J Prima Med Sains (2023) 5(2):164-168
https://doi.org/10.34012/jpms.v5i2.4455

CASE REPORT

Diagnostic challenge of *Pneumocystis jirovecii* pneumonia infection mimicking interstitial lung disease in initially HIV negative patient

Anastasia Kristy[1]*, Ni Made Dwita Yaniswari[1]

Abstract

Background: *Pneumocystis jirovecii* pneumonia (PJP) infections are common in immunocompromised patients and are rarely found in immunocompetent patients. Lung radiology in PJP patients could mimic the appearance of interstitial lung disease (ILD) and could be used to diagnose HIV-negative patients. Clinicians should rule out false negatives in patients with patterns suggestive of opportunistic infections and risk factors for HIV infection.

Case illustration: A 34-year-old man presented with a chief complaint of shortness of breath, had history of 15 years of smoking, and daily chlorine exposure. The radiology pattern and initial HIV-negative test results suggested an ILD diagnosis. Owing to persistent symptoms despite initial management and the presence of risk factors, repeat HIV testing was initiated and was positive. The patient was treated with cotrimoxazole and showed rapid clinical improvement.

Discussion: The diagnosis of PJP in our patient was based on radiology and an HIV-positive status. In patients who are not immunocompromised, the diagnosis of PJP is unlikely, and other diagnoses, such as ILD, should be considered. However, in the HIV testing window period of infection, a poor advanced state of HIV could cause a false negative result. Therefore, clinical judgement is essential in suspecting such a result. The empirical treatment course of cotrimoxazole has been shown to provide better clinical outcomes in PJP.

Conclusion: The possibility of PJP must be considered in patients with initially HIV-negative results, especially in patients with risk factors and clinical symptoms suggestive of immunocompromise. While some ILD showed similar PJP, the risk factors for ILD and PCP could be distinguishing factors. Retesting for HIV infection can confirm the diagnosis and rule out false-negative results.

Keywords: *Pneumocystis jirovecii* pneumonia, interstitial lung disease, HIV

Introduction

Pneumocystis jirovecii pneumonia (PJP) is a typical opportunistic infection in immunocompromised individuals with clinical symptoms ranging from asymptomatic to interstitial pneumonia. In patients with HIV, screening and prevention of PJP infection are mandatory in those with low CD4 counts. In contrast, patients with clinical symptoms of lung infection and typical radiologic features of PJP should also be investigated for HIV infection and other immunocompromised histories. However, in immunocompetent patients, diagnosis of PJP is unlikely; thus, radiological features may suggest other diagnoses such as interstitial lung disease (ILD).

ILD is a group of more than 100 lung disorders that share similar clinical, radiographic, and pathologic features but are often difficult to diagnose. The cystic pattern of ILD shares similar radiological features with those of PJP infections. Therefore, radiologic findings from chest radiography and high-resolution

Affiliation
[1]Department of Pulmonology and Respiratory Medicine, Wangaya General Hospital

Correspondence
anastasia_kristy@hotmail.com

chest computed tomography can be used to diagnose both PJP and ILD, with evaluation of the risk for immunocompromised patients as important. We report the case of 34 years old man with PJP and HIV infection, who was initially diagnosed with ILD in a laboratory that was negative for HIV infection.

Case Illustration

A 34-year-old man presented to Wangaya General Hospital, Denpasar, with a complaint of difficulty in breathing for a few months and worsening in the last month, which worsened with activity and was not relieved with postural changes. The patient reported recurrent episodes of nonproductive cough, subfebrile cough, and lightheadedness. History of smoking cigarettes of one pack per day for 15 years. The patient denied a history of tuberculosis exposure. The patient worked as an engineer with daily exposure to chlorine and has been working for 15 years.

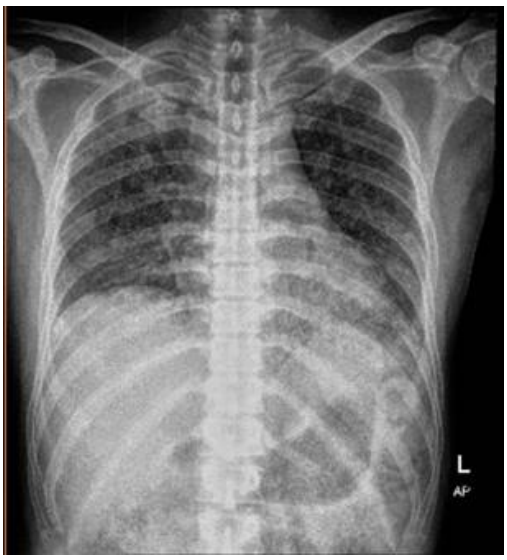

Figure 1. Chest X Ray showed signs of pneumonia

On presentation, the patient appeared moderately ill, with a slight increase in respiratory rate (26 times/min), and peripheral saturation was 88-91% with otherwise normal vital signs. Chest examination revealed rhonchi and wheezing on both sides of the lower lung. The notable laboratory findings were decreased hemoglobin level of hemoglobin 6,0 g/dL and decreased lymphocytes count 0,33 x 10^3/µL). Result for blood gas analysis were: pH 7,48, Pco2 32, Po2 55, Hco3 24, ABE 0, SaO2 91 suggested a chronic respiratory alkalosis.

Chest X ray (Fig.1) suggested pneumonia and computed tomography (CT) scan (see Fig. 2) suggested interstitial lung disease with multiple lymphadenopathies at the left and right to the mediastinum. Spirometry suggested severe obstruction, a moderate degree of restriction, and small-airway disease. The patient tested negative for HIV and the sputum gene Xpert tested negative for tuberculosis.

The patient was diagnosed with interstitial lung disease and treated with inhaled ipratropium bromide, methylprednisolone injection, N-acetylcysteine, combined with pulmonary rehabilitation of deep breathing and pursed lip breathing, chest expansion exercise, and walking exercise. The patient was also administered PRC blood. The patient showed improvement in clinical symptoms, with resolution of shortness of breath. The patient was then managed as an outpatient with inhaled formoterol and low-dose methylprednisolone, and was discharged after 5 days with improvement in clinical signs and symptoms.

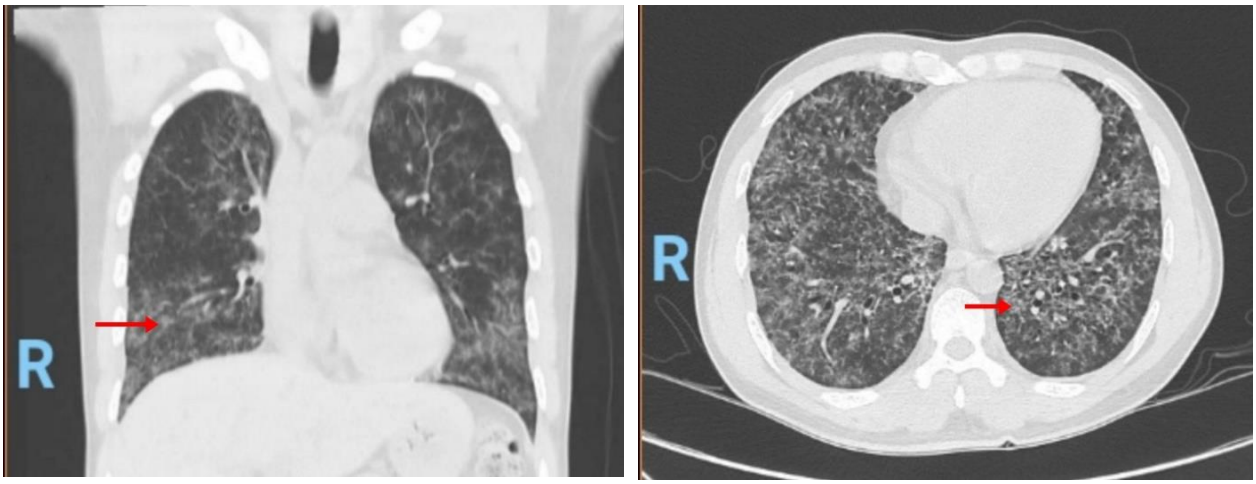

Figure 2. Thorax contrast computed tomography (CT) showed interstitial lung disease (arrow sign)

During the follow-up visit to the outpatient clinic, the patient again appeared to have difficulty breathing and worsened with activity. Due to the high suspicion of PJP infection, the patient was re-tested for HIV infection and returned positive for CD4 (15 cells/mm3). The patient was diagnosed with PJP and treated with cotrimoxazole and prednisone for 21 days. Later evaluation showed improvement in symptoms, and anti-retroviral therapy was planned.

Discussion

Pneumocystis pneumonia (PJP) is a fungal infection, previously termed Pneumocystis jirovecii pneumonia, named after a parasitologist called Otto Jirovec.[1] PJP was found in approximately 20-69% of patients with HIV infection and transmitted from human to human through airborne.[2] Once the cysts are inhaled and shattered, the trophozoite is emitted and adheres to the type I alveolar epithelium.[3] In immunocompetent hosts, the body's inflammatory response of cytokines, chemokines will eliminate the fungus and cause less injury to the lungs. However, in patients with low level of CD4+ T cells, due to poor immune system such as HIV hosts, this mechanism tends to cause more severe lung damage and could interfere with gas exchange.[1]

Clinical presentations of PJP are, at times, insignificant and could be mistaken for other diseases. The classic triad of shortness of breath, subfebrile fever, and dry cough is usually found in HIV-positive patients.[4] a definitive diagnosis of PJP involves recognition of the pathogen in respiratory tract samples with invasive techniques using bronchoscopy to obtain bronchoalveolar lavage fluid (BALF) or open lung tissue biopsy with a sensitivity of 90-99% and 95-100%, respectively.[1,4] The microorganism *P. jirovecii,* however, is difficult to isolate; therefore, several staining methods such as Giemsa or immunofluorescent assays can be used to identify this pathogen. Advancement of molecular techniques offers the option of a quantitative polymerase chain reaction (PCR) to detect *P. jirovecii* with 99% sensitivity and 92% specificity.[5] A less invasive sputum collection by hypertonic solution induction can be used, but with inferior sensitivity of 55-90%.[6] The radiology finding of chest X Ray often manifests as bilateral, diffuse infiltrates and develops as an interstitial alveolar butterfly pattern located to the lungs' apex or bases.[7] High resolution computed tomography (CT) shows a bilateral and ground-glass opacity appearance. These findings often appear along with one or multiple nodules and tissue cavities.[5] Risk factor and suspicion of immunodeficiency state, method for detecting microorganism and radiology findings could be used to guide the diagnosis of PJP.[4]

Interstitial lung diseases (ILD) have various clinical manifestations, management, and outcomes, with reported incidence of ILD in America and Europe ranging from 6.3 to 71 per 100,000 people and was found to be higher by 10.7- 47.3% in Asia, specifically in India.[8,9] ILD often manifests as shortness of breath on exertion, consistent cough, and chest pain. According to the American Thoracic Society (ATS), the classification of ILD can be differentiated by those with known causes such as chemical exposure, occupational exposure, or drug exposure and those without known causes such as idiopathic pulmonary fibrosis (IPF) and sarcoidosis.[8,10] Onset of the disease, radiographic findings, and histopathology patterns could also be the key to classifying the disease. ILD is commonly observed in certain age and sex groups. Those with unknown causes are more likely to appear in elderly and those with known causes like connective tissue related ILD, sarcoidosis is more likely to be diagnosed at a younger age.[10]

Several workups can be performed to support the diagnosis of ILD, including chest radiography, high-resolution computed tomography (HRCT), transbronchial biopsy via bronchoscopy, and surgical lung biopsy.[7] Radiology pattern in ILD could be grouped into peripheral reticular, nodular, ground glass, and cystic patterns. The cystic pattern in ILD is often grouped together with diffuse cystic lung disease (DCLD) and can be distinguished by etiology, pathogenesis, and mode of presentation. PJP is an infectious etiology that presents as a radiologic cystic pattern mimicking that in the ILD group. Radiological changes in PJP can be seen as cystic changes in the form of pneumatoceles. Therefore, in patients without a risk of immunocompromise, such as HIV infection, severe malnutrition, malignancy, or immunosuppressant therapy, the cystic pattern in radiology tends to suggest the possibility of ILD rather than PJP infection. A comprehensive risk factor assessment for immunocompromised patients should be noted by all physicians. False negatives should also be suspected in patients with risk factors but negative HIV test results. Repeat after 12 weeks should be considered in patients with risk factors for HIV infection who initially tested negative. False-negative HIV results are usually seen in the window period, within 12 weeks of HIV infection,

and are rarely encountered thereafter. Severe immunosuppression condition could be one of the factors causing false negative in advanced HIV.[11] The development of next generation HIV testing methods could further reduce the false negative risk.[12]

The clinical presentation of PJP in patients with HIV is characterized by the subacute onset of dyspnea, fever, and nonproductive cough. Even though not as often, immunocompetent patients could also contract PJP, but with a more acute presentation. The identification of microorganisms by staining remains the definitive diagnosis of PJP.[10]

The treatment of PJP must be started immediately without waiting for the diagnostic result in patients at risk of developing PJP and in those with suspicious manifestations of PJP.[6,10] The drug of choice for PJP is *Trimethoprim/Sulfamethoxazole* (TMP/SMX), and the duration of treatment is 21 days with a dosage of TMP 15–20 mg/kg/day and SMX 75–100 mg/kg/day, which can be administered orally divided in 3-4 doses per day. The intravenous route may be an option for patients who cannot tolerate oral therapy. Steroids are recommended as a combination therapy for the treatment course and must be started as soon as possible within 72 hours. The prednisone dose was 40 mg orally twice a day from days 1 to 5, 40 mg orally once a day from days 6 to 10, and 20 mg orally once a day from days 11 to 21. Patients with HIV infection can start antiretroviral therapy (ART) two weeks prior to PJP treatment. Books PJP prophylaxis can be administered to certain populations, especially those with poor immunity, such as HIV patients with CD4+ count <200 cells/µL or <14% or if oral candidiasis appears, people with malignancy, and those who take immunosuppressant medications with a dose of more than 20 mg/day for 1 month or longer. The first line medication for prophylaxis treatment is TMP/SMX with recommended dose of double dose one tablet once a day orally or one single tablet once a day orally.[13]

Conclusion

We report the case of a male 34 years old diagnosed with PJP and HIV-positive infection. As PJP is an opportunistic infection, prompt diagnosis should be made in patients with immunocompromised and suggestive chest radiology findings. However, the diagnosis of PJP with no known history suggestive of immunocompromise could be challenging, as it may be mistaken for other interstitial lung diseases (ILD). The cystic pattern in ILD may share the same radiological pattern as the PJP. Differentiating both these conditions from radiology findings is difficult, and clinical judgement and good history taking for risk factors are essential in confirming the immunity status of a patient for better management of the disease.

References

1. Avino LJ, Naylor SM, Roecker AM. Pneumocystis jirovecii Pneumonia in the Non–HIV-Infected Population. Ann Pharmacother. 2016;50(8):673–9.
2. Dellière S, Gits-Muselli M, Bretagne S, Alanio A. Outbreak-Causing Fungi: Pneumocystis jirovecii. Mycopathologia. 2019;185(5):783–800.
3. Bateman M, Oladele R, Kolls JK. Diagnosing Pneumocystis jirovecii pneumonia: A review of current methods and novel approaches. Med Mycol. 2020;58(8):1015–28.
4. Weyant RB, Kabbani D, Doucette K, Lau C, Cervera C. Pneumocystis jirovecii: a review with a focus on prevention and treatment. Expert Opin Pharmacother. 2021;22(12):1579–92.
5. Cooley L, Dendle C, Wolf J, Teh BW, Chen SC, Boutlis C, et al. Consensus guidelines for diagnosis, prophylaxis and management of Pneumocystis jirovecii pneumonia in patients with haematological and solid malignancies, 2014. Intern Med J. 2014;44(12b):1350–63.
6. Salzer HJF, Schäfer G, Hoenigl M, Günther G, Hoffmann C, Kalsdorf B, et al. Clinical, Diagnostic, and Treatment Disparities between HIV-Infected and Non-HIV-Infected Immunocompromised Patients with Pneumocystis jirovecii Pneumonia. Respiration. 2018;96(1):52–65.
7. Fishman JA, Gans H. Pneumocystis jiroveci in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019;33(9):e13587.
8. Mikolasch TA, Garthwaite HS, Porter JC. Update in diagnosis and management of interstitial lung disease. Clin Med (Northfield Il). 2017;17(2):146–53.
9. Kaul B, Cottin V, Collard HR, Valenzuela C. Variability in Global Prevalence of Interstitial Lung Disease. Front Med. 2021;8.
10. Mathur A, Antin-Ozerkis DE. Interstitial Lung Disease: A Clinical Overview and General Approach. In: Grippi MA, Antin-Ozerkis DE, Dela Cruz CS, Kotloff RM, Kotton CN, Pack AI, editors. Fishman's Pulmonary Diseases and Disorders, 6e [Internet]. New York: McGraw-Hill Education; 2023. Available from: http://accessmedicine.mhmedical.com/content.aspx?aid=1195005403
11. Chuwa F, Kivuma B, Ndege R. Repeated false-negative HIV rapid test results in a patient presenting to care with advanced HIV disease: A case report. IDCases. 2023;31:e01719.

12. Alexander TS. Human Immunodeficiency Virus Diagnostic Testing: 30 Years of Evolution. Pasetti MF, editor. Clin Vaccine Immunol. 2016;23(4):249–53.
13. Truong J, Ashurst J V. Pneumocystis jirovecii Pneumonia. Treasure Island (FL): StatPearls Publishing; 2022.