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CASE REPORT

Systemic lupus erythematosus with initial presentation of empyematous pleural effusion in an elderly male patient: A diagnostic challenge

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Systemic lupus erythematosus (SLE) poses great difficulty in making an early diagnosis in elderly males, often presenting with atypical manifestations. Acute onset of empyematous pleural effusion has rarely been seen. Herein, we report a 66-year-old man with SLE presenting with rapid progression of bilateral pleural effusion. Diagnostic thoracentesis disclosed neutrophil-predominant exudates and chest computed tomography revealed multiple loculated pleural effusions. Nevertheless, optimal antibiotic therapy plus surgical decortication of the pleura did not improve his condition. The diagnosis of SLE was readily established after LE cells were accidentally found in the pleural effusion. Large amounts of pleural effusion subsided soon after high dose corticosteroid therapy.

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease involving multiple organs. It mostly affects young and middle-aged females and is diagnosed by American College of Rheumatology (ACR) criteria. However, a wide spectrum of clinical manifestations is common and early diagnosis is crucial to potentially fatal complications. Male geriatric patients with SLE are easily missed or

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delayed in diagnosis because of the lower incidence in these groups and atypical clinical presentations. We report an elderly male SLE patient who initially presented with empyematous pleural effusion. Interestingly, the rapid diagnosis of SLE was due to the accidental observation of LE cells in the pleural effusion.

Case report

A 66-year-old male with hypertension who previously had medical therapy, was admitted for fever and dyspnea lasting several days. One week previously, he had been hospitalized for left pneumonia with parapneumonic effusion. After treatment with empirical antibiotics for 3 days, even though no specific pathogen was isolated, he felt better and was discharged, against advice, with an oral form of levofloxacin. Physical examination revealed his blood pressure was 140/82 mmHg, blood temperature 37.8°C, pulse rate was 110 beats/minute, and respiratory rate was 24 breaths/minute. Decreased breathing sounds over the bilateral lower lung fields and bilateral pedal edema were recorded, but lymphadenopathy and skin lesions were not noted. The chest film revealed

cardiomegaly, a new right massive pleural effusion and worsening of the previously existing left pleural effusion (Fig. 1A).

Laboratory analysis showed the white blood cell count as 15.5 k/cm³ (normal range = 3.4k–9.1 k/cm³), hemoglobin concentration as 8.8 g/dL (normal range = 13.5–17 g/dL), serum albumin level as 2.5 g/dL (normal range = 3.5–5 g/dL), glucose as 280 mg/dL (normal range = 75–105 mg/dL) and C-reactive protein as 163.9 mg/L (normal <5 mg/L). A positive direct Coombs' test was incidentally noticed while preparing for blood transfusion. Urine analysis showed proteinuria (>300 mg/dL). Diagnostic thoracentesis resulted in an exudate with predominant neutrophils. He was then treated for pneumonia, complicated by parapneumonic pleural effusion after above evaluation.

There was no improvement under the treatment of 3rd generation cephalosporins and doxycycline, and a chest tube was placed, but in vain. Chest computed tomography (Figs. 1C and 1D) which showed bilateral loculated pleural effusion, consolidations and ground glass opacities at the bilateral lower lobes, cardiomegaly and trivial pericardial effusion. Serial analysis of pleural fluids (Table 1) revealed them to be consistently exudative in nature, and there was an incidental finding of LE cells.

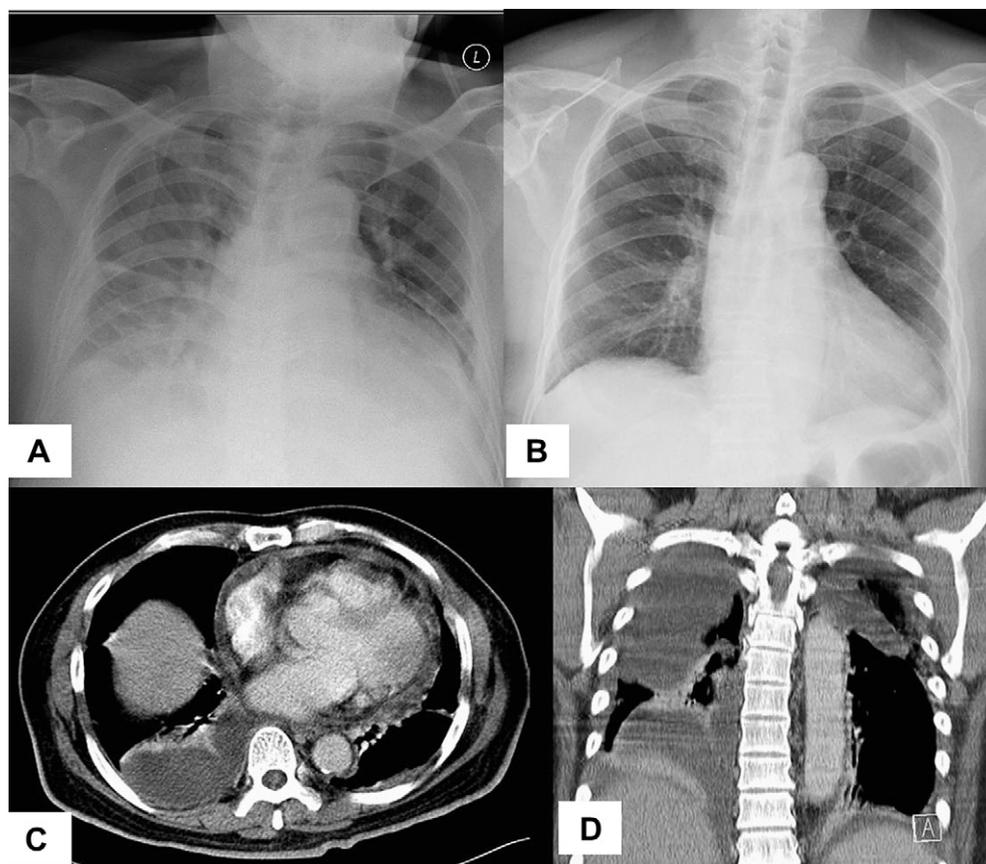


Figure 1. Chest X-ray and chest computed tomography before and after systemic steroid therapy. (A) Chest X-ray on this admission showing cardiomegaly and bilateral exacerbated pleural effusion; (B) chest X-ray after right side decortication and systemic steroid therapy showing obvious improvement; (C, D) chest computed tomography showing lobulated pleural effusions over both lungs, more on the right side with consolidations and with ground glass opacities at bilateral lower lobes as well as cardiomegaly and some pericardial effusion.

Table 1 Serial thoracocentesis data review

Variable	Last admission	Emergency department	On Admission	During operation
Side	Left	Right	Left	Right
Appearance	Yellowish	Reddish	Reddish	Reddish
RBC (cmm)	0	50000	Clot mostly	66000
WBC (cmm)	4000	340	Clot mostly	2950
Differential count(%)				
Neutrophil	20	48	92	90
Eosinophil	2	12	—	—
Monocyte	20	24	4	7
Lymphocyte	2	16	4	3
Mesothelial cell	44	—	—	—
Light's criteria	Exudate	Exudate	Exudate	Exudate
Glucose (mg/dl)	110	85	99	83
pH value	7.03	6.92	6.8	—
Cytology	Negative	Negative	LE cell	Negative
Culture, Gram stain, Acid-fast stain	Negative	Negative	Negative	Negative

Because of the lack of improvement, the patient finally received right side decortication for diagnostic and therapeutic purposes. The pathology of pleura and lung parenchyma disclosed reactive fibroblasts and proliferative endothelial cells, infiltrated by neutrophils, and empyema was suspected (Figs 2A and 2B) but no specific pathogen was isolated. Despite decortication, with concomitant antibiotic therapy, his effusion and fever persisted.

Due to the detection of LE cells in the pleural effusion, a survey for SLE was performed. This disclosed decreased serum complement at the C3 and C4 levels, a high titer of antinuclear antibody (ANA) (1:1280, speckled type), and positive anti-double-stranded DNA antibodies (1:160). After establishing a diagnosis of SLE, high dosage parenteral corticosteroid therapy (methylprednisolone 1 mg/kg/day) was administered. His effusion, fever, and dyspnea significantly improved. The following chest roentgenogram (Fig. 1B) revealed complete resolution of the pleural effusion.

Discussion

SLE is an imitator with various presentations. Overall, 90% of patients with lupus are female and most are between 15 and 50 years of age.¹ Therefore, making an early diagnosis is tough in elderly males without a classical expression. In a case series analysis of 520 patients with SLE conducted by Dubois and Tuffanelli, pleuritis was observed in 45% of patients, and accounted for 3% of the initial manifestations.² In late onset SLE, pleuritis was observed more frequently, especially among male patients,³ and may be the only specific symptom at the initial hospital arrival.

Lupus-related pleural effusion is currently ascribed to immune complex deposition and the binding of anti-dsDNA antibodies to the mesothelium; it is usually exudative with a low pH value, high protein, lactic dehydrogenase (LDH) and negative culture results.⁴ The glucose level is often low in rheumatoid related pleural effusion but indeterminate in lupus.⁵ In addition, systemic high glucose level may

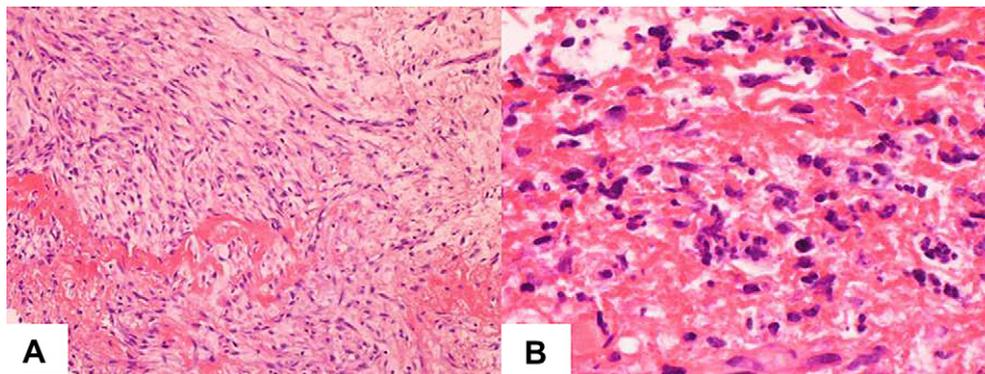


Figure 2. Decortication and lung biopsy. Reactive fibroblasts and proliferative endothelial cells infiltrated by neutrophils, lymphocytes, and plasma cells, with fragments of lung parenchyma due to acute inflammation. (A) Gomori-methenamine-silver, acid fast and Gram stain showing negative findings. There is no evidence of malignancy. HE, $\times 400$. (B) Many polymorphonuclear leukocytes showing aggregation with the necrotic debris. High power view HE, $\times 600$.

interfere with the interpretation. The effusion usually affects both sides and the white blood cell count is observed in a range of 500 to 15,000/cmm. Nevertheless, the differential count did not show a significant predominance of either neutrophils or lymphocytes.⁶

Non-infectious loculated pleural effusion, shown in this case, also called sterile empyema or empyematous pleural effusions, is usually seen in rheumatoid arthritis, pancreatitis and malignancy.⁵ To our knowledge, it is rare in patients with SLE.⁷ To distinguish it from infectious etiologies is crucial, since super-infection in lupus pleural effusion is possible. As for our case, the initial thoracocentesis was performed before antibiotic treatment started and only 3-day therapy was prescribed prior to the 2nd pleural effusion study. The results both implicated empyema (including a pH < 7.2 and elevated LDH, total protein). The patient was initially treated with antibiotics under the impression of infectious empyema, but in vain. Great efforts to identify any microorganism including using decorticated lung tissue failed. The importance of early decortication of infectious empyema has been emphasized, to achieve a better therapeutic response, as well as fewer complications. Conversely, in empyematous pleural effusion, even though decortication tends to decrease the incidence of fibrothorax, trapped lung and symptomatic restrictive disturbance but not superior to anti-inflammatory treatment.⁵ In our case, neither antibiotics nor decortication led to a therapeutic response. The symptoms of the patient were not resolved until SLE was diagnosed and treated. Thus, based on no pathogen being identified in cultures and pathology specimens, treatment with glucocorticoid for lupus related empyematous pleural effusion is reasonable. However, culture-negative bacterial empyema due to prior antibiotic exposure could not be definitely excluded in our case.

Empyematous pleural effusion has been more commonly reported in rheumatoid arthritis than other etiologies, with the histologic characteristics of a "gritty" or "frozen" pleural surface appearance, numerous small vesicles, granules, and nodules. Effusion from ruptured rheumatoid nodules into the pleural space is the supposed pathophysiology. Meanwhile, pleuritis in SLE is a result of a localized immune process, with fewer features to distinguish it from other inflammatory related pleural effusions. In our case, the pathology finding of pleura revealed reactive fibroblasts and proliferative endothelial cells infiltrated by neutrophils, lymphocytes, and plasma cells; Gomori-methenamine-silver and gram stain tests and a malignancy survey showed negative results. The reported characteristics of pleural biopsy in lupus erythematosus pleural effusion have been described as "the replacement of normal mesothelial cells covered by epithelioid cells with nucleated cells" and corresponds to the results in our patient.

The presence of LE cells in the effusion, even though less sensitive, is highly specific for the diagnosis of lupus pleuritis and usually indicates an active disease status.⁸ They are composed of polymorphonuclear neutrophil phagocytosis of apoptotic bodies induced by antinuclear antibodies. Phagocytes from patients with lupus were shown to engulf far less apoptotic material than phagocytes from healthy subjects, implying an impaired "waste disposal" function. C1q and anti-histone H1 antibody play roles in the phagocytosis, by binding to cell debris, which can then be engulfed by macrophages.^{1,8} Besides, some reports indicate that the binding of anti-RNP antibody, as well as anti-SS-A/Ro and anti-SS-B/La antibodies, is predominantly involved in the development of cutaneous LE lesions.⁹ However, LE cells are not frequently observed and cannot be depended on to make diagnoses, no longer belonging to the updating American College of Rheumatology revised criteria.¹⁰

SLE does occur in elderly males with an initial presentation as rapidly-progressive loculated pleural effusion only. If laboratory analyses and thoracocentesis give an indeterminate result, a clinical suspicion of autoimmune disturbance is reasonable and may facilitate early diagnosis.

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