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Case Report

Pneumocystis carinii pneumonia at thirty-eight months after kidney transplantation

Zachariah P. Polachirackal [a], Vavullipathy N. Unni [b,*], Kadevalappil N. Indu [c], George Kurian [d], Rajesh R. Nair [d], Anil Mathew [e]

[a] Resident, Department of Nephrology, Amrita School of Medicine, Kochi, Kerala 682041, India
[b] Professor and Head, Department of Nephrology, Amrita School of Medicine, Kochi, Kerala 682041, India
[c] Physician Assistant, Department of Nephrology, Amrita School of Medicine, Kochi, Kerala 682041, India
[d] Professor, Department of Nephrology, Amrita School of Medicine, Kochi, Kerala 682041, India
[e] Associate Professor, Department of Nephrology, Amrita School of Medicine, Kochi, Kerala 682041, India

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ABSTRACT

Pneumocystis carinii pneumonia is an infection observed in immunocompromised patients. The risk of infection depends on the intensity and duration of immunosuppression and underlying immune deficits. Prophylaxis with trimethoprim-sulfamethoxazole prevents opportunistic infections due to *Pneumocystis carinii*, *Toxoplasma gondii*; in addition to preventing community acquired respiratory, gastrointestinal, and urinary tract infections. The usual presentation of *P. carinii* is during the first three to six months after transplantation at the peak of immunosuppressive therapy. We describe a case of Pneumocystis jirovecii pneumonia in a renal transplant recipient 38 months after renal transplantation.

1. Introduction

The organism *Pneumocystis jirovecii* (formerly carinii) is a ubiquitous fungal pathogen worldwide, identified by Carlos Chagas in 1912. Pneumocystis jirovecii pneumonia (PjP) is a potentially life threatening complication in immunocompromised renal transplant recipients (RTR), commonly manifesting as a severe lower respiratory tract infection. If untreated, the mortality is 90–100% in immunocompromised HIV negative patients, which declines to 35% with treatment.[1] Individual risk factors for susceptibility to PjP remains incompletely understood. Recipients of bone marrow and solid organ transplantation remain at risk for PjP in the first year following transplantation and during treatment for transplant rejection, both periods associated with intensive immunosuppression; in the absence of prophylaxis 6–20% of these patients may develop PjP.[2]

The most abundant surface antigen of *P. jirovecii* is the major surface glycoprotein. Variation of the expressed major surface glycoprotein facilitates the evasion of host immune responses. The course of the disease is extremely rapid and overwhelming; and recovery depends on early diagnosis and prompt treatment. Mortality in RTR is high (27–50%) despite aggressive treatment.[3] Routine PjP chemoprophylaxis with

* *Corresponding author.*
E-mail addresses: unnivn@asianetindia.com, unnivn1@gmail.com (V.N. Unni).
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Trimethoprim-Sulfamethoxazole (TMP-SMX) is advocated in the first 6 months after kidney transplant.[4]

Cumulative incidence of PjP was 0.4%, with median time to development of the infection after transplant being 0.80 ± 0.95 years according to the United States Renal Data System.[4] We report the case of a renal transplant recipient who was diagnosed to have PjP 38 months after transplant surgery when she was on minimal immunosuppression and normal graft function. This case raises the question whether PjP prophylaxis needs to be continued in renal transplant recipients.

2. Case report

A 27-year-old female with Alport's Syndrome, underwent a haplomatched live related donor renal transplantation in March 2010 with her mother as the donor. She was on triple immunosuppressive medications (Tacrolimus, Mycophenolate mofetil, Prednisolone). Her post-transplant period remained uneventful and at discharge her creatinine was 1.4 mg/dl. Two months post transplantation, she developed graft dysfunction and graft biopsy was suggestive of CNI toxicity, hence Tacrolimus was stopped and she was started on Sirolimus. She received TMP-SMX during the initial 6 months after transplantation. Sirolimus was discontinued at 1 year after transplantation. At 36 months she had normal graft function and was on Mycophenolate mofetil 750 mg twice daily and oral prednisolone 5 mg/day. She did not have any episodes of acute rejection or any infections after transplantation.

She presented at 3 years and 2 months post transplant with complaints of exertional breathlessness, dry cough and intermittent fever of one-week duration. On clinical examination she was tachypneic, heart rate 150 per minute, temperature 103° F, blood pressure 90/60 mm Hg and bilateral basal crepitations were heard. Investigations showed hemoglobulin – 7.1 g/dl, WBC – 4580/cu.mm, platelets 70,100/cu.mm, normal serum creatinine and liver functions on admission. Serum lactate dehydrogenase was found to be high (500 IU/ml). X-ray chest showed bilateral reticular shadows predominately in the lower zones (Fig. 1). She was started on parenteral Levofloxacin and Piperacillin/Tazobactam. Clinical response remained unsatisfactory with radiological worsening over 48 h. She was shifted to the intensive care unit and a bronchoscopy examination was done. Histopathological analysis of the bronchoalveolar lavage showed macrophages loaded with tiny refractile structures giving rise to vacuolated appearance, which was suggestive of *P. jirovecii* (Fig. 2a). Transbronchial biopsy revealed lung tissue with dilated alveoli, filled with fluffy eosinophilic granular material; the alveoli show focal type II pneumocyte hyperplasia (Fig. 2b).

She was started on TMP-SMX (15 mg/kg/day). However she deteriorated rapidly, requiring ventilatory, inotropic and hemodialysis supports. Despite our best efforts she succumbed to her illness due to multi organ dysfunction within 10 days.

3. Discussion

Pneumocystis jirovecii pneumonia can be a life threatening complication in patients with impaired immunity. The primary mode of transmission of *P. jirovecii* is uncertain. Interhuman *P. jirovecii* transmission is likely to be mediated by airborne droplets. *P. jirovecii* colonizes the respiratory tract in 10–20% healthy adults, 65% in postmortem lungs, and 31–68% of HIV infected people; frequency of colonization in RTRs remains unknown.[5] Molecular genotyping studies of nosocomial clusters have recently suggested interhuman transmission among immunocompromised renal transplant patients. Studies suggest PjP is the result of the emergence of latent infection during immunosuppression. This carrier state can be eradicated with TMP-SMX in animal models but not in the case of humans.[6]

PjP has an insidious onset, about 7% remain asymptomatic; others present with fever, non productive cough, progressive dyspnea and progressive respiratory failure, with or without constitutional symptoms of fatigue, chills, chest pain, and weight loss. Extrapulmonary manifestations include hepatosplenomegaly, skin lesions and pleural effusion. Blood investigations are mostly inconclusive; an increase in serum LDH activity is generally taken to support the presumptive diagnosis of PjP (the source of LDH being lung parenchyma); this is mostly recognized in the setting of AIDS and is a poor prognostic factor In our patient serum LDH was elevated.

X-ray chest shows diffuse, interstitial or alveolar infiltrates. High resolution computed tomography shows ground glass pattern predominantly in the perihilar and lower zones, reticular opacities, pneumatoceles, pleural effusions, consolidation, nodules which may cavitate and rarely lymphadenopathy may also be seen. Gallium 67 citrate scanning is highly sensitive and demonstrates intense diffuse bilateral uptake of the isotope. Diagnosis of PjP is confirmed by demonstration of the organism in the respiratory tract specimen. Bronchoalveolar lavage with or without transbronchial biopsy is the preferred diagnostic test. The organism exhibits three morphologic forms - cysts, sporozoites and trophozoites; these are easily identified with the help of toluidine blue O, Grocott's methenamine silver or Giemsa stains. At present the commonly employed method is the more sensitive direct

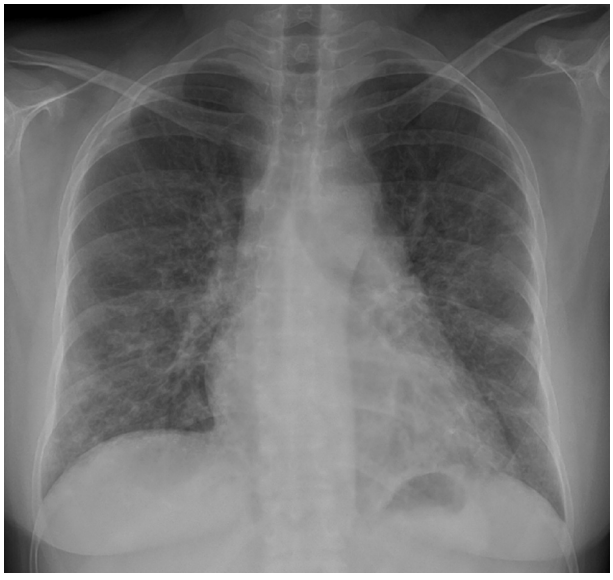

Fig. 1 – X-ray chest showing bilateral reticular infiltrates.