**Pneumocystis jirovecii** pneumonia secondary to chronic steroid use: An uncommon cause of pneumocystis pneumonia

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**Abstract**

Patients on long-term immunosuppression, including corticosteroids or immunomodulatory drugs, are susceptible to opportunistic infections, such as like Pneumocystis jirovecii pneumonia (PJP). Corticosteroid use can increase the frequency of fungal infection, mask symptoms, and delay the diagnosis, and thus warrant preventive measures. Maintaining a high index of suspicion is important, and prophylactic antibiotics, particularly trimethoprim-sulfamethoxazole, should be considered for high-risk patients. This case underscores the diagnosis of PJP in a patient with interstitial lung disease receiving prolonged steroid therapy, despite lacking HIV and conventional risk factors for this infection. Notably, PJP can present as a more severe infection in non-HIV patients, leading to higher mortality rates and stressing the need for swift and effective diagnosis and treatment by healthcare providers.

**Keywords:** Pneumocystis jirovecii; pneumonia; chronic corticosteroid treatment use; fungal pneumonia; interstitial lung disease

**Introduction**

**Pneumocystis jirovecii** pneumonia (PJP) is an opportunistic fungal infection primarily affecting immunocompromised patients, such as those with HIV/AIDS, malignancies, or organ transplants. In HIV-positive patients, symptoms, like cough, fever, and shortness of breath develop gradually, while HIV-negative patients often have a sudden onset of symptoms and rapid decline. A CD4+ count below 200 cells/µL in HIV patients signals a high risk, prompting prophylaxis. Non-HIV patients may also require prophylaxis, especially patients on prednisone at a 20 mg or higher daily or chemotherapy and patients with certain clinical disorders, such as leukemia, immunodeficiency, or status post hematopoietic stem cell or solid organ transplantation. However, guidelines lack consensus on prophylaxis solely for corticosteroid use.

**Case**

A 65-year-old man with a medical history of idiopathic pulmonary fibrosis (IPF) and chronic respiratory failure presented to the emergency department with worsening shortness of breath over a week. He had significant limitations in daily activities and noted bilateral lower extremity swelling, abdominal distention, and a 20-pound weight gain over the last 6–8 months. During the past few months, patient required multiple courses of corticosteroids and antibiotics for ILD flare-ups and superimposed pneumonia. His last admission was a month prior to this current admission when he received pulse dose steroids for 3 days and tapering dose over one week. Chest X-ray at discharge is shown (Figure 1). He was a former smoker with 6 pack-year smoking history, who quit 8 years ago. He denied any recent travel history, sick contacts, or any infection.

On arrival at the ED, the patient was hypotensive (blood pressure 61/83 mmHg) and tachycardic (heart rate 115 beats/minute). He was in moderate respiratory...
distress, with a respiratory rate of 32 breaths/minute. His initial oxygen saturation was 60% which increased to 90% on a non-rebreather oxygen mask.

Significant laboratory results included a white blood cell count of \(21.6 \times 10^3/\mu L\), hemoglobin of 11.2 g/dL, and lactic acid level of 2 mmol/L. He tested negative for COVID-19 and influenza, and BNP and troponin levels were within normal limits. His arterial blood gas analysis showed pH 7.46, PaCO\(_2\) 27.3 mmHg, and PaO\(_2\) 38 mmHg. His chest x-ray revealed diffuse bilateral lung opacities (Figure 2). Computed tomography with angiography ruled out pulmonary embolism but showed multifocal ground glass opacities consistent with pneumonia in the background of chronic ILD (Figures 3, 4). Echocardiogram demonstrated a left ventricular ejection fraction of 65% to 70% with Grade 1 diastolic dysfunction. A strongly positive Fungitell\textsuperscript{®} test raised concern about a fungal infection, including PJP and Aspergillosis, and a galactomannan test was then ordered to rule out invasive aspergillosis. Sputum studies, including Gram stain, cultures, and PJP PCR, were sent. Blood cultures returned negative.

The patient was started on broad-spectrum antibiotics (vancomycin and meropenem), stress doses of corticosteroids, diuretics, and BiPAP. In addition, fluconazole and trimethoprim-sulfamethoxazole (TMP-SMX, initially at prophylactic dose) were added on day 3. The chest x-ray on day 4 showed partial clearing of opacities (Figure 5), but patient’s clinical condition continued to deteriorate, requiring increased oxygen supplementation. Bronchoscopy was considered at this point, but because of high risk of decompensation and possible need of mechanical ventilation, family decided to defer this decision. Fungitell\textsuperscript{®} was positive; galactomannan was negative. On day 4, TMP-SMX was adjusted...
CD4 counts, the incidence of PJP in HIV-infected individuals has significantly decreased in industrialized countries. Unfortunately, the incidence of PJP in patients who do not have HIV infection is increasing, necessitating meticulous evaluation and heightened clinical suspicion. A particularly rare and intriguing cause of PJP is corticosteroid use, and these patients can present with more severe infections than patients with HIV. Glucocorticoids, widely used in management of various rheumatological, pulmonary and autoimmune diseases, increase the risk of infection by decreasing CD4+ lymphocyte counts, especially in the blood and lungs, and by inhibiting T-cell activation and macrophage differentiation among other mechanisms.

Several prophylactic options exist for PJP, the most important being TMP-SMX. Other drugs include atovaquone, aerosolized pentamidine, and dapsone for patients with sulfa-allergies. While CD4 counts <200/µL is the criterion for starting prophylactic antibiotics in patients infected with HIV, there are no such guidelines for patients who are on corticosteroid therapy. However, information in the medical literature suggests that it is appropriate to start prophylaxis when patients have been on prednisone 20 mg or higher for four weeks or more, especially if they are already on other immunosuppressants.

The HIV-negative patients who contract PJP experience higher rates of mortality (30%–40%) and respiratory failure when compared to patients with HIV (1%–15%). LDH levels and the development of respiratory failure can serve as significant markers for identifying patients at risk of mortality, regardless of their HIV status. It has also been noted that higher neutrophil counts in non-HIV patients correlate with increased disease severity.

Diagnosing PJP in this patient was very challenging in the absence of traditional risk factors given a long list of possible differential diagnoses. In addition, his lung disease and heart failure represented significant risk factors and indicated decreased cardiorespiratory reserve. Numerous risk factors, coupled with corticosteroid use, likely contributed to the development of PJP. Multiple studies have shown a correlation between corticosteroids use and PJP, typically involving patients with underlying rheumatological conditions, organ transplantation, and

**DISCUSSION**

With the advent of aggressive anti-retroviral therapy and TMP-SMX prophylaxis for patients with low

![Figure 4. Computed tomography revealing honeycombing and reticulation at bilateral lung bases.](image)

![Figure 5. Chest x-ray of day 4 of hospitalization showing improved bilateral infiltrates.](image)
hematological and solid organ malignancies. However, this case did not have these typical risk factors and instead had only chronic interstitial lung disease (ILD), an uncommon association. While this patient required corticosteroids for managing his lung disease intermittently for ILD flare up, maintaining a heightened clinical suspicion along with early initiation of TMP-SMX therapy for PJP may reduce mortality rates.

**CONCLUSION**

This case report highlights the importance of considering PJP high in the differential diagnosis in patients who have been on long-term corticosteroid therapy, even if it is intermittent but frequent.

**LEARNING POINTS**

1. Extended corticosteroid use poses a notable risk for non-HIV patients to develop *Pneumocystis jirovecii* pneumonia.
2. Vigilant clinical suspicion is crucial for diagnosing PJP in individuals without traditional risk factors, given the higher mortality rate among HIV-negative patients.
3. TMP-SMX prophylaxis should be recommended for those on prednisone 20 mg or higher for over four weeks unless otherwise contraindicated.

**REFERENCES**


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