Systemic Lupus Erythematosus Presenting with Recurrent Pleural Effusion without any Systemic Manifestation


Abstract
Pleural effusion can be the sole presenting manifestation in about 5 percent of cases with SLE. We are reporting a case of SLE which presented with recurrent pleural effusion without other systemic manifestation.

INTRODUCTION
Systemic lupus erythematosus (SLE) affects predominantly women. Pleurisy is the most common thoracic manifestation of SLE. Clinically apparent pleural effusions have been reported in up to 50 percent of patients with SLE and in up to 93 percent of cases at necropsy. Pleural effusion can be the sole presenting manifestation in about 5 percent of cases with SLE. We are reporting a case of SLE, which presented with recurrent pleural effusion without other systemic manifestation.

CASE
A 20 years girl, student nondiabetic nonhypertensive was admitted in our institute in April 2004, with chief complaint of progressive dyspnoea, for last 7 days, without any pleuritic type of chest pain, productive cough or hemoptysis. There was no history of palpitation, PND, dependent edema or oliguria. There was a history of low-grade intermittent fever for seven days without any joint pain or dysuria.

In February 2004 she developed similar episodes of dyspnoea, intermittent fever, weakness, loss of appetite, lethargy, for which she was admitted in local hospital, and diagnosed to have bilateral pleural effusion. At that time there were bilateral palpable axillary lymph nodes, one of which was biopsied, histopathology revealed: reactive hyperplasia. Pleural biopsy was also done and showed nonspecific reaction.

She was treated with four antitubercular drug (ATD), (INH-300mg, Rifampicin 450mg, Ethambutol 800mg, Pyrizinamide 1.5gm, her body weight was 61Kg) + oral steroid (60mg/day) + inj ceftrioxone (2gm/day: for 7 days). As she was improved within 3 weeks she was discharged with four drugs ATD with oral steroid. She continued the ATD and steroid only for 3 weeks after discharge, and thereafter she stopped all treatment by herself without any medical consultation.

In July 2002 there was a similar episode of right sided pleural effusion for which her family physician had prescribed four drug ATD (IREZ) along with oral steroid (60 mg/day). She improved clinico radiologically over 3 weeks, after which she stopped ATD medications without any medical consultation.

On examination she was conscious, pulse was-100/minute, blood pressure was 160/98 mm of Hg, respiratory rate was 32/minute. Anaemia, jaundice, clubbing, and neck glands were absent. Neck veins were not engorged. Lymphoreticular system was normal. On inspection of the respiratory system there was no chest wall deformity or shoulder dropping. There were bilateral intercostal fullness in infraaxillary region. The movement of the chest wall was restricted bilaterally. There was no venous prominence. On palpation trachea was central in position, and percussion note was stony dull (bilateral). On auscultation there was diminished vesicular breath sound bilaterally. Cardiovascular system– apex could not be localized properly, S1 and S2 were audible and there was no murmur or added sounds. Other systems were normal.

On the day of admission her routine blood examination was as follows:
Hemoglobin: 12 gm%, RBC 4.9 million/cumm, WBC 7500 (N 60% L 26% E2% B 0% M 22%), platelet count: 3
lakhs/cumm, ESR: 80 mm/Hr, blood sugar 98mg%, Urea-34mg%, creatinine 0.6mg%, CRP: 9mg/dl (normal upto 5 mg/dl), serum lipid profile, T3, T4, TSH, liver function test, serum LDH were within normal limits. Urine: protein was trace, no RBC, no cast was detected. 24 hour urinary protein leak was 100mg/day, Sputum for AFB: negative (3 consecutive days), sputum culture in Bactec media: was negative. Pleural fluid Adenosine Deaminase (ADA); 23U/L (normal limit; upto 40ng/dl).

Chest X-ray showed: bilateral massive pleural effusion, Ultrasonography of chest was done which revealed multiple fibrous septae in addition to bilateral pleural effusion. Ultrasonography of abdomen showed no abnormality. Routine ECG was normal. Echocardiography showed, a mild pericardial effusion, no chamber enlargement, no evidence of pulmonary hypertension, valves were normal, no vegetation or clot was detected. Pleural fluid Gram stain and culture was negative for microorganism (three occasions). Mantoux test was negative. ELISA for HIV 1 and 2 was negative. Serum antinuclear antibody (ANA) was positive with the titer value 1:160 (done in Hep-2 cell line). In fluorescent microscopy the pattern of ANA was homogeneous. Anti ds DNA was strongly positive in a titer of 98ng/dl (Normal: upto 4ng/dl).

Pleural fluid routine examination done on various occasions are given in Tables 1 and 2.

Pleural fluid ANA was positive in a titer of 1:320. Serum ANA was 1:160, so pleural/serum ANA ratio was >2 (>1), pleural fluid LE phenomena not performed. On the day of admission 500 ml plural fluid was aspirated from right side of chest, next day 450 ml fluid was aspirated from left chest, conservative treatment (with IV antibiotic) was continued. (Fig. 1 shows chest X-ray on admission, Fig. 2 shows chest X-ray after thoracocentesis.) After getting all the reports, she was put on oral prednisolone (1mg/Kg/day) 60 mg per day. Within 14 days she improved clinically and her chest X-ray showed significant radiological improvement (Fig. 3). Four weeks after institution of steroid her chest X-ray showed near complete resolution of pleural fluid (Fig. 4).

Now she is on oral prednisolone, discharged from the hospital, and under our follow-up.

![Fig. 1 : Chest X-ray during admission in our institute, showing bilateral pleural effusion, February 2004.](image_url)

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(Normal pleural fluid protein: 1-2 gm /100ml, Normal serum LDH 100-190 U/L, Light criteria for exudative pleural effusion are: pleural fluid protein/serum protein > 0.5, pleural fluid LDH/serum LDH >0.6, pleural fluid LDH more than two third of the normal upper limit of the serum value)
DISCUSSION

In SLE pleural effusion usually bilateral and small to moderate in size, massive effusion leading to mediastinal shift have also been recorded. Immune complex deposition in pleural microvasculature and activation of complement plays an important role in pathogenesis of pleurisy and pleural effusion.

The pathogenesis of pleural effusion in SLE differs from that of RA, for example, immune complexes in RA are thought to be produce locally in the pleura, whereas immune complexes are derived from the circulation in SLE. In addition, the concentration of soluble interleukin-2 (IL-2) receptors in the pleural fluid in RA is significantly higher than that in SLE. This suggests that a local T-cell mediated immune reaction may be a more important mechanism in rheumatoid pleurisy than in lupus. In an autopsy study 54 of 58 patients (93%) in Ropes series showed pleural involvement, in 33 patients fluid were found in pleural space and adhesion seen in 63% cases. Varying degree of microscopic change were found in 24% cases, which consisted of accumulation of lymphocyte and macrophage, pleural thicking, perivascular fibrinoid necrosis with neutrophilic and mononuclear infiltrates, fibrinous exudates and rare hematoxylin bodies.

Several early studies revealed that reduced levels of hemolytic complement, C1q, C4, C3 in pleural fluid from lupus patient when compared to pleural effusions from patients with cancer, heart failure, and other conditions. This complement level remained low even after
and empyema. This suggests that an immune mediated as well as in non-rheumatic conditions, including cancer associated with other rheumatic diseases, such as RA in the parital pleurae all have been reported in pleurisy complement activation products, and immune deposit in pleural fluid. Furthermore perivascular deposition of immunoglobulins and compliment components in the parietal pleura have been found in patients with lupus pleuritis. The nature of the immune complexes in SLE pleural fluid is not clear, though they may well be DNA-anti-DNA complexes.

Study conducted by Andrew BS, Arora NS, Shadforth MF et al showed that in RA the process occurring in the pleural space appears to be analogous to the joint whereas the mechanism proposed to explain the pathogenesis of malignant effusion includes 1) pleural implantation of tumor cell, 2) obstruction of pleural lymphatic by tumor cells, 3) increases pleural fluid protein which may impair the absorption of the protein by visceral pleural lymphatic and atelectasis leading to reduction of pleural pressure. An immunopathogenic basis for malignant pleural effusion has not been considered in there study. They showed that the degree of immune complexes was higher in the serum than in the pleural fluid in patients with malignant diseases, the converse was true in patients with connective tissue diseases. Activation of C3 and properdin factor B was almost invariable in patients with connective tissue diseases and bacterial infection.

None of the immunologic abnormalities that are described in pleural fluid is diagnostic of lupus pleuritis, thus the presence of immune complexes, complement activation products, and immune deposit in the parial pleurae all have been reported in pleurisy associated with other rheumatic diseases, such as RA as well as in non-rheumatic conditions, including cancer and empyema. This suggests that an immune mediated mechanism is a common pathway by which SLE and other diseases cause pleurisy.

In SLE, the pleural fluid differential cell count varies from predominantly polymorphonuclear (PMN) to mononuclear depending on the time of thoracentoscent and onset of effusion. In SLE characteristics of pleural fluid are: pH > 7.30, with glucose level >60mg/dl, and LDH never exit more than 600 U/L. When pleural fluid ANA >1:160 with pleural fluid / serum (PF/S) ANA ratio is more than 1, the diagnosis of lupus is likely. In most of the patients, the pleural effusion resolves with oral or intrapleural corticosteroid administration.

In our case the patient presented with recurrent exudative pleural effusion, initially which was unilateral and latter bilateral. The tempo of the disease was waxing and waning in nature. When she was admitted in our institute she had moderate bilateral pleural effusion with mild pericardial effusion without any systemic manifestations of SLE, but investigations (pleural fluid and, serum ANA, serum anti dsDNA, pleural fluid cell type, pH, LDH level) supported a diagnosis of lupus.

With steroid she responded dramatically. She will need prolonged follow-up to ascertain whether she develops other clinical features of lupus.

**References**


**Announcement**

**IANCON - 2006**

14th Annual Conference of Indian Academy of Neurology Jointly organized by Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS) and ACIAN (Bangalore) Trust held on 6-8th October, 2006 at Convention Center, NIMHANS, Bangalore.

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