

CASE REPORT

Cytomegalovirus pneumonia in a patient with systemic lupus erythematosus

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ABSTRACT

We presented an interstitial pneumonia case developed due to very rarely seen cytomegalovirus (CMV) in a 66 year-old female patient who had systemic lupus erythematosus (SLE). This patient who was on prednisolone and cyclophosphamide developed high fever, dyspnea and rales in lungs, high CRP, leukopenia, and thrombocytopenia after 11 days of cyclophosphamide treatment. Interstitial infiltration was detected in thoracic tomography. CMV antigen and CMV-DNA by RT-PCR were positive in blood. It was considered as CMV pneumonia. Ganciclovir treatment was started. CMV antigen became negative in the 14th days of the treatment. Clinical improvement was observed at the same time. It is necessary to remember CMV as the agents responsible for causing pneumonia due to high mortality in immunosuppressive host such as SLE. In the blood CMV antigen and CMV DNA investigation may contribute to the diagnosis in that bronchoalveolar lavage cannot be performed. *J Microbiol Infect Dis 2011;1(2): 80-83*

Key words: Systemic lupus erythematosus, cytomegalovirus, pneumonia

Sistemik lupus eritematozusu bir hastada sitomegalovirus pnömonisi

ÖZET

Sistemik lupus eritematozus (SLE) tanısı alan 66 yaşında kadın hastada gelişen ve oldukça nadir görülen sitomegalovirus (CMV)'a bağlı gelişen interstisiyel pnömoni vakası sunuldu. Prednizolon ve siklofosfamid tedavisi almakta olan hastada, siklofosfamid tedavisinden 11 gün sonra ateş yüksekliği, nefes darlığı, akciğerde raller, CRP yüksekliği, lökopeni ve trombositopeni gelişti. Kan gazı incelemesinde hipoksi olduğu ortaya çıktı. Akciğer tomografisinde interstisiyel infiltrasyon saptandı. RT-PCR ile CMV-DNA ve CMV antijeni kanda pozitif. Hastada CMV pnömonisi düşünülerek gansiklovir tedavisi başlandı. Bu tedavi ile kanda CMV antijeni 14 gün sonra negatifleşti. Aynı zamanda hastada klinik düzelme sağlandı. SLE gibi immunosüpresif konakta, mortalitesi yüksek olması nedeniyle pnömoni etkeni olarak CMV'nin hatırlanması gereklidir. Bronkoalveolar lavaj yapılamayan olgularda kanda CMV antijeni ve CMV DNA incelemesi taniya katkıda bulunabilir.

Anahtar kelimeler: Sistemik lupus eritematozus, sitomegalovirus, pnömoni

INTRODUCTION

Infections are common causes for mortality and morbidity in systemic lupus erythematosus (SLE) patients.^{1,2} Risk factors for infections in SLE patients include immunosuppressive treatment with cytotoxic medications or corticosteroids, proteinuria, renal failure, lymphopenia and active SLE.³ Cytomegalovirus (CMV) infection is one of the most important causes of the infections in immunosuppressive host. Cyclophosphamide and azathioprine therapy is sufficient for CMV reactivation.⁴

CMV pneumonia has a serious course. In untreated cases mortality rates reach 85%.⁵ For this reason, early diagnosis and treatment are essential. This case was presented since CMV pneumonia is rarely seen among SLE patients, CMV-DNA and CMV antigen have contributions to the diagnosis in patients for whom bronchoalveolar lavage (BAL) cannot be performed.

CASE

A 66-year-old woman was admitted to our hospital with complaints of fever, fatigue, tenderness

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and swelling in her joints. Laboratory examinations showed a total leukocyte count of 5,000/mm³ with 58% polymorphs and 42% lymphocytes, hemoglobin level of 11.2 g/dL and platelet count of 246,000/mm³. On physical examination, she was febrile and had pallor; left occipital lymph node measured 1x1 cm. Examination of the chest revealed decreased breath sounds on the left hemithorax. She had elevated IgG immunoglobulin in blood and proteinuria. Erythrocyte sedimentation rate (ESR) was 97 mm in the first hour. C-reactive protein was 0.6 mg/dL (<0.8 mg/dL). Direct Coombs' test was positive. C3 and C4 levels were low. ANA, anti-ds DNA, anti-cardiolipin antibodies were positive.

Her chest radiography revealed pleural effusion on the left (Fig. 1). In addition, thoracic CT scan showed mediastinal and axillary lymphadenopathy measured 15x25 mm, pleural effusion, and minimal pericardial effusion. Multiple small retroperitoneal lymph nodes were demonstrated in the abdominal CT. Thoracentesis was performed. ANA and LE cells were positive in her pleural fluid. Central nervous system vasculitis was detected by MR images. Her creatinine clearance was 38 mL/min. SLE was considered in this patient. Renal biopsy was performed, and it revealed Class IV glomerulonephritis according to the World Health Organization's classification of lupus nephritis.

The patient with SLE diagnosis received intravenous methylprednisolone (1 g/d) for 3 days and followed by prednisolone (30 mg/d) and cyclosporine (5 mg/kg/d) for 30 days. After a month her complaints were resolved. However, pleural fluid persisted. Methylprednisolone (1 g/d) for 3 days and cyclophosphamide (500 mg) were administered due to resistant pleural fluid. Corticosteroid therapy was continued (60 mg/d).

Six days after cyclophosphamide therapy, her temperature increased. Chest auscultation revealed bilateral crackles. Laboratory values showed leukocyte was 2,900/mm³ with 64% neutrophils and 31% lymphocytes; platelet count was 91,000/mm³, and ESR was 20 mm/h. C-reactive protein increased to 3.54 mg/dL. Chest X-ray and thoracic CT revealed diffuse interstitial shadow (Fig. 2). Lymphadenopathy was not observed in thoracic CT. Due to probable nosocomial or atypical pneumonia cephoperazon/sulbactam 1g four times a day and clarithromycin 500 mg a day were

initiated. The patient's fever decreased after this therapy. Laboratory examinations revealed a leukocyte count of 3300 /mm³ and C-reactive protein level of 2.2 mg/dL.

Five days later, the patient developed respiratory distress. Her fever increased. Hypoxemia was detected in the analysis of arterial blood gases. No bacterial, mycobacterial or fungal organisms were seen or cultured in her blood or pleural fluid samples. CMV IgM of the patient was found to be negative, CMV IgG was positive, at admission to our hospital. Both CMV IgM and CMV IgG showed positivity six weeks later. Real time PCR for CMV gave positive result (10,370 copies/ml). CMV antigenemia test was positive (25 cells/200,000 leukocytes). A diagnosis of CMV pneumonia was reached and ganciclovir 2.5 mg /kg twice a day was started. Trimethoprim-sulphamethoxazole 160/800 mg, three times a day was added, as she was prone to *P. jirovecii* pneumonia. The symptoms and radiographic abnormalities were resolved after this therapy. Laboratory result of CMV antigenemia had been negative on the 14th day. Ganciclovir and trimethoprim-sulphamethoxazole therapy were completed in 21 days. Two months after initiation of immunosuppressive therapy, her pleural effusion was resolved and she was discharged (Fig. 3). During the follow-up for one year, she was free of CMV infection.



Figure 1. There was left pleural fluid on his chest x-ray,, when the patient admitted our hospital

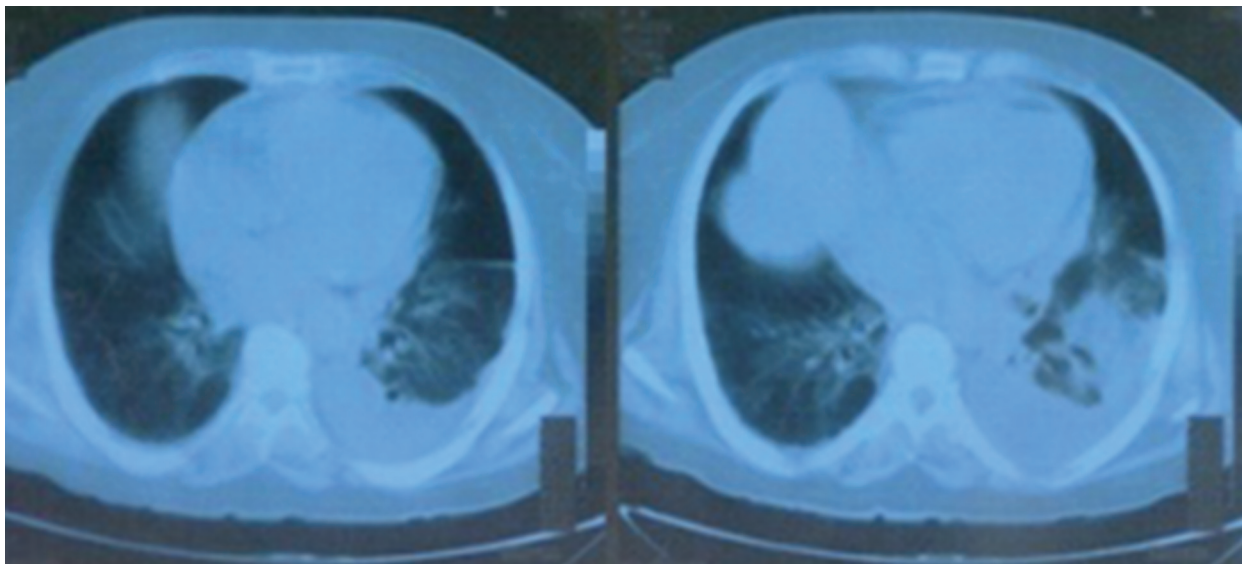


Figure 2. There was diffuse interstitial shadow and left pleural fluid on thorax CT

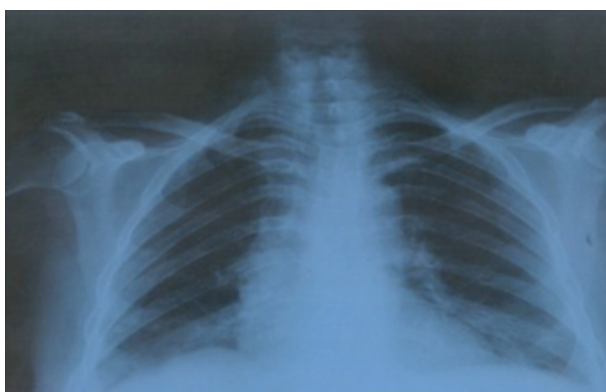


Figure 3. Ganciclovir therapy in 20th days, Chest X-ray

DISCUSSION

SLE is an autoimmune disease affecting many organs. Pleuropulmonary manifestations are seen in about 50-70% of patients with SLE.⁶ Pulmonary infiltrations should be evaluated as infectious until proven otherwise since infections increase morbidity and mortality in SLE patients. The infectious pulmonary infiltrations can be resulted from viruses, bacteria, fungi and protozoa.⁶

For diagnosis of CMV it is required to detect CMV in the tissue together with appropriate clinical symptoms and findings; and in BAL fluid in case of suspected CMV pneumonia. Patients with CMV pneumonia usually have high fever, dry cough, tachypnea, rales, and interstitial infiltrations in chest X-ray.⁷ Our patient was evaluated as CMV pneumonia due to clinical findings, inter-

stitial infiltration in thoracic tomography, CMV antigen (25 cells/200,000 leukocytes), and positivity of CMV PCR (10,370 copies/ml).

CMV antigen can be used in detection of CMV reactivation in immunosuppressive patients.⁸ The number of CMV positive cells in peripheral blood reflects the viral load; and high number of pp65 positive cells is correlated with CMV disease.⁹ Cut-off value of pp65 for estimation of symptomatic infection is reported to be 13 cells/200,000 polymorphonuclear leukocytes. Level of immunosuppression affects the relation between symptomatic CMV disease and CMV DNA replication. It is known that those who developed the disease have high CMV DNA (8,000 copies/ml) in the beginning of reactivation.^{8,9}

Although BAL could not be performed to determine the causative agent in our patient, as a response to the treatment fever dropped, respiratory distress and hypoxia in blood gas improved. In parallel with clinical improvement CMV antigen result in patient's blood was also negative. In the literature, Tokunaga et al. reported in a case report presentation that a patient with interstitial pneumonia was diagnosed due to CMV antigen positivity in blood and clinical improvement was observed after ganciclovir treatment.¹⁰

Many opportunistic infections in SLE patients may appear simultaneously due to severe immunosuppression. *P. jirovecii* pneumonia may occur together with CMV in an immunosuppressed host, and in this case the prognosis is worse.^{1,5}

Trimethoprim-sulfamethoxazole was added ganciclovir therapy of our patients due to the likelihood of coexistence of CMV and P. jirovecii.

As a result, although detection of the causative agent in BAL fluid is necessary for diagnosis of pneumonia, investigation of CMV DNA or CMV antigen in blood seems significant for patients who cannot undergo BAL considering untreated individuals have higher mortalities. To our knowledge, CMV infection is very rare in patients with SLE.^{1,5,11-14} It should be remembered that CMV can be an infection agent in immunosuppressive host and taken into differential diagnosis.

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