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Acute lupus pneumonitis mimicking pulmonary tuberculosis: a case report

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We report a case of systemic lupus erythematosus in a 15-year-old girl with initial presentation as acute lupus pneumonitis. A fulminant course with pancytopenia and respiratory distress were developed 3 weeks after symptom onset. Chest radiographs revealed an interstitial pattern with miliary nodules over bilateral lower lung fields that mimics miliary tuberculosis. The patient was treated with intravenous immunoglobulin and antituberculosis drugs because the infection-associated hemophagocytic syndrome and pulmonary tuberculosis could not be excluded from the clinical course. The response to antituberculosis treatment, however, was poor and her respiratory condition deteriorated rapidly to impending respiratory failure 1 week after admission. Systemic lupus erythematosus with acute lupus pneumonitis was then diagnosed based on the fulminant clinical course and accordant laboratory results. Corticosteroid (methylprednisolone) and cytotoxic agent (cyclophosphamide) pulse therapies were applied twice and once, respectively. She recovered gradually after receiving the immunotherapy.

Key words: Acute lupus pneumonitis, pulmonary tuberculosis (TB), systemic lupus erythematosus (SLE)

Acute lupus pneumonitis is an uncommon pulmonary manifestation of systemic lupus erythematosus (SLE), with an incidence of 1% to 4% in these patients [1]. Acute lupus pneumonitis is an abrupt febrile pneumonic process without an infectious etiology [2], and it may be indistinguishable from other causes of pulmonary infiltrates (eg infection, hemorrhage, and embolism) [3]. The non-specific pictures of acute lupus pneumonitis on chest radiographs, which mimic miliary tuberculosis (TB) and other infectious diseases, may lead to misdiagnosis. Acute lupus pneumonitis can be life-threatening, with a mortality rate as high as 50% [4]. Because of its fulminant course and high mortality rate, early diagnosis and prompt treatment of acute lupus pneumonitis are necessary. Some patients respond to high-dose corticosteroids [4], whereas for those who respond poorly to steroid therapy, other treatments should be tried. Pulse therapy with steroids, immunosuppressants, and plasmapheresis—alone or in combination—may be effective in these corticosteroid-recalcitrant patients [4-6]. In this case report, we describe a patient in whom SLE was diagnosed after an episode of acute lupus pneumonitis. The clinical course of fulminant acute lupus pneumonitis in this patient are described, and reasons for its treatment are provided.

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Case Report

A 15-year-old girl was admitted to the National Taiwan University Hospital because of prolonged fever. She had been healthy until 3 weeks before admission, when she experienced fever and mild cough. Viral infection was initially diagnosed, and supportive treatment was prescribed at a local clinic. The patient, however, developed exertional dyspnea, orthopnea, and myalgia over bilateral thighs 1 week before admission. She had no previous history of operation or trauma, nor had she been traveling in recent months.

Physical examination at admission showed a clear consciousness. The body temperature was 38.5°C, the pulse rate was 106/min, and the respiration rate was 32 /min. The blood pressure was 101/61 mm Hg. Fine rales were present over bilateral lower lung fields. Grade II systolic murmur was noted upon auscultation. No hepatosplenomegaly, skin rash, or mucosal ulcer was found, except for one grain-sized ulcer over the tongue tip. Laboratory data revealed pancytopenia (white cell count: 2010 /mm^3, absolute lymphocyte count: 219 /mm^3, hemoglobin: 5.2 g/dL, platelet: 76 000 /mm^3). Biochemistry revealed elevation of aspartate amoni-transferase 97 U/L (normal range, < 40 U/L). C-reactive protein was mildly elevated (1.36 mg/dL). Tuberculin skin test result was negative. The stool occult blood test result was negative and urinalysis gave normal results. Chest radiography showed an interstitial pattern with miliary nodules over

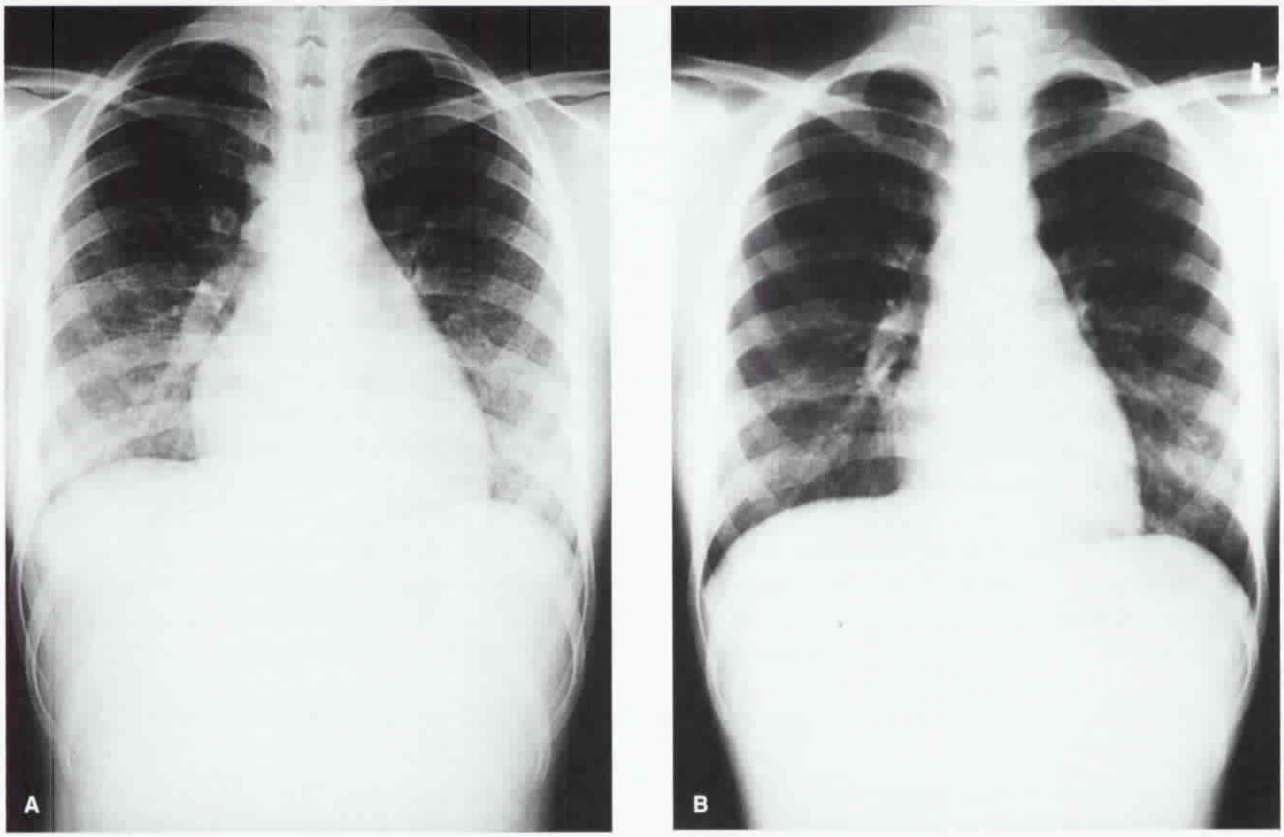

Fig. 1 (A) Acute lupus pneumonitis in a 15-year-old female patient with systemic lupus erythematosus. Chest X-ray showed an interstitial pattern with miliary nodules in bilateral lower lung fields. **(B)** After treatment with two courses of steroid pulse therapy and one course of cyclophosphamide pulse therapy, the chest plain film revealed resolution of the interstitial pattern and miliary nodules in bilateral lung fields.

both lower lung fields (Fig. 1A). Chest computed tomography showed ground-glass opacities with diffusely increased infiltrations and small patchy shadows over bilateral lungs. Prominent pleural effusion at the dependent aspect of the bilateral lung fields was also found. Cardiac echography showed minimal pericardial effusion.

Under the suspicion of infection-associated hemophagocytic syndrome, bone marrow aspiration and biopsy were performed, and intravenous immunoglobulin was then administered. Empirical antibiotic therapy was given with clavulanate-potentiated amoxicillin plus cefotaxime. Because of a family history of pulmonary TB and miliary infiltration on chest plain film, antituberculosis drugs with isoniazid, rifampin, and pyrazinamide were administered. The patient, however, did not respond well to the treatment. Bone marrow examination showed no evidence of infection-associated hemophagocytic syndrome. High spiking fever persisted and respiratory distress, which was aggravated with hypoxemia, developed. Furthermore, hematologic tests still revealed pancytopenia even after blood transfusion. Hence, autoimmune-mediated interstitial pneumonitis was highly suspected. The laboratory results were as follows: antinuclear antibody titer, 1: 5120 (+), speckled pattern; anti-double-stranded (ds) DNA antibodies: 45.4 IU/mL, C3: 14.8 mg/dL, C4: < 6 mg/dL (normal range, anti-dsDNA antibody: < 12 IU/mL, C3: 100 ± 18.6 mg/dL, C4: 19.1 ± 8.3 mg/dL), positive anti-Smith (Sm) antibody, haptoglobin: < 5.83 mg/dL (normal range, 111.1 ± 46.3 mg/dL), Coombs' test: positive, anti-platelet antibody: positive. The laboratory data were suggestive of autoantibodies with intravascular hemolysis. The diagnosis of SLE was made based on the following criteria: hematologic disorder (hemolytic anemia, lymphopenia); serositis (pleural effusion); immunologic disorder (positive anti-Sm antibody, elevated anti-dsDNA antibody); abnormal titer of antinuclear antibody.

Hemogram revealed pancytopenia even under treatment with hematopoietic agents (lenograstim 100 μg/day). To control the acute lupus pneumonitis and hematological crisis, steroid pulse therapy (methylprednisolone 1 g/d for 3 days) was given 1 week

after admission. Because the possibilities of viral pneumonitis and superimposed infection could not be ruled out, ganciclovir was also given for 5 days. Fever subsided 2 days after the steroid treatment. A maintenance dose of methylprednisolone (80 mg/d) was given after the completion of pulse therapy. Visual hallucination, retinal hemorrhage, serositis (pleural effusion, pericardial effusion), ascites, and proteinuria, however, were noted and her respiratory condition deteriorated during this period. A second course of steroid pulse therapy was thus given for 5 days. Her respiratory condition then improved gradually and extubation was performed. Treatment with the cytotoxic agent cyclophosphamide (500 mg/mm^2) was also added once 3 days after the second course of steroid pulse therapy to potentiate the suppression of disease activity. Follow-up chest X-ray performed 25 days after admission revealed resolution of abnormalities in bilateral lung fields (Fig. 1B). Methylprednisolone (80 mg/d) was shifted to oral steroid (prednisolone 60 mg/d) 1 month later. Her clinical condition improved progressively 1 month after admission, although the indicators of disease activity were still abnormal (C3: 45.4 mg/dL, C4: < 6 mg/dL, anti-DNA: 64.2 IU/mL). Treatment with the immunomodulators hydroxychloroquine and aza-thioprine was added 20 and 30 days after admission, respectively. Her hemogram then returned to normal levels gradually, with absolute lymphocyte counts above 500 /mm^3 at 35 days after admission. Urinalysis showed that proteinuria had decreased to 30 mg/dL, and no hematuria was noted at that time. Because of stable condition, the dosage of prednisolone was then tapered to 30 mg/day after 7 days of oral prednisolone treatment, and the patient was then discharged home.

Discussion

The differential diagnosis of pneumonitis with nodular lesions can comprise the following: 1. Miliary TB; 2. *Pneumocystis carinii* pneumonia (PCP); 3. Viral pneumonitis; and 4. Immune-mediated pneumonitis [2, 7-9]. This patient was initially given antituberculosis treatment because of a family history of TB and similar clinical manifestations. The patient, however, did not respond well to antituberculosis agents. Respiratory distress with hypoxemia also became aggravated during the treatment. Both clinical symptoms and laboratory data were then re-evaluated. The clinical features and chest X-ray characteristics made miliary TB seem less likely to be the diagnosis: hypoxemia is rarely found in TB, and the chest plain film of miliary TB usually shows diffusely distributed rather than localized nodules. In this case, PCP was also unlikely because of pleural effusion, a finding that is not common in PCP. Further study of laboratory data revealed that the patient had developed SLE with the initial manifestations of acute lupus pneumonitis and impending respiratory failure. Because respiratory infection is the most common cause of pulmonary infiltrates in patients with SLE [3], primary or superimposed pulmonary infection should be taken into consideration, even if the diagnosis of acute lupus pneumonitis is more favored. In fact, many studies have shown that clinically diagnosed lupus pneumonitis can be explained by other factors such as infection, aspiration, cardiac dysfunction, or uremia [3].

The clinical manifestations of acute lupus pneumonitis may include cough, dyspnea, fever, pleurodynia, and hypoxemia [1,4]. These symptoms result from acute injury to the alveolar-capillary unit [10]. The chest radiographs characteristically reveal unilateral or bilateral patchy acinar infiltrates in the lower lung fields [11]. Interstitial pneumonitis associated with small vessel vasculitis is, however, an unusual feature of acute lupus pneumonitis [1,12]. Because acute lupus pneumonitis is rare, adequate treatment has not been identified [13]. Patients are usually treated with high-dose corticosteroids (prednisone 1-2 mg/kg per day, or its equivalent); those who do not respond to corticosteroid therapy may develop potentially fatal respiratory failure [4]. Pulse methylprednisolone (1 g/d for several days), plasmapheresis, and immunosuppression have been used for patients with poor response to corticosteroids [4-6]. In this case, corticosteroid pulse therapy was used as the initial treatment because of the rapidly deteriorating respiratory failure. The clinical symptoms of this patient did not improve until two courses of steroid pulse therapy and one immunosuppressant (cyclophosphamide) pulse therapy were given. The findings indicate the importance of early intervention for acute lupus pneumonitis.

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