concomitantly with PAP-like reaction. Involvement of lungs is rare in patients with SLE and the most frequently reported thoracic lesion is pleuritis, which is found in 16–60% of

Table 1. Laboratory findings.

Hematology		AST	24 U/L	Anti-dsDNA antibody	19 U/mL
White blood cell	3,400/ μ L	ALT (7-23 U/L)	30 U/L	(<12 U/mL)	
Neutrophil	60.7%	Sodium	141 mmol/L	Anti-ssDNA antibody	514 U/mL
Lymphocyte	24.5%	Chloride	107 mmol/L	(<25 U/mL)	
<u>Monocyte (3-9%*)</u>	<u>11.8%</u>	Potassium	3.6 mmol/L	Anti-Sm antibody	3.2 U/mL
Eosinophil	2.7%	C-reactive protein	0.04 mg/dL	PR3-ANCA	0.5 U/ml
Basophil	0.3%	KL-6	216 U/mL	MPO-ANCA	0.5 U/ml
Red blood cell	445 \times 10 ⁴ / μ L	SP-D	65.4 ng/mL		
Hemoglobin	13.7g/dl			Urine tests	
Hematocrit	41.0%	Immunology		Uric protein	Negative
Platelet	22.7 \times 10 ⁴ / μ L	IgG	1,279 mg/dL	Uric blood	Negative
<u>ESR (3-13mm/hour)</u>	<u>36mm/hour</u>	<u>IgA (93-393 mg/dL)</u>	<u>457 mg/dL</u>		
		IgM	55 mg/dL	Pulmonary function tests (% predicted)	
Blood chemistry		C3	94.0 mg/dL	VC	3.44 L (102.7%)
Total protein	6.8 g/dL	<u>C4 (11-31 mg/dL)</u>	<u>10.7 mg/dL</u>	FVC	3.43 L (106.5%)
<u>Albumin (4.1-5.1 g/dL)</u>	<u>3.8 g/dL</u>	CH50	31 U/ml	FEV ₁	2.68 L (99.3%)
Blood urea nitrogen	13 mg/dL	<u>ANA (<1:40)</u>	<u>1:160</u>	FEV ₁ /FVC	78.1%
Creatinine	0.52 mg/dL	(homogeneous and speckled appearance)			

*Normal ranges are described in parenthesis.

ALT, alanine aminotransferase; ANA, anti-nuclear antibody; ANCA, antineutrophilic cytoplasmic antibody; AST, aspartate aminotransferase; C, complement; CH50, 50% haemolytic unit of complement; ds, double-stranded; ESR, erythrocyte sedimentation rate; FEV_{1.0}, forced expiratory volume in 1 sec; FVC, forced vital capacity; Ig, immunoglobulin; KL-6, Krebs von den Lungen-6; MPO, myeloperoxidase; PR3, proteinase 3; Sm, Smith; SP-D, surfactant protein-D; ss, single-stranded; VC, vital capacity.

patients with SLE [1,2]. Furthermore, in terms of parenchymal lung lesion such as interstitial pneumonia, lung focal involvement is scarce in patients with SLE. We reported 62 patients with SLE with thoracic diseases who visited respiratory departments [5]. In that report, lung focal consolidation on HRCT similar to this case was not found except for infection. Furthermore, neither SLE-related vasculitis nor PAP-like lesion was found [5].

As for vasculitis in SLE, Ramos-Casals et al. studied 670 patients with SLE and vasculitis was identified in 76 (11%) patients [3]. In their report, cutaneous vasculitis accounted for 89% of patients, while lung vasculitis accounted for only 1.3% [3]. Moreover, many of these patients with SLE-related vasculitis presented arthritis (87%), fever (62%), and cutaneous lesions (73%) [3]. Therefore, lung vasculitis without any symptoms, as in our case, is extremely rare.

PAP is caused by abnormal accumulation of phospholipoproteinaceous material in airspace of the lung. Its incidence is estimated to be 0.49–6.2 per million. To the best of our knowledge, only one case report of PAP with

SLE exists [4]. In that report, one patient showed lung diffuse ground-glass opacities consistent with “crazy-paving” pattern on computed tomography (CT) and showed milky bronchoalveolar lavage fluid [4]. Conversely, our case showed focal consolidation opacity on HRCT, although pathological PAP-like reaction was found in surgical lung specimens (Fig. 2E–H). We could not measure anti-granulocyte-macrophage colony-stimulating factor (GM-CSF) antibody. While PAP was not clinically and actively suspected in this case, we believe that histopathological PAP-like reaction is a lung manifestation of SLE. The relationship between PAP and disorders in humoral immunity other than anti-GM-CSF antibody has been unclear [6], and we need further study to clarify this issue.

In conclusion, we experienced a case of SLE with lung vasculitis and PAP-like reaction in which lung consolidation existed for four years. Existence of lung vasculitis and PAP-like reaction is extremely rare in patients with SLE, and we need further study to elucidate the relationship between lung vasculitis and PAP-like reaction.

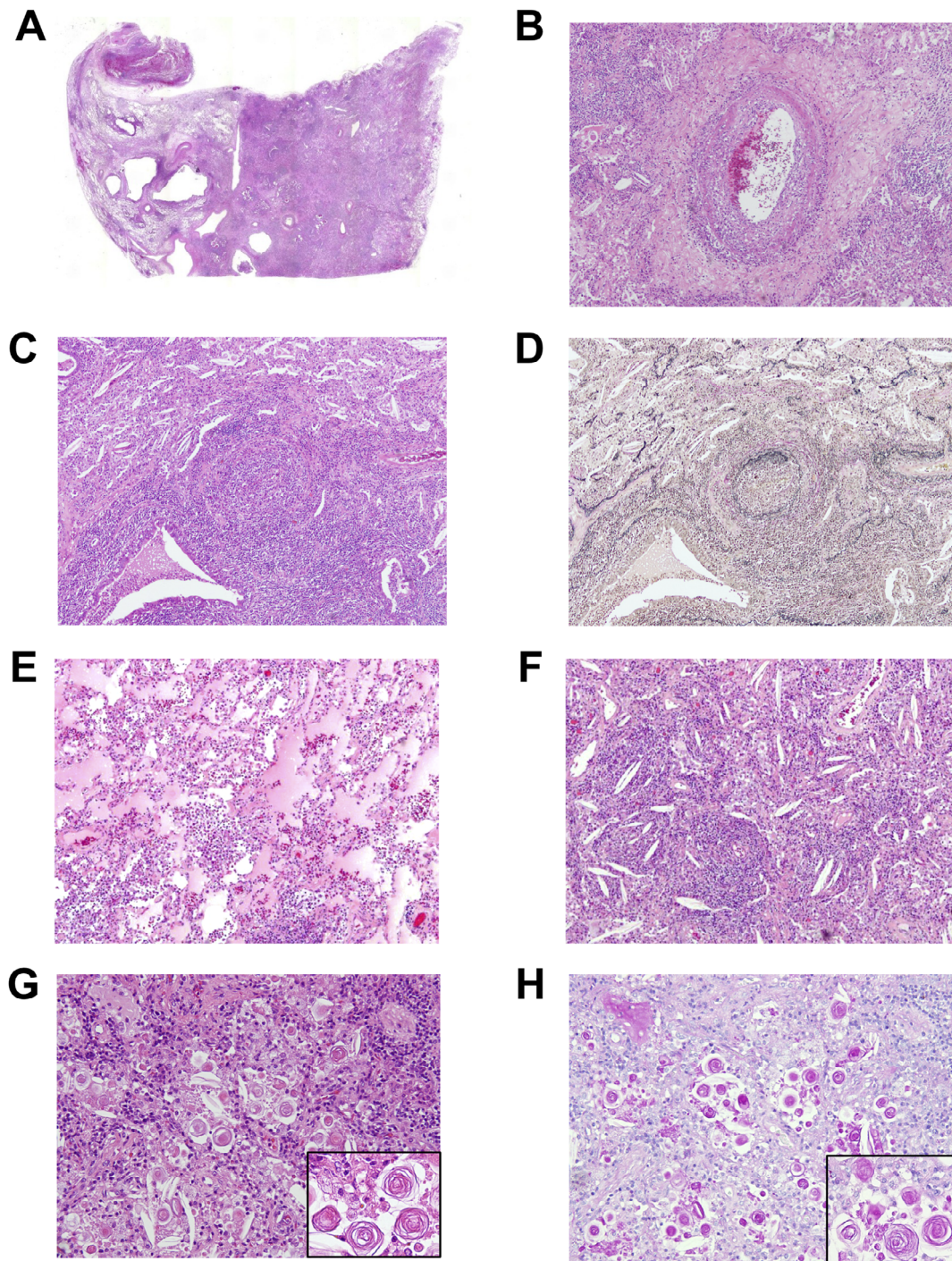


Figure 2. Surgically resected lung specimens. (A) Microscopic examination with lower magnitude shows solid lung lesion. Aggregation of lymphocytes and plasma cells with germinal centres and collagen deposition are found (haematoxylin and eosin (HE) stain: 12.5 \times). (B and C) Lung vasculitis with mononuclear cell aggregation is seen (HE stain: 40 \times). (D) Elastica-Van-Gieson (EVG) stain shows destruction of elastic layers of vasculature (EVG stain: 40 \times). In the other lung lesion, eosinophilic exudate (E) and cholesterol clefts (F) exist (HE stain: 40 \times). (G) Eosinophilic concentric structures and exudate with foamy macrophages and cholesterol clefts exist in air space (HE stain: 100 \times). This concentric structure shows “rose-like appearance” (inset: HE: 200 \times). (H) Eosinophilic concentric structures and exudate are positive for periodic acid-Schiff (PAS) stain and correspond to pulmonary alveolar proteinosis (PAP)-like reaction (PAS stain: 100 \times). This concentric structure also shows rose-like appearance (inset: PAS: 200 \times).

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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