CASE REPORT

Case of *Pneumocystis jirovecii* pneumonia in a non-AIDS patient

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ABSTRACT

Pneumocystis jirovecii is widely known as an important cause of pneumonia in immunocompromised hosts. It remains a leading cause of opportunistic infection, morbidity and mortality in these patients. Here, a case of severe *P. jirovecii* pneumonia in a post-renal transplant patient is described. Giemsa and Gomori methenamine silver stain of sputum showed cysts of *P. jirovecii*. Despite treatment with Trimethoprim- Sulfamethoxazole, the patient developed severe respiratory failure and expired.

Key words: Bronchopneumonia, *Pneumocystis jirovecii*, renal transplant

INTRODUCTION

Pneumocystis jirovecii pneumonia is an opportunistic infection that occurs in immunocompromised individuals. It is a potentially life-threatening infection that occurs primarily not only in HIV patients with CD4 counts below 200 but also in non-HIV patients with immunosuppression. The common underlying factor is deficiency of cellular immunity. Non-HIV patients at risk are those with cancer, particularly haematologic malignancies, patients receiving glucocorticoids, chemotherapeutic agents and other immunosuppressive medications, haematopoietic stem cell and solid organ transplant recipients, patients with primary immunodeficiencies and severe malnutrition.

CASE REPORT

A 43-year-old female, who was a post-renal transplant patient, developed chronic transplant rejection. Renal transplantation was done for systemic lupus erythematosus (SLE)-related chronic kidney disease on October 2010. She presented with graft rejection reaction in July 2012 and was treated with steroids and immunosuppressants.

She was admitted in the nephrology Intensive Care Unit (ICU) with complaints of progressive breathlessness for one week, associated with mild fever and cough. There was no haemoptysis or pleuritic chest pain.

On examination, respiratory rate was 40/min, pulse rate 102/min and blood pressure 120/80 mmHg. Cushingoid facies was present. There was no pallor, cyanosis, clubbing, jaundice, palpable lymph node enlargement or pedal oedema. Chest examination revealed wheeze, rhonchi and crepitations on both sides. Other systems were normal.

A provisional diagnosis of infection-induced asthma with acute exacerbation or a probable lower respiratory tract infection in the form of bronchopneumonia was made. On the day of admission, empirical Amoxicillin-Clavulanic acid 1.2 g intravenous (IV) twice daily, Meropenem 500 mg IV twice daily and Cotrimoxazole DS two tablet thrice daily were started. As the patient failed to respond, two days later, Oseltamivir 75 mg once daily and Valganciclovir 450 mg twice daily were added to the regimen. On day four, Fluconazole 100 mg IV once daily was added as the sputum culture showed predominant growth of Candida species. On day five, Azithromycin 500 mg IV once daily

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was added as the patient continued to have tachypnoea. In view of progressive worsening of respiratory condition and poor saturation, the patient required mechanical ventilation on the sixth day of hospitalisation. Chest X-ray showed bilateral interstitial infiltrates. Fluconazole was changed to tablet Voriconazole 200 mg once daily. The next day, a repeat sputum sample was received in the microbiology laboratory and was stained with Gram-stain, Giemsa stain and Gomori methenamine silver (GMS) stain. Gram-stain showed moderate inflammatory cells and normal upper respiratory tract flora. Giemsa stain showed the presence of cysts, approximately 5–8 micron in diameter and containing up to eight daughter forms (spores or endospores, formerly known as intracystic bodies or sporozoites) [Figure 1]. GMS stain also showed cysts that appear dense, homogeneously black and demonstrating the presence of a small, dot-like thickening in the cyst wall [Figure 2]. The presence of *P. jirovecii* was confirmed by typical morphological features under microscope. Based on this report, antibiotics were modified by adding Clindamycin 600 mg IV twice daily and tablet Primaquine 30 mg once daily. Cytomegalovirus DNA polymerase chain reaction (PCR) and HIV ELISA was negative. On the same day, she developed hypotension requiring inotropic support and later succumbed to cardiac arrest.

DISCUSSION

Pneumocystis describes a genus of closely related unicellular fungi of low virulence found in the lungs of humans and a variety of mammals. Pneumocystis infection is usually, but not exclusively, confined to the lungs presenting as interstitial pneumonia. Fever, non-productive cough and exertional dyspnoea are the typical features.[1] Chest X-ray typically shows bilateral interstitial pattern. The spread of *P. jirovecii* beyond the lungs occurs mainly in patients with advanced HIV infection who are taking no prophylaxis or only aerosolised Pentamidine. The main sites of involvement are lymph nodes, spleen, liver, bone marrow, gastrointestinal tract, eyes, thyroid, adrenal glands and kidneys.

Our patient with a background history of SLE and renal transplantation on immunosuppressants (Tacrolimus and Prednisolone) presented with fever, breathlessness and cough for about a week and got admitted to ICU. Initially, the patient was empirically treated with IV Meropenem, Amoxicillin-Clavulanic acid and Cotrimoxazole. On the seventh day of admission, sputum was reported positive for *P. jirovecii* and antibiotics were modified to IV Clindamycin and Primaquine. Later, the patient succumbed to her illness due to progressive worsening of cardiorespiratory functions on the ninth day of admission.

Diagnosis of Pneumocystis pneumonia (PCP) can be difficult because it cannot be cultured. Sputum induction is the current standard screening tool for Pneumocystis. If induced sputum is negative and index of suspicion is high, bronchoscopy with bronchoalveolar lavage is the diagnostic method of choice and is the gold standard technique.[2] The organism is detected by different staining procedures such as GMS, toluidine blue O, cresyl violet, Gram-Weigert, Wright-Giemsa or its variant, e.g., Diff-Quik and Papanicolaou stains. PCR-based assays increase diagnostic sensitivity in an induced sputum specimen with smaller number of *P. jirovecii*.[3]

In the present case, sputum sample was collected by standard technique and stained with Giemsa stain and GMS stain to demonstrate the presence of *P. jirovecii*.

Trimethoprim-Sulfamethoxazole (TMP-SMX) is the drug of choice for all forms of pneumocystosis. It is administered

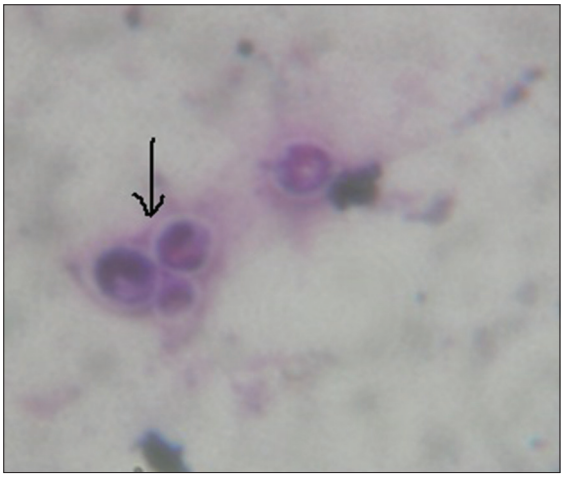

Figure 1: Giemsa stain showing cysts of *Pneumocystis jirovecii*

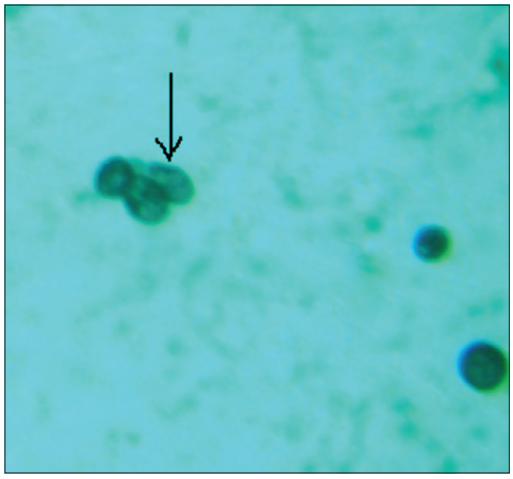

Figure 2: Gomori-methenamine silver stain showing cysts of *Pneumocystis jirovecii*

orally or IV in a dosage of 15–20 mg/kg/day (TMP) and 75–100 mg/kg/day (SMX) in three or four divided doses. Treatment should be continued for 21 days in patients with HIV infection and 14 days in others. Alternative regimens for the treatment of mild to moderate PCP include TMP administered at a dose of 15–20 mg/kg/day orally combined with Dapsone 100 mg/day for 21 days. Other drugs that have been used are Pentamidine isethionate, Trimetrexate, Atovaquone, Clindamycin and Primaquine.[4] Combination of Clindamycin and Primaquine is the preferred alternative regimen to TMP-SMX for moderate to severe PCP.[4,5] Non-HIV patients usually show a clinical response by four days of treatment; if there is no response by four to eight days, it is wise to consider switching to another drug. Clindamycin and Primaquine are the preferred drugs for those patients who fail TMP-SMX. Systemic corticosteroids should be administered within the first 72 h of starting treatment if partial pressure of oxygen in arterial blood is <70 mmHg or alveolar–arterial oxygen gradient is more than 35 mmHg.[5,6]

Recommended drug regimens for HIV patients who cannot tolerate TMP-SMX include for moderate to severe PCP: Pentamidine or Primaquine + Clindamycin and for mild to moderate PCP: Dapsone + TMP or Primaquine + Clindamycin or Atovaquone.[7]

Our patient succumbed despite initiation of Cotrimoxazole empirically on the day of admission. Clindamycin and Primaquine were added after confirmation of the diagnosis on the seventh day of admission. Hence, we recommend empirical parenteral treatment of anti-*P. jirovecii* treatment in suspected cases.

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Conflicts of interest

There are no conflicts of interest.

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