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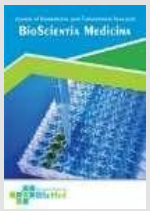

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Delayed SARS-COV-2 Viral Clearance in a Newly Diagnosed HIV Patient: A Case Series

Dimas Bayu Firdaus[1*], Oea Khairsyaf[1], Dewi Wahyu[1], Irvan Medison[1], Deddy Herman[1], Masrul Basyar[1]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Andalas/Dr. M. Djamil General Hospital, Padang, Indonesia

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***Corresponding author:**
Dimas Bayu Firdaus

E-mail address:
bdimasb@gmail.com

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A B S T R A C T

Background: SARS-CoV-2 can infect anyone, but people with HIV have underlying conditions or comorbidities that can make them seriously ill if infected with SARS-CoV-2. HIV attacks and destroys the immune system delays the response of specific antibodies, and even causes failure to thrive, resulting in a long course of the disease. This case report aimed to describe 2 cases of HIV patients co-infected with SARS-CoV-2 with delayed viral clearance. **Case presentation:** There are two HIV patients with co-infection with SARS-CoV-2. The first patient, a 32-year-old man with COVID-19 and HIV-AIDS, was referred from a regional hospital after being treated for 10 days due to clinical deterioration. Physical examination showed that the patient's general condition was moderately ill, and other vital signs were within normal limits. Oral candidiasis was seen in the patient's mouth, crackles were found in both lung fields, and epigastric tenderness was found on abdominal examination. The patient tested positive for COVID-19 based on the results of an antigen swab examination from the previous hospital. The second patient, a 26-year-old man, came with complaints of intermittent fever 1 week before entering the hospital. Complaints began with the body feeling weak and coughing without phlegm 2 weeks ago. The patient tested positive for COVID-19 based on the results of an antigen swab examination. The delayed viral clearance of SARS-CoV-2 in the two patients was possibly caused by the impaired immune response due to HIV infection, as shown by the presence of lymphopenia and decreased CD4+. **Conclusion:** ARV use can suppress HIV viral load and increase immunity so that can help viral clearance of SARS-CoV-2.

1. Introduction

COVID-19 is caused by a virus known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and can spread from person to person. The World Health Organization (WHO) reported that as of Jul 3rd, 2022, more than 546 million confirmed cases and more than 6.3 million deaths have been reported globally.[1] SARS-CoV-2 can infect anyone, but people with human immunodeficiency virus (HIV) have underlying conditions or comorbidities that could make them seriously ill if infected with SARS-CoV-2.[2] The centers for disease control and prevention (CDC) states that compared to the general population, people with HIV are at higher risk of complications and death related to COVID-19.[3] People infected with HIV are at increased risk of infection with SARS-CoV-2, especially people with comorbidities, lower CD4 counts, or high HIV viral loads. Conversely, routine use of antiretrovirals may alter the risk of SARS-CoV-2 infection and clinical presentation in this population.[4,5]

The impact of SARS-CoV-2 co-infection in people with HIV is not fully understood. Research by Mirzei et al. showed HIV patients with mild to moderate COVID-

19 in 141 of 212 patients (66.5%), severe in 46 patients (21.7%), and critical in 25 patients (11.8%). The majority of patients (158 of 244, 64.7%) were hospitalized, and 16.8% of them were admitted to the intensive care unit.[6] HIV attacks and destroys the immune system, delays the response of specific antibodies, and even causes failure to thrive, resulting in a long course of the disease.[7] This study aimed to report two case illustrations of HIV patients coinfected with SARS-CoV-2, which aims to discuss viral clearance of SARS-CoV-2 in newly diagnosed HIV patients.

2. Case Presentation

Case 1

A 32-year-old man with COVID-19 and acquired immunodeficiency syndrome (SIDA) was referred from the regional hospital after being treated for 10 days due to clinical deterioration. During treatment, the patient was given remdesivir for 5 days, co-trimoxazole, and other supportive treatment. The patient has felt shortness of breath since 14 days ago, accompanied by coughing, nausea, and heartburn. Liquid bowel movements and a weight loss of 2 kg were felt by the patient in the last 1 month. Based on the results of examinations at the previous hospital, the patient was diagnosed with SIDA but had not yet undergone ARV treatment. The patient's wife is known by SIDA and is already undergoing treatment. Physical examination showed that the general condition of the patient looked moderately ill, with respiratory rate 26x/minute, oxygen saturation 87% with O_2 15 L/min, temperature 37.7^{O}C, and other vital signs within normal limits. The patient was normoweight, with a body mass index of 27. Oral candidiasis was seen in the patient's mouth, crackles were found in both lung fields, and epigastric tenderness was found on abdominal examination. No significant abnormalities were found on other physical examinations. The patient tested positive for COVID-19 based on the results of an antigen swab examination from the previous hospital. The RT-PCR examination showed a positive result with a CT value of 33/32. Laboratory examination results showed lymphopenia 658.5 mm^3 and increased inflammatory biomarkers (results of laboratory tests can be seen in Table 1). Blood gas analysis results showed respiratory alkalosis with severe ARDS with a pH of 7.5; pCO_2 34; pO_2 43; SO_2 85; HCO_3- 26.7; BE 26.7; and pO_2/FIO_2 61.4. Decreased CD4 levels were found in patients. Serial anti-HIV tests are performed in patients with reactive results. Chest X-ray showed infiltrates mainly at the base of the right lung (Figure 1).

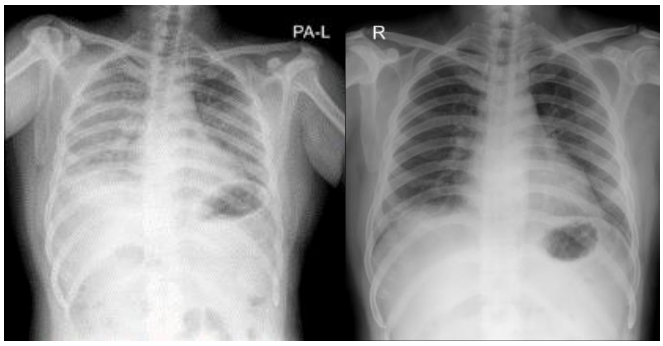

Figure 1. Thoracic X-ray of patient treatment days 1 and 9.

The patient was diagnosed with clinically critical COVID-19 with severe ARDS accompanied by clinical stage III SIDA. Oxygen via high current nasal cannula was given for the first 3 days. Corticosteroids were given for 10 days, and symptomatic drugs and co-trimoxazole were given during treatment. Anti-retroviruses in the form of Tenovofir, Lamivudine, and Dolutegrafir were started on the 5th day of treatment.

The patient's clinical symptoms began to decrease after 3 days of treatment, shortness of breath had decreased, oxygen therapy was reduced, and the patient only complained of an occasional cough. RT-PCR examination on the 11th day of treatment showed positive results with CT-Value 33/32. The RT-PCR examination still showed positive results after being serialized on day 16, day 26, day 32, and day 39 with a decreasing CT-Value pattern until it was declared negative on day 47.

Table 1. Comparison of patient laboratory results.

Laboratory results	**Patient 1**	**Patient 2**
Hb (g/dL)	15,7	6,1
Thrombosis (/ul)	396000	368000
Leukocyte (/ul)	8230	5390
Count type		
Basophils (%)	0	0
Eosinophils (%)	0	0
Neutrophils (%)	90	86
Lymphocytes (%)	8	6
Monocytes (%)	2	8
ALC (/ul)	658,4	323,4
D-Dimers	504	733
Procalcitonin (ng/mL)	<0.05	0,23
Ferritin	821,52	>1200
Interleukin-6	2	72,2
CRP	31	155
LDH	180	196
Antigen SARS-CoV-2	Positive	Positive
CD4+ (cell/uL)	56	6
TCM MTB	Not detected	Not detected

Case 2

A 26-year-old man came with complaints of intermittent fever for 1 week before entering the hospital. Complaints began with the body feeling weak and coughing without phlegm 2 weeks ago. Shortness of breath is not felt in the patient. Liquid bowel movements and a weight loss of 2.5 kg were felt by the patient in the last 2 months. The patient has been known to have acquired immunodeficiency syndrome since 2 weeks ago but has not yet undergone anti-retroviral treatment. The patient has a history of risky sex. Physical examination showed the general condition of the patient looked moderately ill, with respiratory rate 24x/minute, 95% oxygen saturation with free air, temperature 37.7^{O}C, and other vital signs within normal limits. Normoweight patients with a body mass index of 24.2. The patient's conjunctiva looked anemic, and oral candidiasis was seen in the patient's mouth. No significant abnormalities were found on other physical examinations. The patient tested positive for COVID-19 based on the results of an antigen swab examination. Laboratory examination results showed anemia 6.1 g/dL, lymphopenia 323.4 mm^3, and increased inflammatory biomarkers (results of laboratory tests can be seen in Table 2). Decreased CD4 levels were found in patients. Serial anti-HIV tests are performed in patients with reactive results. Chest X-ray showed an infiltrate in the right perihilar (Figure 2).

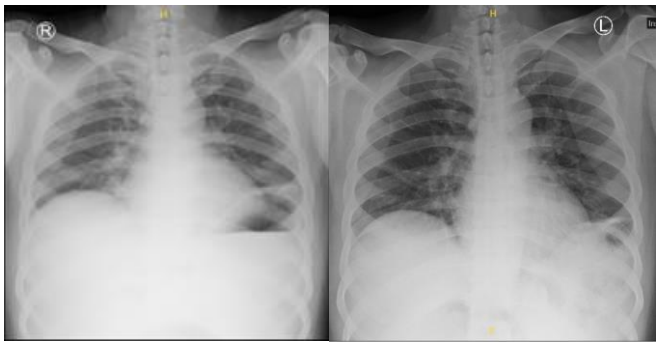

Figure 2. Thoracic X-ray of patient treatment days 1 and 10.

The patient was diagnosed with moderate clinical COVID-19 with clinical SIDA stage III accompanied by anemia of chronic disease. Antivirus in the form of Remdesivir is given to patients for 5 days. Transfusion of a packed red cell is given until Hb reaches ≥10. Symptomatic drugs and co-trimoxazole were administered during treatment. Anti-retroviruses in the form of Tenovofir, Lamivudine, and Dolutegrafir were started on the 7th day of treatment. After 5 days of treatment, the patient's clinical symptoms began to decrease, the fever was no longer felt, and the patient only complained of an occasional cough. RT-PCR examination on the 9th day of treatment showed positive results with CT-Value 15/16. RT-PCR examination still showed positive results after being serialized on day 14, day 22, day 29, and day 36 with a CT-PCR pattern. The value increased until it was declared negative on the 45th day.

3. Discussion

Both patients, in this case, were men in their middle age who were newly diagnosed with HIV infection during their COVID-19 treatment. The incidence rate of COVID-19 among people with HIV differs in each country, from the United States (0.8%), Spain (1.8%), and China (0.68%).[5] A systematic review by Mirzaei et al. showed that out of 252 patients coinfected with COVID-19 and HIV, the majority of patients coinfected with HIV and COVID-19 were male.[6] SARS-CoV-2 is a beta coronavirus consisting of four structural proteins consisting of the nucleocapsid (N) protein, the spike (S), the protein envelope (E), and membrane proteins (M). HIV has a different apparatus as a member of the lentivirus family consisting of two copies of positive-strand RNA. The viral capsid houses enzymes essential for viral replication, such as reverse transcriptase, integrase, and protease. The newly formed virion contains the glycoprotein gp41 on the envelope. Viral glycoprotein ~120 kD (gp120) is attached to gp41, which forms the protein spike HIV is important for interaction with host cell receptors, which causes infection and restarts the full life cycle.[8]

The patient in the first case showed severe clinical symptoms and began to experience clinical improvement after a few days of treatment, while the second case showed mild to moderate symptoms from the start of treatment. Most people with HIV co-infected with COVID-19 show mild to moderate clinical symptoms. In addition, the risk factors for severe COVID-19 among people with HIV are similar to those for COVID-19 without HIV, such as older age and comorbid medical conditions.[5] Research by Ho et al. states that the most common symptoms of COVID-19 in HIV patients are fever (66%), cough (76%), or shortness of breath (61%). This is similar to people without HIV.[9] SARS-CoV-2 and HIV have different disease courses. SARS-CoV-2 infects epithelial cells of the upper respiratory tract, and the virus produced by infected cells travels to the lower respiratory tract, infecting bronchial and alveolar epithelial cells and alveolar macrophages. As a consequence of innate immunity, virus-infected epithelial cells undergo apoptosis and are phagocytosed by the virus antigen presenting cell (APC), such as dendritic cells and

macrophages. APCs migrate to lymph nodes to present viral antigens to T cells. CD4+ and CD8+ T cells play a major role in eliminating SARS-CoV-2. CD4+ T cells activate B cells to promote the production of virus-specific antibodies, while CD8+ T cells can directly kill virus-infected cells.[5] In contrast to SARS-CoV-2, HIV binds to the CD4 receptor of the host cell, followed by co-receptor engagement (i.e., chemokine receptor 5 (CCR5) or chemokine receptor 4 (CXCR4)). The cytopathic effects of HIV include the host's innate immune response to viral DNA produced during abortive infection and endotoxin/microbial translocation of leaky guts, persistent immune activation, immune dysregulation, and failure of CD4 T-cell homeostasis are keys to HIV pathogenesis leading to CD4 T-cell depletion and immunocompromised in HIV.[5] Lymphopenia was found in both cases. One of the effective responses of human innate and adaptive immunity to viruses includes the secretion of several proinflammatory cytokines and the activation of several subsets of T cells that are important for controlling viral replication, restraining viral spread, limiting inflammation, and clearing infected cells. Lymphopenia especially decreased CD4+ T cells, is frequently seen in patients with COVID-19, and is more pronounced in severe cases.[10]

Both patients have time viral clearance, which is slow, seen from the negative serial PCR examination after more than 40 days. Pattern Ct-value differences were observed in the two patients. The first case has a pattern CT-value which decreased until it was declared negative on day 47, followed by an ALC pattern which tended to stabilize around 516-850/µL. Unlike the first case, the second case has a pattern of CT-value which increased, followed by an increased ALC value, until it was declared negative on day 45. Gatechompol et al. mentioned that low CD4 counts and lymphopenia in HIV patients with COVID-19 could inhibit the viral clearance of SARS-CoV-2 and drive the development of the disease.[5] Mascolo et al. demonstrated that HIV-associated lymphopenia may have a protective role from clinically severe COVID-19 in HIV patients. T-cell activation by SARS-CoV-2 is associated with disease severity leading to poorer clinical outcomes.[11] A low CD4 cell count may protect HIV-infected patients from developing a cytokine storm, which is part of the clinical syndrome of COVID-19 and has the potential to reduce some of the severe manifestations of COVID-19.[12]

The study by Ho et al. reported data on HIV patients before and after exposure to COVID-19, showing a significant reduction in $CD4^+$ T cell counts and absolute lymphocyte count. Although lymphopenia associated with COVID-19 can further reduce the number of CD4+ T cells in PLHIV, there is no difference in clinical presentation, outcome, morbidity, and mortality between individuals who have SARS-CoV-2 with or without HIV infection.[9] The differences in the peripheral blood cells of HIV and COVID-19 patients can be seen in Figure 6. Tests for SARS-SoV-2 antibodies were not performed on the two patients. Humoral immunity against COVID-19 is critical not only in recovering from this COVID-19 but also for building and maintaining herd immunity through effective vaccination strategies. The study by Rumpa et al. showed of 30 HIV patients with COVID-19, 16 patients were found to have IgG antibodies on the 20th day after infection, 4 patients on the 35th day, 2 patients on the 50th day, 1 patient on the 65th day after infection, and 7 patients had no detectable specific SARS-CoV-2 antibodies.[7] The second patient had quite high IL-6 levels. The meta-analysis conducted by Lee et al. showed that out of 277 HIV patients with COVID-19, some of them had increased IL-6. In general, a fairly high percentage of studies reported increased baseline values for most inflammatory markers (C-reactive protein, fibrinogen, ferritin, and interleukin-6). A high percentage of cases with elevated biomarkers indicate inflammation, coagulopathy, and tissue damage.[13] Both patients were at clinical stage III based on the presence of oral candidosis, sores, and diarrhea for more than 1 month, accompanied by anemia in the second patient. Both patients were given ARVs during treatment in the form of a fixed-dose combination of Tenofovir,

Lamivudine, and Dolutegravir. Based on the guidelines of the Ministry of Health, ARV therapy should be given to all PLHIV regardless of clinical stage and CD4 count. However, the CD4 count is needed to determine the indication for opportunistic infection prophylaxis.[14] A survey in China showed that people living with HIV were given nucleoside reverse transcriptase inhibitors (NRTI) plus non-nucleoside reverse transfer inhibitors (NNRTI), which do not prevent COVID-19 infection.[6] Several randomized controlled trials have shown that antiretroviral therapy has no beneficial effect among people infected with SARS-CoV-2 compared to standard care.[5] COVID-19 can become more severe in people with immunodeficiency or immune dysregulation. Most people with HIV who are infected with COVID-19 are reported to be using ARVs and have HIV infection that is well controlled so that they can suppress their HIV viral load and CD4 count > 350.[5] Patients with HIV who have been infected for a long time and have comorbidities are still at risk of experiencing severe manifestations of COVID-19 despite taking ARVs.[9]

4. Conclusion

Delayed viral clearance of SARS-CoV-2 in both patients was possibly caused by impaired immune response due to HIV infection, as shown by the presence of lymphopenia and decreased CD4+. ARV use can suppress HIV viral load and increase immunity so, which can help viral clearance of SARS-CoV-2.

5. References

1. WHO. COVID-19 weekly epidemiological update. 2022.
2. Ssentongo P, Heilbrunn ES, Ssentongo AE, Advani S, Chinchilli VM, Nunez JJ, et al. Epidemiology and outcomes of COVID-19 in HIV-infected individuals: a systematic review and meta-analysis. Scientific Reports. 2021; 11(1): 1–12.
3. CDC. What to know about HIV and COVID-19 the centers for disease control and prevention. 2021; 1–11.
4. Vizcarra P, Pérez-Elías MJ, Quereda C, Moreno A, Vivancos MJ, Dronda F, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. The Lancet HIV. 2020; 7(8): 554–64.
5. Gatechompol S, Avihingsanon A, Putcharoen O, Ruxrungtham K, Kuritzkes DR. COVID-19 and HIV infection co-pandemics and their impact: a review of the literature. AIDS Research and Therapy. 2021; 18(1): 1–9.
6. Mirzaei H, McFarland W, Karamouzian M, Sharifi H. COVID-19 among people living with HIV: A systematic review. AIDS and Behavior. 2021; 25(1): 85–92.
7. Rumpa S, Alpana R, Pooja D, Kirti N, Vikas S, Amir Maroof K, et al. Antibody response to SARS-CoV-2 in HIV patients co-infected with COVID-19. International Journal of Virology and AIDS. 2021; 8(2): 1–8.
8. Evans N, Martinez E, Petrosillo N, Nichols J, Islam E, Pruitt K, et al. SARS-CoV-2 and human immunodeficiency virus: Pathogen pincer attack. HIV/AIDS - Research and Palliative Care. 2021; 13(4): 361–75.
9. Ho HE, Peluso MJ, Margus C, Matias Lopes JP, He C, Gaisa MM, et al. Clinical outcomes and immunologic characteristics of coronavirus disease 2019 in people with human immunodeficiency virus. Journal of Infectious Diseases. 2021; 223(3): 403–8.
10. Anka AU, Tahir MI, Abubakar SD, Alsabbagh M, Zian Z, Hamedifar H, et al. Coronavirus disease 2019 (COVID-19): An overview of the immunopathology, serological diagnosis and management. Scandinavian Journal of Immunology. 2021; 93(4): 1–12.
11. Mascolo S, Romanelli A, Carleo MA, Esposito V. Could HIV infection alter the clinical course of SARS-CoV-2 infection? When less is better. J Med Virol. 2020; 92(10): 1777–8.
12. Guo W, Ming F, Dong Y, Zhang Q, Liu L, Gao M, et al. Driving force of COVID-19 among people living with HIV/AIDS in Wuhan, China. Res Sq. 2020; 3(1): 1–16.
13. Lee KW, Yap SF, Ngeow YF, Lye MS. COVID-19 in people living with HIV: A systematic review

and meta-analysis. International Journal of Environmental Research and Public Health. 2021; 18(7): 1–25.
14. Ministry of Health of the Republic of Indonesia. National guidelines for HIV management medical services. Jakarta; 2019.
15. Peng X, Ouyang J, Isnard S, Lin J, Fombuena B, Zhu B, et al. Sharing CD4+ T cell Loss: When COVID-19 and HIV collide on immune system. Frontiers in Immunology. 2020; 11(2): 1–8.