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Case report

Pneumocystis pneumonia in a treatment-naive rheumatoid arthritis patient

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ABSTRACT

A HIV-negative, newly diagnosed patient with rheumatoid arthritis (RA) was found to have *pneumocystis jiroveci* pneumonia. The infection was treated with three weeks of atovaquone and corticosteroids. Clinicians should be aware of pneumocystis pneumonia as an infection in RA patients not receiving treatment.

Introduction

Pneumocystis pneumonia (PJP) is a pulmonary infection caused by *Pneumocystis jiroveci (P. jiroveci)*, formerly known as *Pneumocystis carinii (P. carinii).* The fungus resides in the alveoli of the lungs and is considered an opportunistic infection in immunosuppressed patients [1,2]. PJP was initially recognized in premature infants, malnourished children, or patients with acute leukemia and other hematological malignancies. However, in the 1980s, the incidence rate of *P. jiroveci* increased exponentially with the human immunodeficiency virus (HIV) epidemic [1]. *P. jiroveci* is extremely uncommon in healthy people; about 20% of adults are reportedly asymptomatic carriers of this fungus in the lungs, and after several months, is eliminated by the immune system [3]. The infection is higher in immunocompromised individuals. About 40% of people infected with PJP are HIV/AIDS (acquired immunodeficiency syndrome) patients, with the remaining burden in individuals receiving immunosuppressive agents to treat malignancies, autoimmune disorders, organ transplantation, and chronic inflammatory diseases [4]. We report a case of a patient with newly diagnosed rheumatoid arthritis (RA) found to have PJP. To our knowledge, this is the first reported case in the literature of *P. jiroveci* infection occurring in an HIV-negative, treatment naïve patient with RA.

Case report

A 32-year-old female with a history of diabetes mellitus presented to the emergency department with a 3-month history of shortness of breath, palpitations and productive cough with white sputum. The shortness of breath initially occurred with moderate exertion but progressively worsened. There was a 10-pound weight loss in 2 months. The patient did not report fever, chills, night sweats, wheezing or sick contacts. She had a several year history of joint pain and tested positive for rheumatoid factor a few months prior to presenting at the current hospital.

The patient presented to another hospital 2 months previously during which a computerized tomography (CT) of the chest showed mediastinal and hilar lymphadenopathy with alveolar and interstitial infiltrates. She was treated with levofloxacin and referred to a pulmonologist for evaluation of interstitial lung disease. An endotracheal ultrasound and fine needle aspiration of a lymph node was unremarkable. However, the symptoms persisted. On presentation, the heart rate was 127 beats per minute, blood pressure 114/73 mmg Hg, respiratory rate 19 breaths per minute and temperature 37 °C. Physical exam was significant for decreased breath sounds bilaterally. The leukocyte count was 9400 /uL with 80% polymorphonuclear cells, hemoglobin 11 g/dL, platelets 506,000/uL, blood urea nitrogen 6.0 mg/dl, creatinine 0.6 mg/dl. CT angiogram of the chest with intravenous (IV) contrast showed multiple diffuse small, nodular opacities bilaterally and mildly prominent bilateral axillary and right hilar lymph nodes. The patient was treated with methylprednisolone 60 mg IV daily with improvement in symptoms. A test for HIV was negative. The

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pulmonary team performed a bronchoalveolar lavage. The sample was tested for both respiratory and AFB (acid-fast bacteria) culture and smearm; which tested negative. Due to the findings of the CT angiogram of the chest, the pulmonary team tested the sample for *P. jiroveci* by direct fluorescent antibody; the test was found to be positive. Treatment with atovaquone 750 mg twice a day and prednisone 40 mg oral daily was given. The patient was discharged home on hospital day 3. At follow-up two weeks after discharge, the patient reported significant improvement in symptoms. She was subsequently diagnosed with RA for which she is receiving treatment.

Discussion

Patients with RA are nearly twice as likely to get infections, and pneumonia is a common cause of death [5,6]. PJP is the leading cause of morbidity and mortality in this population after immunosuppressive therapy has begun [7]. Non-HIV related PJP generally has a more acute and serious course than HIV related PJP which in patients with HIV, the onset of the *P. jiroveci* is more gradual. In contrast, among non-HIV PJP individuals, the onset of the infection is more sudden and often associated with respiratory failure [8]. Previous studies have reported a lower mortality rate (10–20%) in patients who have HIV PJP compared to those without HIV (35–55%) [9], perhaps related to non-HIV PJP patients having a longer duration between admission and initiation of PJP treatment [10].

Notably, the presentation of *P. jiroveci* in the current case differs from previous reports as the patient had a slower onset of infection compared to others with non-HIV PJP [8]. Poor prognostic factors such as bacteremia, increased blood urea nitrogen and pre-existing chronic lung disease were absent in our case [2]. Other poor prognostic factors including lower lymphocyte count, older age and coexisting lung involvement during immunosuppressive treatment were absent as well [11].

Corticosteroids promote depletion of CD4+T cells which leads to promotion of PJP. Patients with RA who are receiving anti-TNF-alpha agents, methotrexate and humanized monoclonal anti-IL6 (interleukin-6) receptor antibody, advanced age or pre-existing RA lung involvement have been associated with a higher incidence of PJP [5,12]. However, our patient was treatment naïve when she was diagnosed with PJP. It has been suggested that the immunomodulatory effect of RA itself can contribute to increased risk of infection, and we hypothesize that this may have been the plausible causal mechanism of increased susceptibility to *P. jiroveci* in our patient [13]. Based on our review of the literature, our study represents the first case report of PJP in a treatment naïve RA patient.

The treatment of *P. jiroveci* is well elucidated in literature. Trimethoprim-sulfamethoxazole and pentamidine are the most commonly used medications for the treatment of PJP [14], with the former regarded as the first-line treatment. However, depending on the severity of the disease and underlying conditions, second-line agents such as atovaquone may be initiated [14]. We opted to use atovaquone in our patient because of hyperkalemia with an excellent response.

In HIV-positive patients, steroids have been well established as a useful adjunct therapy, especially in those with significant hypoxemia (arterial oxygen partial pressure < 70 mmHg or alveolar-arterial gradient > 35 mmHg), but its benefits have not been proven by current literature for HIV-negative immunocompromised patients [15]. Corticosteroid treatment has been shown to avert early and reversible worsening of respiratory conditions and become commonly used as an adjunct therapy in non-HIV patients [15].

Conclusion

PJP is a life-threatening infection with a high mortality rate in immunosuppressed patients, however it is emerging as a concern in individuals with rheumatoid arthritis. Unlike previous reports of PJP in RA patients, we report a case in which the patient was not on treatment for RA. RA patients can be immunosuppressed without being on treatment, and thus, PJP should also be considered in these patients.

Ethical statement

Our study did not require an ethical board approval; however, this study was performed in accordance to the ethical standards of the institution.

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Declaration of Competing Interest

We have no known conflicts of interest to declare.

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