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# Superinfection by Pneumocystis Jirovecii and SARS-COV-2 in Non-HIV/AIDS Immunosuppressed Patient

*Case Report*

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## Abstract

Pneumonia by Pneumocystis jirovecii is a potentially life-threatening infection in immunosuppressed patients.

We present the case of a 38-year-old man who was readmitted with a febrile illness 3 weeks after discharge following hospitalization for severe bilateral SARS-CoV-2 pneumonia. His condition deteriorated until he was diagnosed with an infection by Pneumocystis jirovecii, which was treated successfully. SARS-CoV-2 and Pneumocystis jirovecii infections may have overlapping clinical and radiological findings. Hence, the objective of this case report is to highlight the importance of being alert to potential cases of superinfection by this microorganism in previously immunosuppressed patients with SARS-CoV- 2 pneumonia whose condition deteriorates despite appropriate treatment.

**Keywords:** Pneumocystis jirovecii; SARS-CoV-2; superinfection; Immunosuppression; lymphopenia; Bronchoalveolar lavage

## Introduction

Pneumonia due to Pneumocystis jirovecii is a potentially life-threatening infection in immunosuppressed patients [1]. Numerous animal and human studies suggest that this microorganism is transmitted through the airways, non-immunocompromised patients being asymptomatic hosts and a reservoir for transmission to immunosuppressed patients. Its diagnosis has been traditionally associated with patients carrying Human Immunodeficiency Virus (HIV) and those with a CD4 lymphocyte count below 500x103 cells/μL. Additionally, this type of infection has been described in other patients who are immunocompromised, either due to blood disorders or because they are on immunosuppressive therapy [2], among other causes. The microbiological diagnosis of this type of pneumonia requires good quality respiratory samples generally obtained through Broncho Alveolar Lavage (BAL) during bronchoscopy [2].

## Case Report

We present the case of a 38-year-old man who sought medical attention for fever and productive cough. He had a medical history of immunoglobulin A nephropathy for which he had received a kidney transplant, and hence, was on immunosuppressive therapy (prednisone 5mg/d and tacrolimus 2mg/d); nonetheless, at the time, the patient had returned to hemodialysis after graft failure. Twenty days earlier he had been discharged from our department following hospitalization for severe bilateral SARS-CoV-2 pneumonia with coinfection by Streptococcus pneumoniae. During his hospital stay, he had required High Flow Oxygen Therapy (HFOT) and dexamethasone at a dose of 20mg daily for 5 days, which was subsequently tapered to his usual dose of 5 mg of prednisone daily. He was readmitted due to new-onset fever of up to 38.8°C, mucoid sputum and dyspnea on exertion, with an oxygen saturation of 95% at rest on arrival. The chest X-ray showed the presence of bilateral interstitial infiltrates, and notably, lab tests found a C-Reactive Protein (CRP) value of 130mg/L and Lactate Dehydrogenase (LDH) level of 366U/L. Empirical broad spectrum antibiotic therapy (piperacillin- tazobactam) was initiated given the recent admission. Sputum and blood culture and a further PCR for SARS-CoV-2 were performed, all yielding negative results; additionally, a SARS-CoV-2 antibody test was carried out and this was positive for IgG antibodies.

A few days later, given the persistence of the fever, we decided to perform BAL and the PCR of the sample obtained revealed the presence of 996,000 copies of P jirovecii (real-time quantitative PCR; FTD-

PCR kit). The PCR tests for other viruses and cultures for other bacteria and fungi were all negative. After initiation of a specific treatment (trimethoprim-sulfamethoxazole), as well as methylprednisolone at a dose of 125mg daily for 3 days [3], the patient´s condition improved significantly clinically, radiologically and in terms of lab results, and he was discharged 7 days later. In follow-up after discharge, the patient´s condition continued to improve, the lung infiltrate having disappeared by the time of the radiological check-up (Figure). Further, a fortnight after discharge, the patient underwent pulmonary function tests, yielding the following results: Forced Vital Capacity (FVC) 4990 ml (91%), Forced Expiratory Volume at 1 sec (FEV1) 4160 ml (94%), and FEV1/FVC 83.4%. These tests were repeated at 4 months, showing further improvement: FVC 5990 ml (109%), FEV1 5000 ml (114%), and FEV1/FVC 83.3%, with a diffusing capacity for carbon monoxide (DLCO) of 92% (also within the normal range).

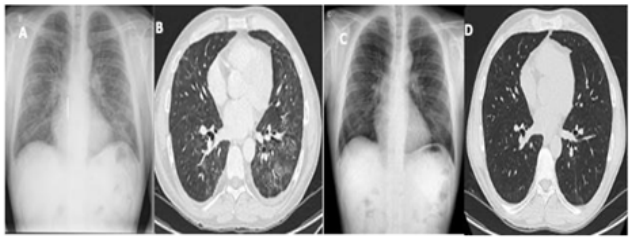


**Figure 1**:

A) Chest X-ray image of the Pneumocystis jirovecii infection.

B) Chest computed tomography image showing ground glass infiltrates attributable to Pneumocystis jirovecii.

C) Chest X-ray image obtained at 1 month after receiving treatment.

D) Chest computed tomography image at 6 months after the treatment.

## Discussion

Pneumocystis jirovecii is an intracellular fungus that may cause severe pneumonia in patients with underlying cellular immunosuppression. An absolute CD4 lymphocyte count of <500 x 103 cells/μL, has traditionally been associated with a 19-fold higher risk of developing this complication [4]. The role of this species as a cause of superinfection in the context of SARS-CoV-2 pneumonia remains unknown. To date, few cases of SARS-CoV-2 and P jirovecii coinfection or superinfection have been reported [5], and most have been in patients hospitalized in intensive care units [6-8] and/or infected by HIV [8-11], except in a few cases similar to ours [12,13], in patients with other causes of immunosuppression. Pneumonia by SARS-CoV-2 and Pneumocystis jirovecii often have similar clinical, lab and radiological characteristics, which may hinder the diagnosis of superinfection by this fungal species in some patients with severe SARS-CoV-2 infection and poor clinical course [12].

Lymphopenia is a common finding during SARS-CoV-2 infection. This finding has been associated with the development of more severe forms of the illness and has been observed to be a predictor of poor course in numerous studies [14]. The cause of this reduction in lymphocyte count during SARS-CoV-2 infection has not yet been clarified, though various hypotheses have been put forward:

1) A direct cytopathic effect of the virus on these cells, given that the angiotensin-converting enzyme 2 (ACE 2) is expressed in these cells.

2) A possible migration of lymphocytes to the lungs in response to the inflammation process itself.

In relation to this, a direct relationship has been described between interleukin-6 levels and the degree of lymphopenia. In the context of our patient, it would be reasonable to suppose that the lymphopenia associated with SARS-CoV-2 would be a mechanism that might increase the risk of a patient with underlying immunosuppression, developing infection by P jirovecii or other fungal species [15]. Our patient had a lymphocyte count of 470x103 cells/μL on first admission for SARS-CoV-2 pneumonia and 310x103 cells/μL when diagnosed with P. jirovecii, having been on high-dose corticosteroids between hospitalizations. The enzyme LDH is involved in energy production and is present in nearly all human cells. The finding of high serum LDH levels is indicative of tissue damage and is considered a reliable marker of inflammation or cell damage. Elevated levels of this enzyme may be observed in patients with pulmonary fibrosis, especially during exacerbations, and also in patients with Legionnaires' disease, viruses such as varicella and, classically, P. jirovecii pneumonia. Recently, this enzyme has been described as a predictor of severity in the context of a patient with SARS-CoV-2 pneumonia [16].

The main value of our clinical case lies in it underlining how potentially important it is to suspect and diagnose pulmonary superinfection in patients with underlying immunosuppression and SARS-CoV-2 pneumonia whose condition deteriorates. The performance of BAL providing good quality respiratory samples may enable us to reach an accurate bacteriological diagnosis, instigate appropriate antibiotic therapy and improve the prognosis of these patients.

## Conflicts of interest

On behalf of all the authors, the corresponding author declares that there are no conflicts of interest.

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