Lupus Nephritis Associated with Bacterial Panperitonitis and Lung Alveolar Hemorrhage

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A 36 year-old woman was admitted to the hospital with the diagnosis of nephrotic syndrome due to lupus nephritis. The patient had panperitonitis caused by *Staphylococcus aureus* as a complication, and an emergency laparotomy was performed. After the operation, the patient developed a massive lung alveolar hemorrhage. Methylprednisolone pulse therapy showed a marked effect on the lung hemorrhage. It is known that lung alveolar hemorrhages associated with systemic lupus erythematosus have a very high mortality; the present case is relatively rare because of the good response to steroid pulse therapy.
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Key words: SLE, steroid pulse, MRSA, vancomycin

Introduction

Systemic lupus nephritis is known to be a polymorphic disease which involves many organs (1). Its clinical picture is often complex. Some cases show latent morbidity occasionally interrupted by acute intermittent flares, and others have very slowly evolving lesions. Both bacterial panperitonitis and lung alveolar hemorrhage are rare but these are some of the most life threatening complications of SLE (2–4). The latter in particular has been shown to have a very high mortality rate in several case reports published in the last two decades (3–5).

Here, we report a patient with lupus nephritis associated with panperitonitis and massive pulmonary hemorrhage, who appeared to respond to therapy with methylprednisolone.

Case Report

A 36-year-old woman was admitted to the hospital with a one-month history of morning stiffness, persistent pain in the limb joints, peritibial or facial edema and intermittent fever which rose to 39.0°C. Physical findings on admission included mild dyspnea with bilateral crackles over the bilateral pulmonary bases, abdominal cramping pain without obvious peritoneal signs and prominent butterfly rashes on the face. Routine laboratory tests disclosed elevated levels of serum anti-DNA antibody (320 IU/ml, RIA) and antinuclear antibodies (2+, diffuse

and speckled pattern). Rheumatoid factor was positive and serum complement component, C3, C4 and CH50 levels were very low (6 mg/dl, 9 mg/dl and <9.1 U/dl, respectively). Anti-extractable nuclear antigen (ENA) antibodies, anti-RNP antibody, anti-Sm-antibody, tests for LE cells, the Venereal Disease Research Laboratory (VDRL) test and direct Coombs' test were all negative. Circulating lupus anticoagulant was not detected. Serum levels of IgG, A and M were 2,700, 276 and 127 mg/dl, respectively. Serum creatinine and urea nitrogen levels were moderately elevated (2.0 and 71 mg/dl, respectively). Serum total protein was 3.8 g/dl (albumin: 2.0 g/dl). Hemoglobin was 12.6 g/dl, the total white cell count 3,200/mm³, and platelet count 15 × 10⁴/mm³. Erythrocyte sedimentation rates (ESR) were 90 mm in the first hour and C-reactive protein (CRP) has risen to 13.1 mg/dl. There were no abnormalities in the blood coagulation test. The blood gas in room air showed an arterial oxygen pressure (PaO₂) of 60.2 mmHg and an arterial carbon dioxide pressure (PaCO₂) of 46.0 mmHg. The oxygen saturation was 94.1%. Total daily urinary protein was 8.33 g and microhematuria was detected as 2+ in urinalysis. Large amounts of red blood cells, white blood cells and hyaline or granular casts were observed in urinary sediment. The glomerular filtration rate on admission was 51.3 ml/min. The initial chest X-ray film demonstrated moderate lung vascular congestion and a small amount of bilateral pleural effusion. The patient was diagnosed as having nephrotic syndrome due to

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Lupus Nephritis with Lung Hemorrhage

Fig. 1. Summary of the clinical course.

Fig. 2. A) Marked diffuse proliferation of glomerular mesangial cells with lobular shapes and wire loop lesions (PAS stain ×200). B) Immunofluorescence microscopy. Granular mesangial and capillary deposits of IgG are present (×200). C) Electron microscopic observations revealed marked electron dense deposits in the mesangial and subendothelial areas (×4,000).

lupus nephritis based on the findings mentioned above. Oral administration of prednisolone (40 mg daily) combined with parenteral antibiotics was started on the day of admission.

The clinical course after admission is summarized on Fig. 1. On the second hospital day, the patient complained of severe abdominal pain accompanied by muscular rigidity. Body temperature had risen to 40°C. On suspicion of panperitonitis, laparotomy for diagnosis and therapy was performed immediately. About 1,000 ml of purulent ascites was found in the abdominal cavity. Methicillin-resistant *Staphylococcus aureus* (MRSA) was detected by bacterial culture of ascites, but neither perforation of the gastrointestinal tract nor the original infectious focus was found in the abdominal cavity despite a careful investigation during the operation.

Renal biopsy was performed simultaneously with the laparotomy. Microscopic finding of the renal specimen showed that the patient had diffuse proliferative lupus nephritis with typical wire-loop lesions (Fig. 2A). By immunofluorescence microscopy, mesangial granular "lumpy" depositions of IgG, IgA, IgM, and complements (C1q, C3, C4 and C5) were observed (Fig. 2B). Electron microscopy revealed large amounts of electron dense deposits in the mesangial and subendothelial areas (Fig. 2C).

On completion of the operation, the blood gas on mechanical ventilation (tidal volume: 600 ml, respiration rate: 12/min, FiO₂: 50%) showed PaO₂ of 61.0 mmHg and PaCO₂ of 38.5 mmHg. After transfer to the intensive care unit (I.C.U.), hypoxia persisted and the patient could not be removed from the respirator. On the next day (the third hospital day), massive bleeding through the tracheal tube occurred and severe infiltrative shadows on both lungs were seen in a chest XP film (Fig. 3a). A bronchofiberscopic examination revealed peripheral lung bleeding and hemosiderin-laden macrophages were identified in bronchoalveolar lavage fluid, and the findings were compatible with pulmonary alveolar hemorrhage. Result of lavage fluid culture was negative for pathogens. Lung biopsy was not performed on the patient. Both PT and APTT at the time were within normal limits. Platelet count was $12 \times 10^4/\text{mm}^3$, and serum levels of FDP were not elevated. A diagnosis of massive alveolar hemorrhage associated with SLE was made and the patient was given pulse methylprednisolone (1 g daily for 4 days) with additional use of 500 mg/day of parenteral vancomycin prophylactically for the MRSA general infection. On the third postoperative day (the second day of the steroid pulse), the amount of bleeding through the tracheal tube became remarkably small, but the chest XP findings persistently indicated infiltrative shadows. Weekly steroid pulse therapy was repeated 2 times (total dose of methylprednisolone was 8 g/month). Improved findings in serial chest XPs became obvious after the first steroid pulse. The patient could be weaned

Fig. 3. Subsequent chest radiographs showing severe alveolar, interstitial infiltrates of pulmonary hemorrhage and its resolution.

from the respirator on the 10th postoperative day. Blood gas had recovered to PaO₂ of 72.0 mmHg and PaCO₂ of 46.3 mmHg in room air by the 20th postoperative day. By that time, the lung infiltrative shadows had almost disappeared (Fig. 3b). Since then she has shown a good recovery from the respiratory crisis.

Discussion

Acute abdominal complications are not rare in systemic lupus erythematosus (2, 6). Several case reports of bowel ischemia (2), gastrointestinal hemorrhage (7), bowel obstruction (8), spontaneous rupture of the spleen (9), spontaneous rupture of the liver (10) and acute pancreatitis (2), which required surgical therapy have been published. A common factor in these abdominal complications is acute or chronic inflammatory changes in the arteries and veins distributed in the abdominal organs. In the present case, massive ascites was observed as in the formerly reported cases (11–13), but it was strange that *Staphylococcus aureus* was detected in the

ascites of the present patient without perforation of the bowel or any infectious foci in the abdominal cavity as a whole. Several routes of bacterial invasion, such as via the genital organs and contamination by acupuncture needles in the abdomen which she underwent for her chronic constipation, were possible, but no decisive evidence for these routes was found.

Lung alveolar hemorrhage is one of the rare but life threatening complications of SLE (3, 4). Some authors have reported that the mortality of the complications is as high as seventy percent (3). The cause of this complication has not been clarified, but some authors have suggested that lupus anticoagulant, vascular fragility due to focal vasculitis and/or presence of antibasement membrane antibody are involved in the development of alveolar hemorrhage (14). Some episodes of extensive pulmonary hemorrhage complicated with SLE were thought to be secondary to thrombocytopenia, uremia or sepsis (14). These contributory factors were absent in our patient and the pulmonary hemorrhage was almost certainly due to the disease process, i.e., focal vasculitis itself. Although the complication is almost always fatal, some patients have recovered from alveolar hemorrhages by steroid pulse therapy (15), immunosuppressive agents (16) or plasmapheresis (14, 16). In the present case, the most serious problem with these treatments was that they were disadvantageous for her recovery from systemic infection and/or wound-healing after abdominal surgery. We chose methylprednisolone pulse therapy because the therapy seemed to be safer and more reliable than immunosuppressive therapy or plasmapheresis in this patient with an infection and in a life-threatening state. Steroid pulse therapy and antibiotic administration showed remarkable effects on the pulmonary bleeding without worsening of the infection. After two courses of steroid pulse therapy (8g of methylprednisolone in total was administrated) followed by maintenance doses of prednisolone, the lung bleeding completely ceased, and the patient recovered from the severe respiratory distress. The present case and other cases previously reported suggested that lung alveolar hemorrhage, although a serious complication of SLE, sometimes responds to therapies such as steroid pulse, immunosuppressive agents or plasmapheresis. Therefore, it is

important to consider the use of therapy in such cases, as the advantages appear to outweigh the disadvantages.

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