CMV Pneumonitis in an Immunosuppressed Patient With C-ANCA Positive Glomerulonephritis

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Abstract
Cytomegalovirus (CMV) pneumonitis is an important cause of morbidity and mortality in HIV and post-transplant patients, and is rare in patients with autoimmune diseases treated with immunosuppressive therapy. We report the first case of a patient with Cytoplasmic anti neutrophil cytoplasmic antibodies positive glomerulonephritis who developed CMV pneumonitis after treatment with cyclophosphamide and prednisone. The CMV infection developed simultaneously with bacterial respiratory infection. All symptoms resolved rapidly under treatment with gancyclovir and immunoglobulins.

ABBREVIATIONS
C-ANCA=cytoplasmic anti neutrophil cytoplasmic antibodies
BAL=bronchoalveolar lavage
CMV=cytomegalovirus

INTRODUCTION
CMV pneumonia is an important cause of morbidity and mortality in HIV and immunosuppressed post-transplant patients. This entity is rare in patients with autoimmune diseases treated with immunosuppressive agents. In a review of the medical literature, we have found only two reports that describe patients with systemic lupus erythematosus who developed CMV pneumonia while on corticosteroids and cyclophosphamide. As best as we can say, we report the first case of CMV pneumonia in a patient with C-ANCA positive glomerulonephritis who was treated with oral corticosteroids and cyclophosphamide.

CASE REPORT
A seventy-seven year old male was admitted with prolonged fever, confusion and a productive cough. Past medical history was notable for ischemic heart disease and hypertension. Three months prior to his admission, the patient was diagnosed with C-ANCA positive glomerulonephritis, which presented as unrelenting fever and renal failure. CMV serology (IgG and IgM) at that point was negative. Treatment with oral cyclophosphamide, prednisone and haemodialysis were initiated. At the time of admission he was receiving 150mg/day cyclophosphamide and 20mg/day prednisone.

On physical examination the patient appeared confused and agitated. Body temperature was 37.8°C, Oxygen saturation was 85% in room air. Examination of the lungs revealed prolonged expirium and bilateral rales. The rest of the physical examination was unremarkable.

Complete blood count was significant for mild normocytic anemia (Haemoglobin 10.7g/dL, MCV 84), with no additional abnormalities. LDH was markedly elevated (1032 units, normal range: 300-620 units). The chest X-ray was normal.

Sputum cultures were positive for Serratia marcescens. Intravenous antibiotics were initiated and the dialysis catheter removed for presumed line-associated bacteremia. Despite these measures, the patient's condition continued to deteriorate, with progressive dyspnea and worsening hypoxemia. High-resolution CT demonstrated non-specific interstitial changes in the apices of both lungs and diffuse ground glass appearance (Fig. 1). Bronchoscopy with bronchoalveolar lavage (BAL) was done; a positive shell vial assay established the diagnosis of pulmonary CMV infection. Bacterial culture was once again positive for Serratia marcescens. Staining for Pneumocystis carinii, acid fast staining and culture for Mycobacterium tuberculosis were negative.

In view of these findings, intravenous gancyclovir and immunoglobulins were administered, cyclophosphamide was...
stopped and steroids were tapered, with rapid resolution of the fever and hypoxemia. Treatment with intravenous gancyclovir was continued for 3 weeks, followed by oral ganciclovir for another four weeks; IV Immunoglobulins was given over seven weeks. CMV IgG after resolution of the disease turned positive.

**Figure 1**
Figure 1: thoracic CT scan demonstrating the interstitial changes in the apices of both lungs. High resolution CT scan of the lungs shows non-specific interstitial changes at the apices of both lungs, and diffuse ground glass appearance.

**DISCUSSION**
CMV infection is very common and usually asymptomatic in the general population (1). In adults, severe CMV disease usually results from a significant defect in cellular immunity, as observed in immunosuppressed, post-transplant and HIV patients. CMV pneumonitis occurs in 17-38% of solid organ recipients; in bone marrow transplant patients the disease tends to be more severe, though it is somewhat less frequent (2, 3). Cytotoxic immunosuppressants and depressors of T-cell function increase the risk of infection, steroids are not considered to so (4).

In a search of the literature, we have found only two case report of CMV pneumonitis in a patients treated by intensive combined therapy with cyclophosphamide and corticosteroids for lupus nephritis (5, 6). To our knowledge, our patient is the first described case of CMV pneumonitis in the context of immunosuppressive therapy for C-ANCA positive glomerulonephritis. The reason for the decreased propensity of immunosuppressed rheumatologic patients to develop CMV pneumonitis, compared to post-transplant patients, is not known, and may relate to the latter's worse general condition and multiple co morbidities, as well as to the extent of immunosuppression.

**In our patient, pulmonary involvements of Wegener's granulomatosis as well as infection were viable explanations for the observed clinical course. Interestingly, the white blood count on admission was normal, despite a combination of CMV infection and treatment with cyclophosphamide.**

In the bowel, CMV has been shown to colonize areas of mucosal inflammation secondary to various aetiologies (7). A similar situation may exist in the respiratory tract. In our case, underlying infection with Serratia marcescens may have predisposed the patient to colonization with CMV. The rapid response to specific treatment for CMV infection, the positive shell vial test and the sero-conversion leads us to believe that CMV had a central role in the pathogenesis of this patient's illness.

**CONCLUSIONS**
We conclude that CMV pneumonitis, while uncommon, may complicate the disease course of rheumatologic patients treated by immunosuppressive agents. Bacterial infection may predispose the patient to CMV pneumonitis. Bronchoscopy may be essential to establish the diagnosis. We also suggest, that blood count alone may not be a reliable parameter for monitoring the immune suppression of patients receiving cyclophosphamide.

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