



Pneumocystis Pneumonia in COVID-19 Outbreak: A Case Report - It's not all about COVID-19

Julisman Hasiholan Situmorang¹, Ginanjar Arum Desianti²

¹Resident Medical Officer, MRCCC Siloam Hospital, Jakarta

²Departement of Pulmonology, MRCCC Siloam Hospital, Jakarta

Corresponding Author:

Julisman Hasiholan Situmorang | MRCCC
Siloam Hopital, Jakarta |
situmorangjulisman@gmail.com

Submitted: February 19th, 2021

Accepted: March 24th, 2021

Published: June 23th, 2021

Respir Sci. 2021; 1(3): 194-201

<https://doi.org/10.36497/respirsci.v1i3.17>

Abstract

One of the phenomena during the current COVID-19 pandemic is Early Detection of In-Patient Deterioration by public health services, especially general hospitals for early detection patients who admit respiratory tract infections (RTIs) symptoms. However, there is a risk of misdiagnosis in differential diagnoses. Pneumocystis Carinii Pneumonia (PCP) is an opportunistic infection that can occur in immunocompromised patients. Symptoms that often appear are similar to COVID-19, such as fever, cough, runny nose, dyspnoea, diarrhea, or others. It makes some difficulties to early diagnosing PCP infection during the COVID-19 pandemic, whereas if it is not early treated it is could be a fatal case. Thus, during the COVID-19 pandemic, it is necessary to consider other differential diagnoses in patients with RTIs symptoms or respiratory distress. It can be supported if other characteristic signs are found during clinical examination, especially if the nasopharyngeal and oropharyngeal swab results are negative.

Keywords: COVID-19, pneumocystis carinii pneumonia, HIV

INTRODUCTION

Cases of Severe Acute Respiratory Syndrome (SARS) Coronavirus 2 infection were first reported in Wuhan, Hubei Province, China in December 2019.¹ These cases of infection had spread to other regions in China. The spread of sporadic cases had led the World Health Organization (WHO) to declare a global pandemic and called this disease "coronavirus disease 2019" (COVID-19).²

COVID-19 causes signs and symptoms that vary in each case. The main

symptoms that most often appear are fever, dyspnoea, cough, painful swallowing, headache, and runny nose. These symptoms can be exaggerated if there is damage to lung tissue and other organs because the inflammation that occurs can be systemic. This severe condition can result from a widespread inflammatory pathological condition called "cytokine storm".³

Cytokine storm is a term that describes the maladaptive process of cytokine release in response to a viral infection or another stimulus.

Dysregulation of the immune response causes tissue damage that can occur in cases of COVID-19 infection.³

Pneumocystis Carinii Pneumonia (PCP) or what is now known as Pneumocystis jirovecii is an opportunistic infection in HIV patients. Most PCP cases are seen in HIV cases were not yet known to be or who have not received antiretroviral therapy (ARV).⁴

In PCP cases, lung damage is due to the accumulation of polymorphonuclear neutrophils (PMNs), not by the exposure of infection itself. This will cause surfactant dysfunction which interferes with alveolar development and can result in respiratory failure. The clinical manifestations are usually dyspnoea, cough, or fever. Pneumocystis jirovecii cannot be cultured, so the definitive diagnosis of PCP is by microscopic examination of induced sputum, bronchoalveolar lavage (BAL), or lung tissue.⁵

The PCP case is interesting to be discussed during the COVID-19 outbreak for its similar symptoms. As the COVID-19 pandemic continues to spread throughout the country, hospitals have focused on the early detection of patients who present with symptomatic respiratory tract infections. At the same time, there is a risk of misdiagnosis by another differential diagnosis. Therefore, as clinicians, it is necessary to understand that the signs and symptoms of RTIs are not only about COVID-19.

CASE ILLUSTRATION

A man, aged 50 years old, came with complaints of fever, dyspnoea and dry cough 2 weeks before entering the Emergency Room. Worsening dyspnoea happened by last week. When at home, oxygen saturation can drop to 80% without losing the ability to talk and still be able to do routine. The patient had a weight loss of approximately 3 kg within this month. The patient does not have a history of previous diseases such as heart disease, tuberculosis, hypertension, diabetes, asthma and others. The patient does not have a history of routine drug consumption.

Examination revealed tachypnea, tachycardia and decreased oxygen saturation (SpO₂ 80%) and white plaque on the oral mucosa. Oxygen saturation has improved after receiving oxygen therapy. On lung auscultation examination, rough wet rhonchi were found in both lung fields. Chest X-ray shows extensive airspaces consolidation in the right lung and more patchy airspaces opacities in the left lung, possible extensive pneumonia likely due to viral infection.

On non-contrast chest computed tomography (CT) was found extensive ground-glass opacities (GGOs) bilateral and crazy paving appearance. SARS Cov-2 RT-PCR results performed on the same day when the patient arrived and the next 24 hours were negative. Due to the suspicion of immunocompromise, the anti-HIV serum was checked with reactive results.

The working diagnosis for the patient is PCP and HIV. This is based on the symptoms experienced by the patient, including sub-acute fever, cough, and dyspnoea. The immunocompromised sign was demonstrated by the presence of oral candidiasis and significant weight loss. In the CT Thorax supporting examination, there was a crazy paving picture, several times the RT-PCR SARS CoV-2 negative results, HIV laboratory test positive result, and the patient experienced clinical symptoms improvement after receiving treatment. BAL examination could not be done because the patient refused it. In BAL examination, ideally, *P. jirovecii* will be found as the cause of PCP.

The patient received cotrimoxazole therapy for 21 days with a dose equivalent to Trimethoprim 15 mg/Kg, divided into 3-4 doses. The patient also received a corticosteroid, namely Methylprednisolone 62.5 mg intravenously twice a day from the first day the patient was diagnosed with HIV until the patient went home. The patient experienced an improvement in clinical condition and oxygenation, eight days post-treatment. On the 14th day, the patient was discharged and carried out further treatment through outpatient care.

DISCUSSION

During the COVID-19 pandemic around the world, patients who come to health facilities with symptoms of respiratory tract infections (RTI) will be considered to have COVID-19 infection until proven negative. This is to prevent

transmission. The initial screening and diagnostic tests are carried out to establish or rule out the diagnosis of COVID-19, such as laboratory, radiology (chest X-ray or non-contrast chest CT) and RT-PCR SARS Cov-2.⁶

COVID-19 can cause a variety of symptoms ranging from no symptoms to severe symptoms and life-threatening. These symptoms can include fever, cough, runny nose, anosmia, ageusia, dyspnoea, nausea, vomiting, diarrhea and other symptoms. The typical symptom that often appears in moderate to severe cases is "Happy Hypoxia". This symptom occurs when a patient with extremely low blood oxygenation, but no sensation of dyspnoea. When the brain receives the signal of internal hypoxia, it gives rise to a sensation of "air hunger", which is curiously absent in severe COVID-19 cases.

The patient showed respiratory symptoms such as fever, dyspnoea and cough which can lead to COVID-19 infection. The phenomenon of happy hypoxia was also shown by the patient. Symptoms were acute, namely 1-2 weeks before hospital admission and had no previous similar symptoms. During the last 2 days, the patient's oxygen saturation was always below 95%.

The results of radiological examinations, both chest X-ray and non-contrast chest CT also pointed to COVID-19 infection was shown through an infiltrate, ground-glass opacity (GGOs) and crazy paving appearance. On this basis, RT-PCR SARS Cov-2 tests have been held twice where the results were

negative/undetectable. This led to the need for other supporting examinations to confirm the differential diagnosis.

The discovery of white plaque on the oral mucosa led to the diagnosis of oral candidiasis, which is common in immunocompromised patients. This was also supported by the symptoms of significant weight loss within the last month. As a comparison, the symptoms of worsening dyspnoea in patients were gradual, but COVID-19 is generally progressive. Therefore, an anti-HIV serum test was performed and the results were reactive.

Symptoms and clinical signs in the patient also result of supporting examination that the diagnosis led to another RTIs (RTI) namely pneumocystis carinii pneumonia. PCP symptoms can appear in varying degrees, ranging from mild and can worsen within days to weeks. However, about 7% of patients are asymptomatic.⁴ The physical examination findings in PCP patients are nonspecific, such as tachypnea, tachycardia, use of the auxiliary muscles and rhonchi. The result of

CRP (C-Reactive Protein) which increased very high indicates the presence of severe inflammation in the patient's body. Thus, this patient is also given antibiotic therapy.

In addition, the radiological examination can help guide the diagnosis of PCP. The chest X-ray can indeed show a picture of pneumonia (Figure 1). However, this examination is not specific because one in three patients usually shows normal chest X-ray results. Another radiological examination, namely chest CT is a more accurate consideration for detecting PCP because of its high density and sensitivity. On chest CT examination, a ground-glass appearance (crazy paving) will be revealed, which shows the intra-alveolar accumulation of fibrin, debris and organisms (Figure 2 and 3).

In PCP patients without HIV infection, the image of ground-glass opacity will usually be found more often.⁶ In this case, the results of the radiological examination such as chest X-ray showed a wide infiltrate, also on chest CT there was a crazy paving image that could match the radiological image on PCP.⁵

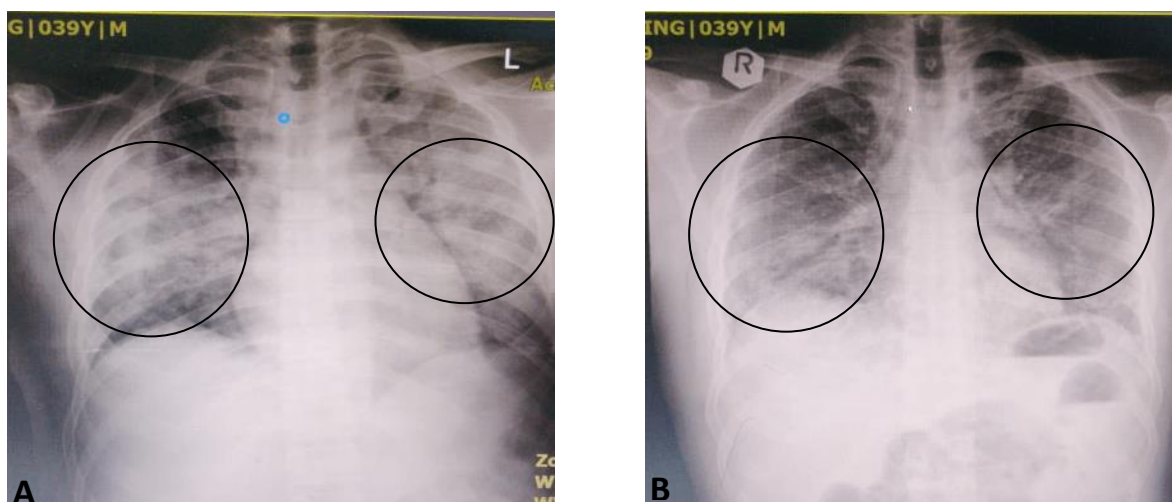


Figure 1. Chest X-ray on A) day 0 of treatment and B) day 14 of treatment



Figure 2. Chest CT scan of the patient's axial cut

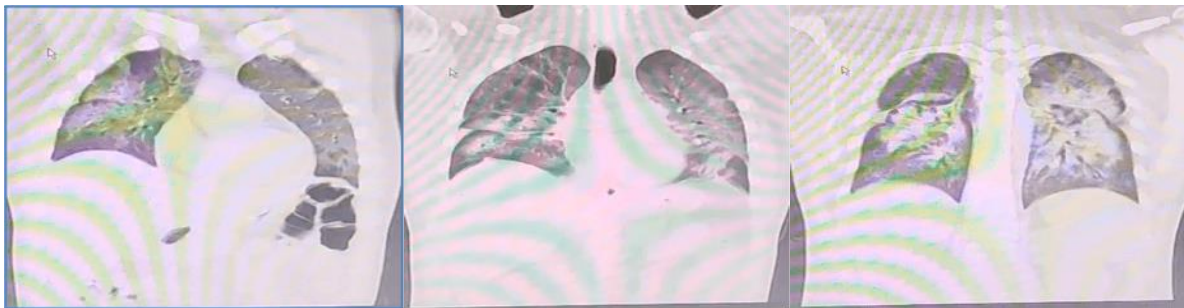


Figure 3. Chest CT scan of the patient's coronal cut

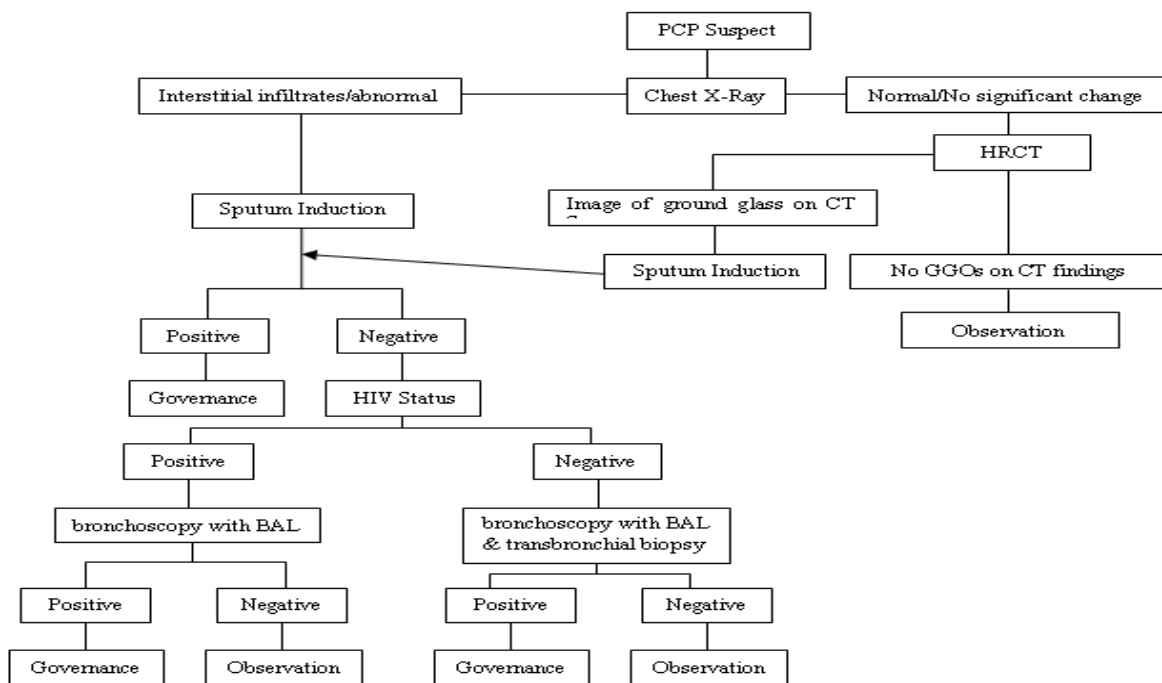


Figure 4. Algorithm of PCP Diagnosis⁴

Table 1. Stratification of disease severity in PCP⁵

	Mild	Moderate	Severe
Signs and symptoms	Dyspnoea on exertion with or without cough and sweats	Dyspnoea on minimal exertion and occasionally at rest; cough and fever with or without sweats	Dyspnoea and tachypnoea at rest; fever and cough
PaO ₂ room air	>83%	61-83%	<60%
SpO ₂ room air	>96%	91-96%	<91%
Chest X-ray	Normal or minor perihilar shadowing	Diffuse interstitial shadowing	Extensive interstitial shadowing with or without diffuse alveolar shadowing

The definitive diagnosis of PCP is by finding organisms on the histopathology of sputum that are induced or BAL (Figure 4).⁵

In this patient, sputum induction was performed to examine the PCP organism and also AFB (Acid-fast bacillus). Inevitably, TB infection (Tuberculosis) is also an opportunistic infection in a patient with HIV, but in this one there was no sputum specimen obtained, so no microbiological examination was carried out. Histopathological data from BAL also could not be obtained because the patient refused the procedure with several considerations.

Considering the severe symptoms that lead to PCP and if the therapy is fatal, this patient is still given PCP therapy and other comorbid diseases. Oral or intravenous trimethoprim-sulfamethoxazole (TMP-SMX) for 21 days is the treatment option for PCP with or without HIV. For mild PCP ($\text{PaO}_2 \geq 70$ mmHg room water), TMP-SMX was administered orally, while moderate-severe degrees ($\text{PaO}_2 \leq 70$ mmHg room water) were given intravenously. The recommended dosage for PCP therapy is 15-20 mg/kg TMP per day and 75-100 mg/kg SMX per day, divided into 3-4 doses (Table 1).

Patients with a $\text{PaO}_2 < 70$ mmHg or $\text{SpO}_2 < 92\%$, need to get prednisone 40mg twice a day on days 1-5, then 40 mg once a day on days 6-10, followed by 20 mg once a day on days 11-21. If the patient can allow for oral therapy then methylprednisolone 75% of the dose is given. The effects of corticosteroids have

only been reported when administered 0-72 hours after PCP-specific therapy was started (Table 2).

Table 2. TMP-SMX Desensitization Protocol⁷

Step	Dose
Day 1	80 mg sulfamethoxazole + 16 mg trimethoprim (2 ml oral suspension)
Day 2	160 mg sulfamethoxazole + 32 mg trimethoprim (4 ml oral suspension)
Day 3	240 mg sulfamethoxazole + 48 mg trimethoprim (6 ml oral suspension)
Day 4	320 mg sulfamethoxazole + 64 mg trimethoprim (8 ml oral suspension)
Day 5	400 mg sulfamethoxazole + 80 mg trimethoprim
Day 6	800 mg sulfamethoxazole + 160 mg trimethoprim

The therapeutic response will usually occur on day 7 or so. Especially in PCP patients with HIV, the response to therapy appears longer but not longer than the first eight days. For this patient, cotrimoxazole therapy was equivalent to 20 mg/kg of trimethoprim in 3 divided doses. Treatment response was seen at 7-8 days. The results of chest X-ray evaluation also showed improvement after therapy. This can be seen from the repeat chest X-ray examination on the 14th day of treatment and it was found that the infiltrate intensity was reduced in both lung fields. After the clinical condition improved, the patient could then go for outpatient treatment on day 14.⁷

PCP cases often result in serious infections and a high mortality rate. This makes prevention is very important in risk groups. Trimethoprim-sulfamethoxazole is primary and secondary prophylaxis in addition to dapsone, pentamidine and atovaquone. HIV patients with $\text{CD4} < 200$ cells/ μL or with a history of oropharyngeal candidiasis should receive

chemoprophylaxis. Chemoprophylaxis is recommended for life time but can be discontinued in HIV patients if CD4 cell count increases from <200 cells/ μ L to >200 cells/ μ L for 3 months, and resumed again if CD4 cell count <200 cells/ μ L. The dosage given is 1x960mg orally or 1x480mg orally.⁷

According to research, the two doses are equally effective, although side effects are more likely to occur at larger doses. The desensitization process was carried out in patients who were intolerant of TMX-SMX. Desensitization was performed 2 weeks after a mild allergic reaction, which resulted in a temporary interruption of TMX-SMX. Desensitization was not performed for patients with a history of stage 4 hypersensitivity reactions. The following is a desensitization protocol from the World Health Organization (WHO).⁷

CONCLUSION

Since the COVID-19 outbreak occurred throughout the country, hospitals have focused on screening and early detection of patients who come with symptoms of respiratory tract infections leading to COVID-19. Symptoms of respiratory tract infections caused by COVID-19 are indeed similar to symptoms of other respiratory infections. The main symptoms most often present are fever, dyspnoea, cough, painful swallowing, headache, and runny nose. This might cause misdiagnosis with other differential diagnosis risks. Patients presenting with the symptoms listed above, but with

negative nasopharyngeal and oropharyngeal swabs, need to be considered of other possible diagnoses. significant weight loss as well as a positive HIV laboratory test result led to an HIV diagnosis.

In patients with or suspected of HIV, if there are complaints of fever, dyspnoea, and/or cough, PCP should be suspected. The clinical picture that appears can vary. PCP symptoms are usually mild and worsen within days to weeks. However, about 7% of patients are asymptomatic. The definitive diagnosis of PCP was confirmed by the BAL test by finding *P. Jirovecii*. However, in this case, the patient refused to undergo the BAL procedure. The drug therapy for PCP was TMP-SMX for 21 days with a response to therapy generally occurring in the first 7-8 days after starting therapy, as shown in this case. Prophylaxis in PCP-risk groups such as HIV-infected patients is very important as it is associated with significant mortality and morbidity.

REFERENCES

1. Zu ZY, Di Jiang M, Xu PP, et al. Coronavirus Disease 2019 (COVID-19): A Perspective from China. *Radiology*. 2020;296(2):E15-E25.
2. Handayani D, Hadi DR, Isbaniah F, Burhan E, Agustin H. Corona Virus Disease 2019. *J Respirologi Indones*. 2020;40(2):119-129.
3. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the 'Cytokine Storm' in COVID-19.' *J Infect*. 2020;80(6):607-613.

4. Agustina DR, Efiyanti C, Yuniastuti E, Ujainah A, Rozaliyani A. Diagnosis dan Tata Laksana Pneumocystis Carinii Pneumonia (PCP)/Pneumocystis Jirovecii Pneumonia pada pasien HIV: Sebuah Laporan Kasus. *J Penyakit Dalam Indones.* 2017;4(4):209.
5. Yudhawati R, Wijaksono W. Peran Steroid pada Pneumocystis Pneumonia Ditinjau Berdasarkan Immunopatogenesis. *J Respirasi.* 2020;5(2):57.
6. Choy CY, Wong CS. It's not all about COVID-19: pneumocystis pneumonia in the era of a respiratory outbreak. *J Int AIDS Soc.* 2020;23(6).
7. Dockrell DH, Breen R, Lipman M, Miller RF. Pulmonary opportunistic infections. *HIV Med.* 2011;12(SUPPL. 2):25-42.