

A double whammy in an immunocompromised patient

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Abstract

Pneumocystis jirovecii pneumonia (PCP) is a common opportunistic infection in immunocompromised patients, especially those with human immunodeficiency virus (HIV) infection. *Cytomegalovirus* (CMV) pneumonia most often occurs as a coinfection with another opportunistic pathogen especially in patients with severe immunosuppression. We present a case of PCP-CMV coinfection in a newly diagnosed HIV patient who was treated with the recommended therapy for both diseases and had a favorable outcome. The presence of CMV in the context of another opportunistic respiratory tract infection is often to be not treated, due to conflicting evidence of its therapeutic benefit. Our report highlights the importance of CMV treatment to achieve clinical stability and recovery in newly diagnosed patients with HIV and severely immuno-compromised status.

Key words: *Cytomegalovirus*, human immunodeficiency virus, *Pneumocystis jirovecii* pneumonia

INTRODUCTION

Pneumocystis jirovecii pneumonia (PCP) is one of the most common opportunistic respiratory infections in patients with human immunodeficiency virus (HIV) infection. *Cytomegalovirus* (CMV) pneumonia is another opportunistic infection presented by these patients when they are in a state of severe immunosuppression. The purpose of this report is to describe a patient with PCP and CMV coinfection who was treated with the recommended therapy for both diseases and had a favorable outcome.

CASE REPORT

An 18-year-old female student presented with dry cough, exertional dyspnea and low-grade fever of 2 weeks' duration. The patient had received intravenous (IV) antibiotics for similar complaints 2 months back with partial resolution of symptoms. There was no prior history of treated tuberculosis or recent travel or pets at home. On examination, she was febrile and normotensive, with a respiratory rate of 26 breaths/min and pulse rate of 100 beats/min. Her body mass index was 19 kg/m². Oxygen saturation was 88% on room air with active use of accessory muscles of respiratory examination revealed bilateral fine crepitations over the infrascapular regions. The rest of the physical examination was unremarkable. Her hemogram, liver function tests, renal function test and blood sugar levels were within normal limits; Her erythrocyte sedimentation rate was slightly raised (50 mm in 1st h). Arterial blood gas showed severe hypoxia with an elevated alveolar-arterial (A-a) oxygen gradient of 56. Chest x-ray (CXR) [Figure 1] showed bilateral lower zone nonhomogeneous opacities. Sputum was negative for acid-fast bacilli (AFB) on two occasions by Ziel-Nielsen (ZN) staining. Bacterial aerobic cultures of sputum samples were also negative. The patient was further worked-up HIV infection which came back positive for HIV 1/2 antibodies with a CD4 count of 9 cells/mm³ and serum lactate dehydrogenase (LDH) of 332 U/L. High-resolution computed tomography (HRCT) of the thorax [Figure 2] showed diffuse ground glass opacities in bilateral lung fields predominantly in the middle and lower lobes with a few areas of confluent consolidation noted in the posterior basal segment of both lower lobes. In view of her HIV-positive status, symptoms, elevated LDH levels and imaging findings, the presumptive diagnosis of PCP was made and the patient was started on a therapeutic dose of co-trimoxazole along with IV methylprednisolone at a dose of 2 mg/kg/day along with supplemental oxygen. After X days with the above treatment, the patient's clinical condition did not improve with worsening

radiological shadows on reimaging. She was then started on IV piperacillin-tazobactam 4.5 g three times daily out of concern for possible bacterial coinfection. Routine blood (hemogram, liver and renal functions) investigations were repeated and were normal. Fundus examination after 4 days of admission was normal.

Bronchoscopy and bronchoalveolar lavage (BAL) were done as the patient was stable and failed to improve in oxygen saturation despite the above treatment. BAL showed multinucleated giant cells with inclusions and margination of chromatin. Foamy and granular casts of *P. jirovecii* were also present [Figure 3a]. BAL fluid smear and cytological tests were negative for bacteria, AFB and fungus. Transbronchial lung biopsy showed alveolar macrophages with intracytoplasmic and predominantly intranuclear inclusions resembling the classic owl eye appearance of CMV [Figure 3b]. Thus, a diagnosis of HIV with PCP-CMV pneumonia was made.

Soon after (or specify the timeline more precisely) the patient was started on IV ganciclovir 5 mg/kg/twice daily, her clinical condition and oxygen saturation improved. At discharge, he was also started on antiretroviral therapy (ART-tenofovir, lamivudine and efavirenz). Ganciclovir was planned to continue until her CD4 count recovered to >100 and co-trimoxazole was planned to continue for a total of 21 days. At 1 month follow-up, she had an oxygen saturation of 98% on room air, CD4 count of 102 cells/mm³ and a radiological resolution of lung lesions.

DISCUSSION

HIV patients are at a risk of developing opportunistic infections especially with severe immunological suppression [Table 1]. PCP is strongly suspected in these patients with a CD4 cell count <200 cells/mm³ and symptoms or signs characteristic of the infection such as dyspnea, hypoxemia, and cough as well as diffuse, bilateral, interstitial, or alveolar infiltrates on chest imaging. A definitive diagnosis of PCP requires visualization of the cystic or trophic forms in respiratory secretions. However, some clinicians may elect to forego obtaining a definitive diagnosis if the clinical presentation and radiographic findings are highly consistent with PCP and to start empiric treatment. The initiation of empiric therapy does not preclude obtaining a definitive diagnosis as cysts may persist for days to weeks after appropriate therapy has been administered.^[1,2]

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Corticosteroids given in conjunction with anti-Pneumocystis therapy in patients with moderate-to-severe disease with A-a gradient of ≥ 35 mmHg can decrease the incidence of mortality and respiratory failure associated with^[3] from the increased inflammation of PCP as a response to the dying organisms. Several randomized trials have demonstrated outcome benefits of steroid use in PCP patients who have abnormalities in oxygen exchange at the time of presentation.^[4-6]

Although CMV may cause serious sequelae and death among organ transplant recipients, its significance as a pulmonary pathogen in HIV-infected patients is unclear. Autopsy studies are the major source of evidence for CMV as a cause of pulmonary disease in these patients.^[7] Pulmonary infections caused by CMV as a sole pathogen occur only in patients in advanced stages of immunosuppression, when CD4+ is below 50 cells/mm³. The more common presentation of pulmonary CMV is coinfection with another opportunistic pathogen. CMV infection can also result in a wide variety of clinical presentations such as retinitis, encephalitis, hepatitis and ulceration of the gastrointestinal tract, which are associated with high morbidity and mortality.^[8] Histologic evidence of CMV infection in the lungs was described in 29%–93% of HIV positive patients.^[8] The diagnosis of CMV infection can be confirmed by serology, isolation, detection by PCR, by culture methods, or direct visualization of the pathogen in transbronchial biopsies.

A central question in the care of HIV-infected patients with pneumonia and isolation of CMV is whether anti-CMV therapy improves outcome. The preponderance of data suggests that anti-CMV treatment of HIV-infected patients with pneumonia and BAL cultures positive for CMV is not associated with improved survival in comparison with patients not treated with anti-CMV therapy.^[9] However, studies by Salomon *et al.*, and Waxman *et al.*, demonstrated improvement in patients treated for biopsy proven CMV pneumonia.^[10,11]

CONCLUSION

PCP-CMV coinfection should be considered in patients with severe hypoxemia and low-CD4+ count. Appropriate and early treatment reduces the mortality and morbidity associated with the coinfection. In addition to evidencing support for the treatment of CMV infection in HIV patients, our report also supports the use of a moderate dose of steroids for the treatment of PCP.

Table 1: Opportunistic infections in HIV patients at different CD4 count

Any value	Tuberculosis and bacterial infection
200-500	Pulmonary tuberculosis, Herpes zoster
50-200	PCP, Histoplasmosis, Coccidioidomycosis, Kaposi's sarcoma, Miliary/extrapulmonary tuberculosis
<50	MAC, CMV, non Hodgkin's lymphoma

PCP=Pneumocystis jirovecii pneumonia; MAC=Mycobacterium avium complex; CMV=Cytomegalovirus

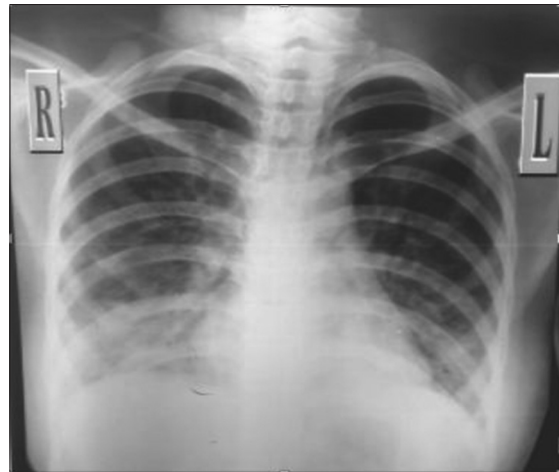


Figure 1: Chest radiography showing bilateral lower zone infiltrates

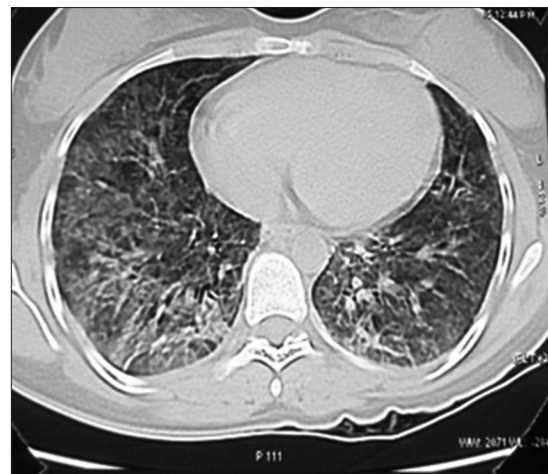


Figure 2: High resolution computed tomography-Thorax: Diffuse ground glass opacities in bilateral lung fields predominantly in the middle and lower lobes with a few areas of confluent consolidation noted in the posterior basal segment of both lower lobes

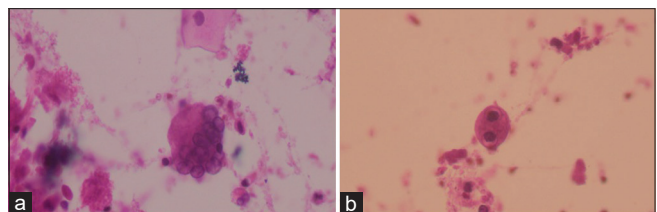


Figure 3: (a) Hematoxylin and eosin staining of bronchoalveolar lavage fluid showing multinucleated giant cells with inclusions and margination of chromatin. Foamy and granular casts of *Pneumocystis jirovecii* are also present. (b) transbronchial lung biopsy sample showing alveolar macrophages with intracytoplasmic inclusions and intranuclear inclusions resembling the *Cytomegalovirus* owl eye appearance

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patient(s) understand that his/her/their name(s) and initials will not be published and due efforts will be made to conceal his/her/their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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