

[CASE REPORT]

Bilateral Pleuritis as the Initial Symptom of Systemic Lupus Erythematosus: A Case Series and Literature Review

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Abstract:

We documented four cases of systemic lupus erythematosus (SLE) presenting with pleuritis as the initial disease manifestation. The diagnosis was challenging because, atypically, all patients were elderly and 3 of the 4 patients were men. Furthermore, SLE pleuritis, characterized by lymphocytic pleural effusion and high ADA activity, is difficult to differentiate from tuberculous pleurisy. A detailed physical examination, blood tests, and urinalysis are therefore indispensable to ensure an accurate diagnosis. We also reviewed the previously published case reports on SLE patients presenting with pleuritis and discussed the relevant findings.

Key words: SLE, systemic lupus erythematosus, pleuritis, pleural effusion

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Introduction

Systemic lupus erythematosus (SLE) is a common autoimmune disease that adversely affects multiple organs. Pleuritis occurs in 43% of patients diagnosed with SLE (1) and is often associated with chest pain, with or without pleural effusion. However, pleural effusion as the initial presenting clinical sign of SLE is rare, occurring in only 1% of patients during the course of disease (2). This makes the diagnostic process more complex, and can lead to incorrect diagnoses. We herein report four cases in which SLE patients presented with pleuritis as the initial manifestation of disease and review the pertinent literature on similar adult cases.

Case Reports

Case 1

A 75-year-old man with a past medical history of coronary artery bypass grafting (CABG), chronic heart failure, chronic obstructive pulmonary disease, chronic kidney disease and type 2 diabetes presented to our outpatient clinic with a 3-week history of progressive dyspnea and productive cough despite treatment for congestive heart failure. He also

had a slight fever (37.0°C), leukocytosis (17,100/μL) and bilateral pleural effusion on a thoracic radiograph. The patient was admitted to our hospital with a tentative diagnosis of heart failure exacerbated by acute bronchitis, and antimicrobial and diuretic therapy were initiated. The initial treatments were, however, ineffective and the pleural effusion progressed. Echocardiography and cardiac catheterization showed no evidence of left-sided congestive heart failure or pulmonary arterial hypertension. Contrast-enhanced computed tomography was negative for pulmonary thromboembolism. Thoracentesis revealed lymphocytic exudate without evidence of malignancy, and microbiologic cultures were negative. The pleural effusion adenosine deaminase (ADA) level was 54.2 U/L (8.6-20.5). Pancytopenia and urinary red blood cell casts were also identified, leading to a differential diagnosis of SLE. Further laboratory testing revealed rising anti-double stranded DNA (anti-dsDNA) antibody levels [7 ng/dL, (0-6)] and hypocomplementemia, confirming a diagnosis of SLE pleuritis. The administration of methylprednisolone (60 mg, daily) improved his general condition and enabled him to be successfully discharged from the hospital.

Case 2

A 69-year-old man with a past medical history of ulcerative colitis and CABG for myocardial infarction presented to

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Table. Clinical Features of SLE Cases with Pleuritis as the Initial Presenting Clinical Sign.

Reference	3	4	5	6	7	8	Case 1	Case 2	Case 3	Case 4
Age	20	23	66	80	20	33	75	69	80	83
Gender	Female	Female	Male	Male	Male	Female	Male	Male	Female	Male
C.C.	Dyspnea	Chest pain	Dyspnea	Dyspnea	Dyspnea	Dyspnea	Dyspnea	Chest pain	Fever	None
ANA	1:160	1:320, Speckled	1:1,280	1:320	1:350	Positive	1:40	1:2,560	1:2,560	1:40-1:80
Anti-dsDNA	98 ng/dL	1:320	1:160	119 ng/dL	Positive	1:640	7 ng/dL	95 ng/dL	4 ng/dL	33-84 ng/dL
Classification Criteria*	N/R	N/R	N/R	N/R	N/R	N/R	Leukopenia Thrombocytopenia Low complement Urinary RBC cast	Proteinuria Anti-cardiolipin	Proteinuria Low complement	N/A
Pleural effusion	Bilateral Exudate Neut 80%, Lymph 20%	Left side Exudate	Bilateral Exudate Neut 92%, Lymph 4%	Bilateral Exudate	Bilateral Exudate Lymph 70%	Bilateral Exudate	Bilateral Exudate Lymph 82.5%	Bilateral Exudate Neut 35.5% Lymph 24%	Left side Exudate Lymph 4-60%	Bilateral Exudate Lymph 73%
ADA	23 U/L	N/R	N/R	N/R	N/R	22.8 U/L	54.2 U/L	89.0 U/L	22.5 U/L	175.1 U/L
Treatment	mPSL 1 mg/kg/day	mPSL 2 mg/kg/day +MTX 7.5 mg/week	mPSL 1 mg/kg/day	mPSL (500 mg×3 days) followed by mPSL 1 mg/kg/day +HCQ+MMF	PSL 50 mg/ day	mPSL (500 mg ×3 days) followed by mPSL 1 mg/kg/day +HCQ	mPSL 60 mg/day	mPSL 60 mg every other day	mPSL 30 mg/day	Aspirin 600 mg/day
Outcome	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improve	Improved

* Systemic Lupus International Collaborating Clinics classification criteria

C.C.: chief complain, N/R: not reported, N/A: not applicable, RBC: red blood cell, ANA: antinuclear antibody, Neut: neutrophil, Lymph: lymphocyte, PSL: prednisolone, mPSL: methylprednisolone, MTX: methotrexate, HCQ: hydroxychloroquine, MMF: mycophenolate mofetil

our hospital with a 3-month history of exertional dyspnea. A chest X-ray image showed bilateral pleural effusion. Thoracentesis revealed lymphocytic exudate without evidence of malignancy, and microbiologic cultures were negative. A high ADA level was noted (89.0 U/L), and thoracoscopy was performed. No evidence of tuberculosis or cancer was identified and pleural biopsy showed only lymphocytic infiltration. Further investigations revealed anti-nuclear antibody (ANA), anti-dsDNA antibody [95 ng/dL, (0-6)], and anti-phospholipid antibody positivity, leading to the diagnosis of SLE. His symptoms and pleural effusion improved after the administration of methylprednisolone (60 mg, every other day).

Case 3

An 80-year-old woman with a past medical history of right-sided breast cancer and scleroderma was referred for further evaluation of bilateral pleural effusion. Thoracentesis revealed lymphocyte-predominant exudate without evidence of malignancy, and microbiologic cultures were negative. The ADA level was 22.5 U/L. Further evaluation revealed proteinuria, hypocomplementemia, and leukopenia. Tests for ANA revealed positive results, confirmed that SLE was the cause of her pleuritis. The administration of methylprednisolone (30 mg, daily) improved her general condition.

Case 4

An 83-year-old man with a 30-year history of hypertension, hyperlipidemia, diabetes, and chronic kidney disease who had undergone CABG for angina twenty years previously presented to our division for a routine checkup after recovering from Legionella pneumonia. Investigations revealed bilateral pleural effusion and a slightly elevated C-reactive protein level (2.47 mg/dL). Thoracentesis revealed lymphocytic exudate without evidence of malignancy, and microbiologic cultures were negative. The level of ADA in the patient's pleural effusion was elevated (175.1 U/L). Thoracoscopy revealed no evidence of tuberculosis or cancer and pleural biopsy showed only lymphocytic infiltration. Further testing revealed anti-dsDNA antibody [33 ng/dL, (0-6)] positivity. We strongly suspected SLE and began administering aspirin (400 mg, daily) as a diagnostic treatment, after which his pleural effusion disappeared. One year later, his ANA titer became positive (1:80, homogenous) and his dsDNA antibody level increased to 84 ng/dl (0-6). We therefore thought that SLE was the most likely diagnosis.

Discussion

The four SLE patients described in this report presented with pleuritis as their initial clinical sign. In all four patients, testing unrelated to the pleural effusion ultimately led to the diagnosis of SLE.

Although pleuritis is a common feature of SLE, Dubois et al. showed that pleuritis associated with or without effusion occurs as the initial clinical sign of SLE in only 3% and 1%

of SLE patients, respectively (1). Pleural effusion typical of SLE is usually yellow-tinged and may be turbid or serosanguineous. It may be neutrophilic or become lymphocytic with time (2) and the adenosine deaminase (ADA) activity in pleural effusion from patients with SLE is often high. Thus, it is difficult to differentiate SLE from tuberculous pleurisy, pulmonary embolism, congestive heart failure, parapneumonic effusion, and nephrotic syndrome (2).

To date, there have only been 6 reported cases of SLE with pleural effusion as the initial manifestation reported in the English literature (Table) (3-8). Two of the six cases involved elderly patients, and in all cases, the effusion was bilateral and exudative. In addition, all previous case reports noted little systemic involvement apart from pleural effusion, making an accurate diagnosis challenging. All of the patients in our cases were elderly, and three of the four patients were men with cardiovascular disease and bilateral pleural effusion resulting in an initial, erroneous clinical diagnosis of congestive heart failure.

Previous studies have described that patients with late-onset SLE experience less mucocutaneous and renal effects, but more serositis (9, 10). Another study reported that SLE most commonly affects women, with the percentage of females in affected populations ranging from 88.3 to 96.2% (11). Thoracentesis is important for further evaluating elderly patients with bilateral pleural effusion that is resistant to diuretic treatment for suspected heart failure.

As all of the pleural effusions in our patients were lymphocytic, and as the ADA activity was high in 3 of the 4 patients, it was difficult to differentiate SLE from tuberculous pleurisy. Good et al. reported that 50% of patients with lupus pleuritis have a predominance of mononuclear leukocytes in their effusion (2). It has been demonstrated that pleural fluid ADA activity is often high in SLE (mean value, 33.3 U/L) (12). Cultivation tests and histopathology must be considered when tuberculous pleurisy is suspected.

In conclusion, we reported four cases in which pleuritis was the initial manifestation of SLE. In all cases, clinical findings unrelated to the pleural effusion ultimately led to an accurate diagnosis. Consequently, it is important to focus on other findings besides the pleural effusion when investigating pleural effusion of unknown origin. Physical examinations, blood tests, and urinalyses often provide important clues that can lead to a correct final diagnosis.

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

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