

Pneumocystis jirovecii Pneumonia in a Patient With Newly Diagnosed HIV and a High CD4 Count

Michelle Koifman¹, Bhavyakumar Vachhani¹, Krishna S. Haridasan¹, Mossammat Mansur²

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1. Internal Medicine, The Brooklyn Hospital Center, New York, USA 2. Infectious Disease, The Brooklyn Hospital Center, New York, USA

Corresponding author: Michelle Koifman, mkoifman94@gmail.com

Abstract

Pneumocystis jirovecii pneumonia (PCP) is a rare, life-threatening opportunistic fungal infection that rarely occurs with CD4 counts greater than 200 cells/mm³. We present a case of PCP in a young male who presented with fever, weakness, dyspnea, and a non-productive cough. He was initially treated for community-acquired pneumonia but was then noted to be HIV positive with signs of immunosuppression such as oral thrush. The CD4 count was found to be very high, at 646 cells/mm³ and 281 cells/mm³ on repeat. The patient was treated with trimethoprim/sulfamethoxazole (TMP/SMX) and fluconazole and further started on highly active antiretroviral therapy (HAART) with TMP/SMX as a means of secondary prophylaxis in the outpatient setting.

Categories: Internal Medicine, Infectious Disease, Pulmonology

Keywords: human immuno-deficiency virus (hiv), acquired immune deficiency syndrome (aids), pneumocystis jiroveci pneumonia prophylaxis, cd4 t-cells, opportunist infections in hiv, pneumocystis jiroveci pneumonia

Introduction

The immunocompromised status of patients with undiagnosed or untreated HIV leads to many opportunistic infections. *Pneumocystis jirovecii* pneumonia (PCP) is one of these life-threatening opportunistic fungal infections that is airborne but only affects those that are immunocompromised, and it rarely occurs with CD4 counts greater than 200 cells/mm³. It often presents with signs and symptoms such as tachypnea, dyspnea, cough, and fever. Trimethoprim/sulfamethoxazole (TMP/SMX) is considered the gold standard for prophylaxis against PCP when CD4 counts are less than 200 cells/mm³. It is also considered the preferred drug for PCP treatment [1,2]. We present an interesting case of a young male with an elevated CD4 count on two occasions who was diagnosed with PCP.

Case Presentation

A 32-year-old male with a past medical history of tobacco use presented to the hospital with fever, weakness, dyspnea, and a non-productive cough that had been ongoing for one week. He reported being vaccinated with the COVID-19 vaccine and denied any recent sick contacts. Vital signs were significant for a fever of 38.7 degrees Celsius, a heart rate of 105 beats per minute, a respiratory rate of 20 breaths per minute, and an oxygen saturation of 90% on room air. The arterial blood gas was noted to have a pH of 7.45, a partial pressure of carbon dioxide (pCO₂) of 40, a partial pressure of oxygen (pO₂) of 91, a bicarbonate (HCO₃) of 28, and an oxygen (O₂) saturation of 97 on 2 L of nasal cannula. The alveolar-arterial gradient (A-a gradient) was 58.6 mm Hg. A physical examination revealed mild respiratory distress. Initial laboratory findings showed no leukocytosis, slight anemia, elevated inflammatory markers, and no lactic acidosis. The laboratory findings are documented in Table 1.

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Test	Value	Reference Range
White cell count	7.4 K/cmm	4.8-10.8 K/cmm
Hemoglobin	12.3 g/dL	13.1-15.5 g/dL
Erythrocyte sedimentation rate	80 MM/HR	0-15 MM/HR
C-reactive protein	64.43 mg/L	<5.00 mg/L
Lactate dehydrogenase	538 U/L	125-220 U/L
Lactic acid	1.4 MMOL/L	0.5-2.2 MMOL/L

TABLE 1: Pertinent laboratory values on initial presentation

The COVID-19 and influenza tests were negative. A septic workup, including urinalysis, blood cultures, a methicillin-resistant *Staphylococcus aureus* (MRSA) swab, and respiratory culture, was collected. An electrocardiogram (EKG) showed sinus tachycardia. A chest radiograph (chest X-ray) showed pulmonary vascular congestion (Figure 1). The computed tomography angiography (CTA) chest with contrast was negative for pulmonary embolism but showed diffuse bilateral ground-glass opacities with a more confluent region of consolidation in the right posterior lower lobe (Figure 2).

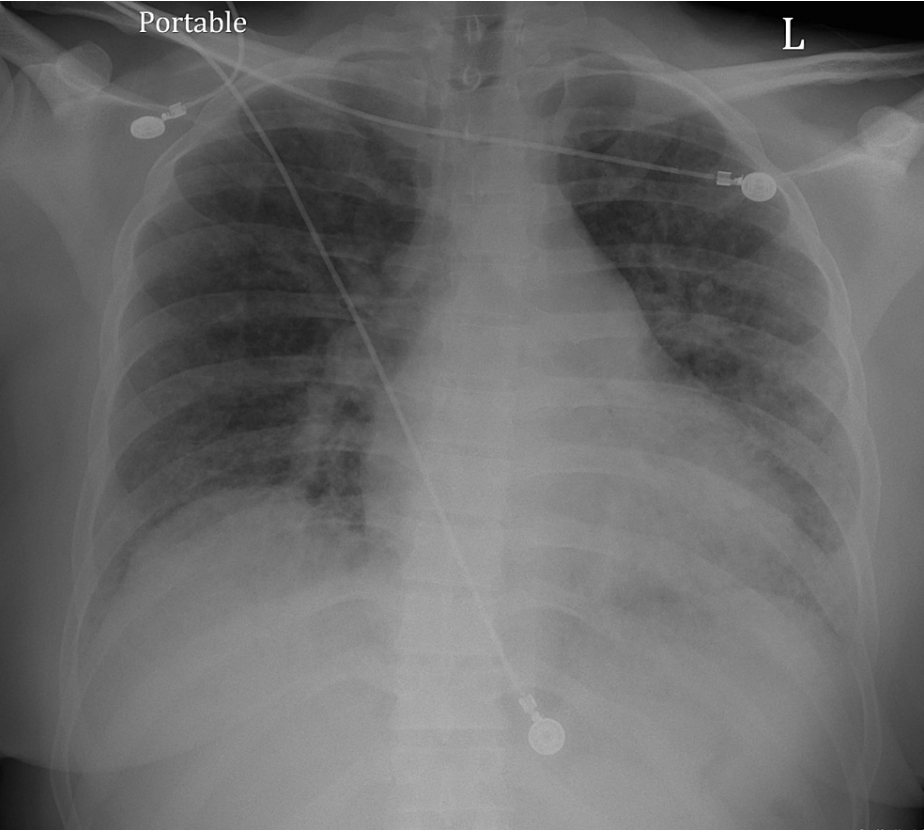


FIGURE 1: Anterior-posterior chest X-ray showing moderate pulmonary vascular congestion

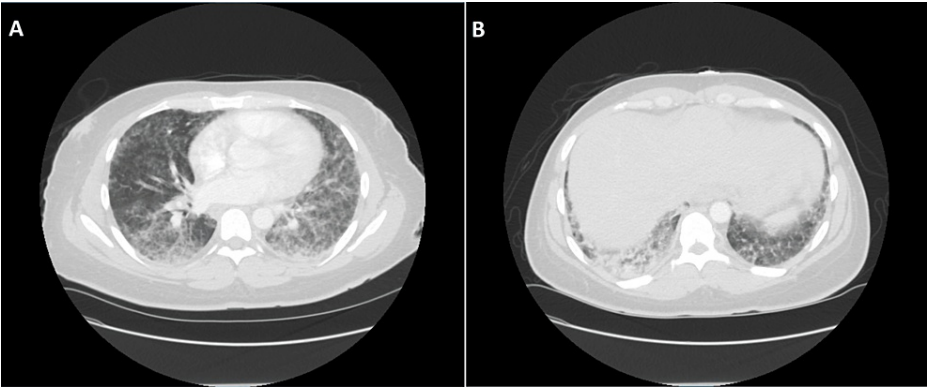


FIGURE 2: CTA chest

A: Extensive diffuse bilateral ground-glass opacities; (B) Confluent region of consolidation in the right posterior lower lobe compatible with an infectious or inflammatory process

CTA: Computed tomography angiography

The patient was started on ceftriaxone and azithromycin for community-acquired pneumonia coverage. Further laboratory values were collected (Table 2), including the HIV antigen/antibody test, HIV viral load, and an absolute CD4 lymphocyte count. The infectious disease team noted oral thrush and recommended intravenous TMP/SMX as a treatment for possible PCP due to signs of immunosuppression despite the high CD4 count. The patient was also started on fluconazole and nystatin suspensions. Prednisone was also started due to the elevated A-a gradient. As the respiratory culture grew *S. aureus*, the patient was also started on linezolid as per infectious disease recommendations while pending sensitivities. The remainder of the septic workup was negative.

Test	Value	Reference Range
HIV antigen/antibody combo	Reactive	Nonreactive
HIV viral load	697000 copies/mL	Not detected
Absolute CD4 cells	646 cells/mm3	490-1740 cells/mm3

TABLE 2: Further laboratory values

The repeat CD4 count two days later was 281 cells/mm3, and the repeat chest X-ray showed no significant change in the diffuse opacities, which did not fit with the presentation (Figure 3). The final growth of the respiratory culture did not show MRSA, and linezolid was further discontinued. Pulmonology performed bronchoscopy with bronchoalveolar lavage (BAL), and PCP was confirmed by Gomori methenamine silver (GMS) stain. Gastroenterology did not recommend endoscopic evaluation as symptoms of dysphagia had improved. On discharge, the patient was given three weeks of oral TMP/SMX double strength (DS) and fluconazole for esophageal candidiasis. The patient was also given a prednisone taper. Antiretroviral therapy was not started to avoid immune reconstitution inflammatory syndrome (IRIS). When the patient followed up two weeks later in the outpatient setting, he was started on bictegravir, emtricitabine, and tenofovir alafenamide (Biktarvy), and the dose of TMP/SMX was reduced to the daily prophylactic dose. The patient continued on this dose of TMP/SMX until the HIV viral load was negative.



FIGURE 3: Anterior-posterior chest X-ray showing no significant change in diffuse bilateral patchy opacities compared to the initial chest radiograph on presentation

Discussion

Pneumocystis jirovecii pneumonia is caused by the human pathogen *P. jirovecii*, which is a spherical, oval, cup-shaped, thick-walled cyst that usually measures 6 to 8 μm in diameter and is classified as a fungus [1]. It is transmitted through an airborne route from person to person. Individuals who are immunocompetent may unknowingly carry *P. jirovecii* due to lung colonization and spread it to the immunocompromised. Despite being one of the most common and serious opportunistic infections in patients with AIDS, prophylaxis and highly active antiretroviral therapy (HAART) have reduced its incidence. The TMP/SMX is the gold standard for prophylaxis, and regimens usually include daily and three times a week dosing with single or DS doses that should be initiated when the patient has a CD4 count less than 200 cells/mm³ and a detectable viral load [2,3].

Patients with PCP present with dyspnea, a nonproductive cough, and fatigue, progressing over a few days to weeks. Physical examination may include tachypnea, tachycardia, fever greater than 38.1°C, oral thrush as a co-infection, crackles, and rhonchi. Markers such as lactate dehydrogenase (LDH) are related to prognosis, as non-survivors had a higher LDH. Arterial blood gas in hypoxic patients often shows a high A-a gradient. Chest X-rays can show diffuse bilateral perihilar interstitial infiltrates, and CT chest may show ground glass attenuation [3,4].

Interestingly, one study found that only three (5%) of 61 cases of PCP occurred above a CD4 count of 250 cells/mm³, while another study showed that only four (9%) of 43 patients with PCP had CD4 counts greater than 250 cells/mm³, and 75% of these had CD4 counts that were less than 333 cells/mm³ [5]. In another study with 100 patients, only three (6%) of 49 patients with PCP had CD4 counts greater than 200 cells/mm³ [6]. Our patient had accompanying signs of immunosuppression, which aided in diagnosis and prompted us to consider PCP, despite an initial CD4 count of 646 cells/mm³. In a study with 346 individuals, out of which a total of 168 participants had oral lesions, oral candidiasis was the only lesion found to have a significant association with a CD4 count of less than 350 cells/mm³ and the only lesion significantly predictive of immunosuppression [7]. The repeat CD4 count in the case of our patient was 281 cells/mm³. On repeat six months later in the outpatient setting, the CD4 count was 262 cells/mm³.

Clinicians need to be vigilant for opportunistic infections such as PCP, even with high CD4 counts, to avoid potential morbidity. Nevertheless, it is still important to account for the potential reason there have been other higher-than-expected CD4 counts in the literature in addition to this case. For instance, it has been found that there is a diurnal variation in the CD4 count, with the lowest counts being in the morning and the highest in the evening [8]. It can also be influenced by any factors that lead to an increase or decrease in the WBC count, such as infection, medications, or other chronic conditions. More specifically, leukocytosis may increase the CD4 count, while leukopenia may result in a decreased count. A patient's immunological status may also not be accurately reflected due to factors such as laboratory variability that may falsely increase or decrease CD4 counts [9].

Demonstration of PCP through histopathology or cytopathology is necessary for diagnosis through either

sputum induction or bronchoscopy with BAL [10]. The preferred treatment includes TMP/SMX for 21 days. For patients with gas exchange abnormalities receiving antibiotics for less than 72 hours, corticosteroids improve survival. Following PCP treatment, TMP-SMX is recommended as a secondary prophylaxis. If the patient is on HAART, has an undetectable viral load, and has a CD4 count that is greater than 200 cells/mm³ for at least three months, secondary prophylaxis can be discontinued [11,12]. In our case, TMP/SMX was later discontinued as a secondary prophylaxis due to an undetectable viral load.

Conclusions

This case of PCP demonstrates the importance of considering many differential diagnoses that could contribute to a patient's symptoms. It highlights the importance of paying close attention to the entire patient presentation for early detection of life-threatening opportunistic infections in susceptible patients. Aside from what is known to contribute to either the increase or decrease in the CD4 count, such as the time of day, WBC count, medications, chronic conditions, or lab variability, the reason why such anomalies may occur still needs to be further explored, as there are limited case reports on this.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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