PNEUMOCYSTIS CARINII PNEUMONIA IN SYSTEMIC LUPUS ERYTHEMATOSUS: A REPORT OF TWO CASES
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Abstract: Patients with systemic lupus erythematosus (SLE) have increased susceptibility to infection by Pneumocystis carinii, but this condition has rarely been reported in Taiwan. Here, we describe two cases of patients with SLE who developed Pneumocystis carinii pneumonia (PCP). The first patient was a 39-year-old woman presenting with fever and dyspnea that had lasted 2 weeks. Chest roentgenography disclosed bilateral interstitial and alveolar infiltrates. The second patient was a 22-year-old woman presenting with a 4-day history of malaise, cough, dyspnea, and fever. She had concomitant Mycobacterium tuberculosis infection. Both patients had been treated with varying doses of corticosteroids and/or cytotoxic drugs within 4 months before presentation. Diagnosis was established based on the findings of bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB). Both patients received trimethoprim-sulfamethoxazole (20 mg kg⁻¹ d⁻¹ trimethoprim), but finally died of nosocomial septicemia (Acinetobacter baumannii and Pseudomonas aeruginosa bacteremia in one, P. aeruginosa bacteremia in the other). These two cases demonstrate that PCP should be included in the differential diagnosis of patients with SLE presenting with pneumonic processes. In addition, a second opportunistic pathogen should be suspected. Bronchoscopic examination should be performed if the diagnosis is not clear and should include TBLB and BAL.

Case Report

Case 1
A 39-year-old woman with a 2-year history of SLE was admitted because of fever and dyspnea that had lasted for 2 weeks. SLE had been diagnosed based on the presence of malar rash, nephrotic syndrome, high titer of anti-double strand DNA antibodies, and positive anti-nuclear antibody [14]. Recent therapy prescribed by a general practitioner are associated with poor prognosis. Here, we report two patients with SLE who developed P. carinii lung infection, one of whom had a coexisting infection of Mycobacterium tuberculosis.
consisted of 60 mg oral prednisolone daily until 3 months prior to admission, when she visited our outpatient department and the regimen was switched to oral prednisolone 40 mg daily and methotrexate 7.5 mg weekly due to lack of effectiveness of, and poor compliance with, the previous regimen. Monthly pulse therapy with intravenous cyclophosphamide and methylprednisolone were also given simultaneously for the 3 months prior to admission for treatment of active lupus nephritis (WHO class VI). At admission, examination revealed a body temperature of 38.8°C, blood pressure of 107/41 mm Hg, and pulse rate of 137. Bilateral crackles were heard on lung auscultation, and edema of the lower legs was present. She had no history of seizure or loss of consciousness, and no evidence of arthritis was observed. Laboratory examination showed a total white cell count of 7.3 x 10⁹/L, lactate dehydrogenase (LDH) 10.8 µkat/L (normal, 1.6–3.4 µkat/L), Na 128 mmol/L, and plasma sugar 9.8 mmol/L (normal, 3.6–11.4 mmol/L). Chest roentgenography disclosed bilateral interstitial and alveolar infiltrates (Fig. 1). Arterial blood gases assessed using a non-rebreathing mask (FiO₂ 100%) showed pH 7.469 (normal, 7.38–7.44), pCO₂ 3.0 kPa (normal, 4.7–5.9 kPa), and pO₂ 3.9 kPa (normal, 11–13 kPa). The hypoxemia worsened despite the use of supplementary oxygen and antibiotics (piperacillin and gentamicin), necessitating assisted ventilation within hours after admission. Bronchoscopy was performed on day 3 after admission. BAL was negative for *P. carinii* cysts, but TBLB identified *P. carinii* cyst by Grocott’s Gomori methenamine silver stain. Cultures of endobronchial aspirates for bacteria, mycobacteria, fungi, and viruses were negative. Serum HIV test using an enzyme-linked immunoassay was non-reactive. The patient was treated for miliary tuberculosis empirically despite a negative smear of gastric aspirates on acid-fast stain. On day 2 after admission, she developed acute respiratory distress syndrome on day 2 after admission and acute renal failure requiring hemodialysis 1 week after admission. On day 29 after admission, she developed nosocomial septicemia with Acinetobacter baumannii and Pseudomonas aeruginosa and died.

**Case 2**

A 22-year-old woman presented with a 4-day history of malaise, cough, dyspnea, and fever. SLE had been diagnosed at the age of 16 years and fulfilled six items of the 1982 ARA revised criteria for the classification of SLE [14]. She had been treated with prednisolone 40 mg every day for unknown periods after a course of high-dose methylprednisolone for flare-up of disease at age 16. Two years prior to this admission, monthly methylprednisolone and cyclophosphamide pulse therapy were administered for active lupus nephritis (WHO class IV and V). One year later, she developed uremia and required hemodialysis. Other notable history before hemodialysis included a seizure attack in January 1998 and abdominal vasculitis in December 1998, which was controlled successfully with high-dose steroids. One year prior to admission, she underwent surgical intervention for bleeding of Meckel’s diverticulum with resection of distal ileum and end-to-end anastomosis. In the following weeks, abdominal wound dehiscence and gastrointestinal bleeding recurred and required wound debridement and ileostomy. One month before admission, she experienced sudden onset of blurred vision. Acute retinal necrosis caused by herpes simplex virus infection was diagnosed, and successfully treated with intravenous acyclovir. The CD4 count was 139/mm³ and HIV test using an enzyme-linked immunoassay was negative. She was maintained on prednisolone alone at a dose of 15 to 30 mg/day at the outpatient department.

On examination at this admission, she appeared mildly ill. Body temperature was 36.5°C, blood pressure 120/73 mmHg, pulse rate 105, and respiration 24 per minute. Bilateral basal crackles were heard on lung auscultation. Skin manifestations, heart murmur, abdominal pain, seizure, loss of consciousness, and symptoms of arthritis were absent. Laboratory evaluation revealed a white cell count of 5.16 x 10⁹/L, hemoglobin 7.3 g/dL, platelet count 12.3 x 10⁹/L, lactate dehydrogenase (LDH) 10.8 µkat/L (normal, 1.6–3.4 µkat/L), Na 128 mmol/L, and plasma sugar 9.8 mmol/L (normal, 3.6–11.4 mmol/L). Chest roentgenography disclosed bilateral interstitial and alveolar infiltrates (Fig. 1). Arterial blood gases assessed using a non-rebreathing mask (FiO₂ 100%) showed pH 7.469 (normal, 7.38–7.44), pCO₂ 3.0 kPa (normal, 4.7–5.9 kPa), and pO₂ 3.9 kPa (normal, 11–13 kPa). The hypoxemia worsened despite the use of supplementary oxygen and antibiotics (piperacillin and gentamicin), necessitating assisted ventilation within hours after admission. Bronchoscopy was performed on day 3 after admission. BAL was negative for *P. carinii* cysts, but TBLB identified *P. carinii* cyst by Grocott’s Gomori methenamine silver stain. Cultures of endobronchial aspirates for bacteria, mycobacteria, fungi, and viruses were negative. Serum HIV test using an enzyme-linked immunoassay was non-reactive. The patient’s condition deteriorated despite administration of intravenous trimethoprim-sulfamethoxazole (20 mg·kg⁻¹·d⁻¹ trimethoprim) and high-dose corticosteroids (1.2 mg·kg⁻¹·d⁻¹ prednisolone). She developed acute respiratory distress syndrome on day 2 after admission and acute renal failure requiring hemodialysis 1 week after admission. On day 29 after admission, she developed nosocomial septicemia with Acinetobacter baumannii and Pseudomonas aeruginosa and died.

**Fig. 1.** Chest roentgenogram showing diffuse interstitial and alveolar infiltrates.
Pneumocystis carinii

Pneumonia in Systemic Lupus Erythematosus

Fig. 3. Pneumocystis carinii cyst on Grocott’s Gomori methenamine silver stain. (x 350).

diagnosis including opportunistic lung infection, and PCP is among the most frequent of these opportunistic infections. Collagen vascular diseases are associated with PCP in about 5% of cases [4, 15]. Fatal infections in SLE patients are correlated with the use of prednisolone and cytotoxic drugs in the 3 months before death and with prednisolone doses greater than 40 mg/day [16, 17]. Yale and Limper reported respiratory failure in 50 of 116 patients with HIV-negative PCP (43%), and these patients had an in-hospital mortality rate of 66% [18]. The authors also noted that respiratory failure was associated with 100% mortality in patients with solid malignant lesions. In both of our patients, respiratory failure was associated with mortality due to the late diagnosis and the development of hospital-acquired infection.

PCP in immunosuppressed patients without HIV infection has a fulminant clinical course, in contrast to the typical, subacute presentation familiar to clinicians caring for AIDS patients. Immunosuppressed patients with PCP have a lower fungal burden in the BAL fluid, rapid response to therapy, higher mortality rate (40%–50%), and higher treatment failure rate (20%–40%) compared to AIDS patients [19]. Radiographic findings in HIV-seronegative patients are similar to those seen in AIDS patients. Chest roentgenography findings are characteristically interstitial initially, then become alveolar or both alveolar and interstitial. In severe cases, diffuse, bilateral alveolar infiltrates consistent with acute respiratory distress syndrome can occur, as in both of our patients. Pleural effusion and/or lymphadenopathy are rare in both HIV-seronegative and HIV-associated PCP. Extrapulmonary manifestations of P. carinii in the HIV-seronegative population are rare [20].

The mechanism of immune suppression in patients with SLE who have PCP is usually multi-factorial, and may be related to underlying diseases, cytotoxic therapies, or malnutrition. However, the development of PCP in most patients with SLE is associated with daily administration of corticosteroids and with the development of lymphopenia. Both of our patients were lymphopenic. Case 2 maintained low-dose treatment with prednisolone (15–30 mg/d) during the 12 months before PCP was diagnosed. This is consistent with a previous report by Godeau et al that PCP can develop in patients taking low-dose corticosteroids only [21]. They also found that two patients with SLE who developed PCP had never received any immunosuppressive treatment and one of these was not lymphocytopenic. Their findings show that use of immunosuppressive drugs and lymphopenia are not necessary prerequisites for the development of PCP in patients with SLE.

In one of our two patients, BAL fluids were negative for PCP. Chechani and Bridges diagnosed PCP compli-
cating a connective tissue disease by fiberoptic bronchoscopy in four patients [9]. However, only one of the specimens (BAL or TBLB) was positive for PCP in two of these patients, despite the collection of adequate specimens. In both of these patients, only a single focus of \( P. \) carinii cysts was noted in the BAL or TBLB. Their findings suggest that diagnostic fiberoptic bronchoscopy in patients with SLE and suspected PCP should include both BAL and TBLB.

Concomitant pulmonary infections in HIV-seronegative patients with PCP are common, occurring in 20% to 40% of patients, and may account for some treatment failures [4, 6, 15]. Yale and Limper identified other pathogenic organisms in 57.8% (67/116) of HIV-seronegative patients with PCP [18]. Among these organisms, cytomegalovirus was the most frequent pathogen, and was detected in 35.3% (41/116) of HIV-seronegative patients with PCP. Other pathogens included \( Pseudomonas, Hemophilus influenzae, Branhamella, Legionella, Proteus, Streplococcus pneumoniae, Staphylococcus aureus, Neisseria, Nocardia, \) herpes simplex virus, \( Aspergillus, Candida, \) and \( Cryptococcus. \) Our case 2 had concomitant pulmonary infection with tuberculosis. Whether the withdrawal of anti-tuberculosis therapy contributed directly to mortality could not be determined due to lack of autopsy. Physicians caring for SLE patients with PCP should consider tuberculosis as a possible coexisting pathogen, especially in endemic areas. Anti-tuberculosis treatment should be given when infection is identified.

**References**