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Case Report

Pneumocystis jirovecii pneumonia in rheumatologic disease: A case report indicating possible need of prophylaxis

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Abstract

An 81-year-old female with Granulomatosis and polyangiitis on immunosuppression with methotrexate, steroids, and Rituximab but not on prophylaxis, developed findings of *Pneumocystis jirovecii* pneumonia (PJP). She was treated with an alternative regimen, clindamycin and primaquine along with caspofungin and corticosteroids. Secondary prophylaxis with cotrimoxazole was initiated after completion of treatment. This case highlights the importance of early diagnosis, treatment difficulties, and the need for prophylaxis for HIV-negative patients on immunosuppressive treatment.

Introduction

Pneumocystis jirovecii Pneumonia (PJP) is a life-threatening opportunistic fungal infection. It occurs mainly in immunocompromised hosts, such as HIV-positive patients, and patients on corticosteroids, chemotherapy, and other immunosuppressive therapy. We report a case of PJP in a patient with Granulomatosis with Polyangiitis (GPA) on immunosuppressive treatment and highlight the need for prophylaxis for PJP.

Case history

An 81 year old female presented to Jupiter Hospital on 5/10/2023 with fever, cough, and shortness of breath for 2 weeks. She was a known case of GPA on treatment with methotrexate initially 25 mg per week which was modified to 10 mg per week 6 months prior and prednisolone 5 mg per day. She had also received Rituximab 2 doses in 2021 and was not on prophylaxis with cotrimoxazole.

On presentation, the patient had respiratory distress, tachypnea, and hypoxia (PO2 -36 mmHg), which required ICU admission and non-invasive ventilation. Hemoglobin was 8.4 gm/dl, WBC 2870/µL, serum LDH 357 and BDG was elevated at 360pg/ml. Anemia and leukopenia were probably due to long-term methotrexate use. The patient's HIV status was negative.

Chest x-ray showed bilateral infiltrates which had increased compared to radiographs 2 weeks earlier. High-resolution Computed Tomography (CT) thorax revealed ground glass opacities and fibrotic changes (Image 1). The latter could be

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due to treated GPA. Although classical CT findings of PJP such as extensive ground glass opacities with peripheral and basal sparing were absent, there was high suspicion considering the clinical presentation and the immunosuppressed status. Bronchoscopy and BAL fluid GMS stain showed a 'crushed ping pong ball' appearance of *Pneumocystis jirovecii* (Image 2) and BAL PJP PCR was positive (C_T value 25). The patient-matched host factors, clinical, radiological, and microbiological criteria for PJP as per revised EORTC/MSGERC criteria.

In view of neutropenia trimethoprim-sulfamethoxazole (TMP SMX) was avoided for treatment and the patient was started on an alternative regimen of oral clindamycin 600mg thrice daily plus oral primaquine 15mg twice daily along with IV Caspofungin 70mg once daily. Initially, high-dose IV methylprednisolone (500mg/day) was used and tapered in due course. The patient responded well to treatment and the oxygen requirement was reduced to 2 litres/min over a period of 1 week. Treatment was continued for 21 days but low-dose steroids were required to be continued for her primary disease. After the improvement of neutropenia and completion of treatment, secondary prophylaxis with TMP SMX was started.

Discussion

The incidence of PJP is rising in non-HIV patients due to chemotherapy for malignancy, organ transplantation, and immunosuppressive therapy. In the non-HIV population disease tends to be more acute with rapid progression to respiratory failure. Also due lack of suspicion for PJP in these patients, diagnosis is often delayed which leads to increased mortality [1,2].

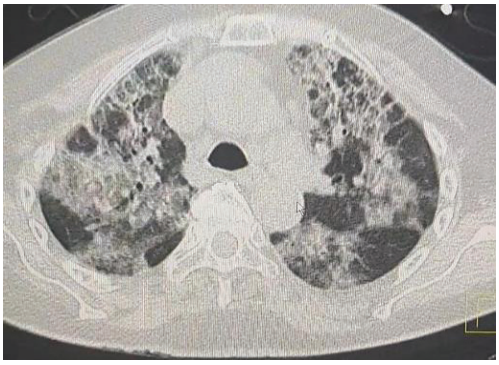

Image 1: HRCT thorax showing ground glass opacities with fibrotic changes.

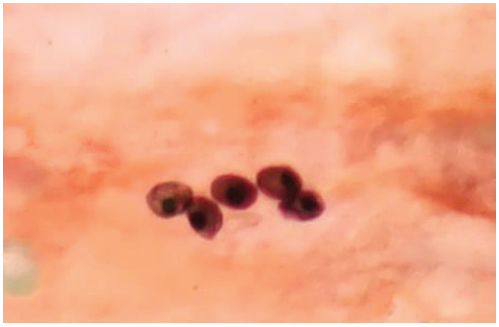

Image 2: GMS stain showing the 'crushed ping pong ball' appearance of *Pneumocystis jirovecii*.

Risk factors for the development of PJP in non-HIV patients include T cell-mediated immunity defects, primary immunodeficiencies, hematological malignancies, hematopoietic stem cell transplant, solid organ transplants and drugs including corticosteroids, purine analogs, tumor necrosis factor α-inhibitors, temozolomide, alemtuzumab, fludarabine, cladrbine, mycophenolate mofetil, azathioprine, methotrexate and cyclophosphamide [3,4].

Rituximab is a monoclonal antibody against CD20 B-cells and is not commonly considered a major risk factor for PJP. However, there are many cases of PJP reported after treatment with Rituximab [5,6].

Patients on prednisolone > 20 mg/day for more than 2–3 weeks have a significant risk of PCP, the presence of other immunosuppressive drugs such as cytotoxic agent increases it further and prophylaxis with TMP SMX dosed as one double-strength tablet or one single-strength tablet given once per day, or one double-strength tablet taken three times per week should be considered [7-9].

Clinical differentiation between worsening GPA vs. PJP was challenging. As there was rapid progression of symptoms and immunosuppression with methotrexate was not reduced, progression of GPA as a cause of current illness was less likely as compared to PJP.

Although PJP PCR has high sensitivity, it is difficult to differentiate between colonisation and disease. C_T value of 25, as in this case is indicative of disease in the non-HIV patient [10].

Neutropenia was a relative contraindication for TMP SMX, which is the drug of choice for PJP hence alternative treatment was used.

While the folate synthesis pathway is targeted by TMP SMX, additional echinocandin may be useful because it has a different target of action, namely glucan synthase of fungal cell wall. It also has good tolerability and low drug-to-drug interactions [11-13].

Drugs for prophylaxis of PJP include TMP/SMX, Dapsone, pentamidine, and Atovaquone [14]. However, unlike the HIV population, there is a lack of established guidelines for prophylaxis in non-HIV immunocompromised patients. Further research on the risk factors, exact incidence, and efficacy of prophylaxis is needed to establish guidance. The duration of this prophylaxis also needs to be defined as prolonged immunosuppression may persist even after discontinuation of these drugs.

In summary, with the increased usage of immunosuppressive and immunomodulating drugs in rheumatologic diseases, the risk of PJP increases, and offering prophylaxis to these patients may be lifesaving. It is necessary to differentiate between primary disease progression and the development of new opportunistic infections in these patients. PJP remains a diagnostic challenge, and there may need for invasive methods, biomarkers, and appropriate interpretation molecular assays

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to diagnose this disease [15]. Choice of alternative treatment should be decided considering toxicities, drug interaction, and possible use of combination therapy.

Conclusion

The number of drugs and conditions associated with risk for PJP is constantly expanding. The selection of treatment, dose, duration, combination, and use of steroids, all need further standardization. Prophylaxis with appropriate drugs and duration can help in preventing this dreaded complication.

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Ethical consideration

Jupiter Hospital's institutional ethical Committee approval was taken.

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