Acute Lupus Pneumonitis With Normal Chest Radiograph*

Irawan Susanto, MD, FCCP; and Jay L. Peters, MD, FCCP

Patients with acute lupus pneumonitis (ALP) usually have hypoxemia, patchy infiltrates evidenced on a chest x-ray film, and an incomplete response to corticosteroids with high mortality. In contrast, lupus patients with a syndrome of acute reversible hypoxemia (SARH) have hypoxemia with normal chest x-ray films and a rapid response to corticosteroids. We present a case of biopsy-proven ALP with normal initial chest x-ray films, and a normal CT scan. We hypothesize that a continuum of vascular and parenchymal abnormalities may exist in the lungs of lupus patients. This case also illustrates the insensitivity of routine chest radiographs in demonstrating mild or early pneumonitis.

(CHEST 1997; 111:1781-83)

Key words: corticosteroids; hypoxemia; lupus; pneumonitis

Abbreviations: ALP=acute lupus pneumonitis; SARH=syndrome of acute reversible hypoxemia

Acute lupus pneumonitis (ALP) traditionally has been characterized by the presence of fever, dyspnea, tachypnea, hypoxemia, and patchy infiltrates evidenced on a chest x-ray film. This diagnosis can be made only after excluding other causes, especially infections. Histologically, ALP presents as acute alveolitis, with alveolar wall necrosis, hemorrhage, edema, hyaline membrane formation, interstitial pneumonitis, capillaritis, or capillary thrombi.¹ In contrast, lupus patients with a syndrome of acute reversible hypoxemia (SARH) were reported to have acute hypoxemia without any pulmonary parenchymal involvement.² The hypoxemia was rapidly reversed by corticosteroids. However, histologic specimens were not available from any of these patients. We present a case of histologically proven ALP with a normal chest x-ray film and CT scan on presentation.

CASE REPORT

A 56-year-old woman presented with dyspnea and bilateral pleuritic chest pain of 2 weeks' duration. She had no orthopnea, paroxysmal nocturnal dyspnea, leg swelling, fever, chills, cough, or hemoptysis. Seven months earlier, she was treated for facial cellulitis which was painful, erythematous, and swollen over the malar areas. Her past medical history was significant for uncomplicated hepatitis C-related cirrhosis, chronic sinusitis, and hypertension. She had no history of smoking. At the time of admission, she was receiving nadolol, thiamine, and folic acid. Physical examination revealed a well-nourished woman in no acute distress with a BP of 140/80 mm Hg, a pulse of 60 beats per minute, a respiratory rate of 20 breaths per minute, and a temperature of 36.3°C. Physical examination revealed non-tender sinuses. Her lungs were clear, and her heart rate was regular with

*From the Department of Medicine, Division of Pulmonary Diseases/Critical Care Medicine, the University of Texas Health Science Center at San Antonio and, the South Texas Veterans Health Care System, Audie L. Murphy Memorial Veterans Hospital Division, San Antonio, Tex.

Manuscript received September 16, 1996; revision accepted December 16.
the presence of an $S_4$ gallop. Results of an examination of the abdomen and the extremities were within normal limits. On admission, the WBC count was 7,500/mm$^3$, the hemoglobin level was 13 gm/dL, the platelet count was 73,000/mm$^3$, prothrombin time was 14 s, partial thromboplastin time was 34 s, total bilirubin value was 2.4 mg/dL, aspartate aminotransferase was 115 IU/L, alanine amino transferase was 107 IU/L, alkaline phosphatase was 75 IU/L, and erythrocyte sedimentation rate was 111 mm/h. With the patient breathing room air, blood gas determinations were as follows: pH, 7.48; PCO$_2$, 25 mm Hg; and PO$_2$, 65 mm Hg. The patient's initial chest x-ray film revealed no parenchymal infiltrates (Fig 1), which was confirmed by a CT scan of the chest with contrast medium. She had normal spirometry values and lung volumes, reduced diffusion capacity (29% predicted), and a 14.2% shunt. A pulmonary angiogram showed no abnormalities. Her electrocardiogram showed no ischemic changes; an echocardiogram demonstrated normal left ventricular size and function. The antinuclear antibody titer was 1:2,560. Her C$_3$ and C$_4$ levels were depressed. The IgG antiphospholipid antibodies were present in moderate titer. Two days after admission, her blood cell counts revealed leukopenia (2,700/mm$^3$) and lymphopenia (1,026/mm$^3$) in addition to thrombocytopenia.

Bronchoscopy was performed less than 24 h after the chest CT scan. Transbronchial lung biopsy revealed alveolar hemorrhage, focal areas of pneumonitis, and capillaritis (Fig 2). The patient developed persistent postbronchoscopy fevers without an infectious source despite extensive workup. Empiric therapy with intravenous antibiotics was started. Her chest x-ray films still showed no infiltrates. Another chest CT scan 5 days after bronchoscopy showed significant changes with vascular prominence and bibasilar alveolar interstitial infiltrates in the dependent regions (Fig 3).

The patient was treated with prednisone, 40 mg po bid, and intravenous administration of antibiotics was continued. She subjectively improved and defervesced despite the persistence of hypoxemia. Her diagnosis at discharge was ALP. On outpatient follow-up 3 months after discharge, her diffusion capacity had increased to 58% of predicted. Fifteen months after discharge, her diffusion capacity was 65% of predicted, and the patient's hypoxemia had slowly improved.

**FIGURE 1.** Normal admission chest x-ray film, posteroanterior view.

**FIGURE 2.** This transbronchial biopsy specimen shows focal infiltrates of neutrophils and monocytes (double arrows). An alveolar wall abruptly merges into the area of capillaritis (single arrow)=[hematoxylin-eosin, original ×450].

**FIGURE 3.** Another chest CT scan showing vascular prominence and bibasilar alveolar interstitial infiltrates in the dependent regions.

**DISCUSSION**

The patient fulfilled the American College of Rheumatology criteria for the diagnosis of systemic lupus erythematosus (rash; serositis; leukopenia, lymphopenia, and thrombocyto-
penia; and antinuclear antibody positivity). Her lung biopsy was consistent with ALP, although her initial chest x-ray film and CT scan lacked parenchymal infiltrates. This case illustrates the lack of correlation between pulmonary radiographic and histologic findings and that absence of radiographic infiltrates does not rule out histologic abnormalities.

The patient's hypoxemia may be partially explained by the presence of cirrhosis. Shunt fractions up to 28% have been reported with severe cirrhosis. This may explain the residual mild hypoxemia despite significant improvement in the diffusion capacity following steroid therapy.

Lupus patients with SARH were reported to present with transient hypoxemia and a clear chest x-ray film or CT scan and to respond to steroids within 72 h. In contrast, patients with ALP usually present with patchy infiltrates, and the response to steroids is slow. Many patients with ALP require mechanical ventilatory support. In the early series described by Matthay et al., out of the 12 patients with ALP receiving high-dose steroids required salvage therapy with azathioprine, and mortality remained at 50%. Although the patient described here had histologic findings consistent with ALP, her clinical course was less severe than that of the patients in the series by Matthay et al.

Central to the pathophysiology of SARH and ALP is pulmonary vascular involvement. Acute injury to the alveolar capillary unit forms the basis for ALP. In SARH, transient leukocyte sequestration with complement activation is thought to occur in the pulmonary microvasculature.

Recently, endothelial cells from the skin biopsy of lupus patients were found to demonstrate increased expressions of adhesion molecules. These molecules are involved in local leukocyte trafficking across the endothelium and may participate in the pathogenesis of vascular inflammation. Treatment with corticosteroids early may significantly attenuate vascular injury, partly due to its ability to downregulate the expression of endothelial adhesion molecules. However, the vascular inflammatory cascade may progress to frank microangiitis and hemorrhage, leading to serious tissue damage and less steroid responsiveness, the way ALP has traditionally been described. We hypothesize that ALP may represent an extension of SARH in the continuum of pulmonary microvascular inflammation.

We conclude that routine chest radiographs may be insensitive to the presence of ALP. Since a high-resolution chest CT scan is superior to routine chest radiographs and conventional CT scans in demonstrating pulmonary interstitial opacities, it also may aid in the evaluation of lupus patients who present with hypoxemia and a normal chest x-ray film. Finally, it is possible that SARH and ALP may not represent distinct clinicopathologic entities but rather different levels of severity within the spectrum of the pulmonary vascular inflammatory process associated with lupus.

ACKNOWLEDGMENT: The authors wish to thank Dr. Jacqueline J. Coalson, Professor and Interim Chair of Pathology at the University of Texas Health Science Center at San Antonio, for her assistance in the evaluation of transbronchial biopsy specimens and the preparation of the photomicrographs.

REFERENCES