DOI: 10.1002/jmv.26102

JOURNAL OF MEDICAL VIROLOGY WILEY

A case of SARS-CoV-2 infection in an untreated HIV patient in Tokyo, Japan

To the Editor,

Coronavirus disease 2019 (COVID-19) is ongoing and spreading worldwide after cases of COVID-19 were reported in Wuhan, China in December 2019.[1] Older age, diabetes, hypertension, and smoking have been reported as aggravating factors,[2] and human immunodeficiency virus (HIV) infection is considered to be a potentially aggravating factor. There are very few reports of COVID-19 in untreated HIV patients[3-5] HIV patients are known to be susceptible to respiratory viruses and to have more severe symptoms, but the clinical course and prognosis of COVID-19 in HIV patients are not known yet. We report a case of COVID-19 with untreated HIV infection.

On 23 March 2020, a 28-year-old male living in Tokyo suffered from persistent fever and nonproductive cough for 8 days before coming to our hospital. He told us he had an HIV infection but had not received any antiretroviral therapy (ART). He was diagnosed with HIV infection 2 years prior and was then noted to be seropositive for syphilis and hepatitis B virus. However, he was lost to follow-up by the hospital before starting ART. The HIV-1 viral load and the $CD4^+$ T lymphocyte count were 1.28×10^4 copies/mL and 491/μL, respectively, at the last visit. He had no other past medical history, but he was a heavy smoker of two packs per day and a heavy drinker. A patient is a man who has receptive sex with men and the last intercourse was 2 months prior. He had no recognized contact with any confirmed COVID-19 patients and had not traveled abroad for a year.

Physical examination was as follows: body temperature, 39.2°C; pulse rate, 130 beats per minute; respiratory rate, 20 breaths per minute; blood pressure, 110/78 mm Hg; and oxygen saturation, 97% while breathing room air. There were no abnormalities in his bilateral lung sounds. However, chest computed tomography showed multiple ground-glass opacities (Table 1). Blood testing revealed mild lymphopenia (981/μL), decreased $CD4^+$ T lymphocyte counts (194/μL), elevated lactate dehydrogenase (529 U/L), and elevated C-reactive protein (10.97 mg/dL). The HIV-1 viral load was 1.00×10^2 copies/mL. Cytomegalovirus was not detected in peripheral blood. A salivary *Pneumocystis jirovecii* polymerase chain reaction (PCR) assay was negative. The nasopharyngeal specimen tested negative by a BioFire Diagnostics Respiratory Panel (BioFire Diagnostics; Salt Lake City, UT), however, positive for SARS-CoV-2 by reverse transcription PCR assay. Therefore, we confirmed that this patient was coinfected with HIV and SARS-CoV-2, and he was hospitalized. We administered 200 mg hydroxychloroquine twice a day for 14 days. On day 3, his fever subsided. However, on day 4, he needed additional oxygen due to difficulties in breathing without desaturation, but he recovered the next day. SARS-CoV-2 was not detected in nasopharyngeal specimens obtained on either day 7 or 8. He was discharged on day 9. One month after his discharge, the HIV-1 viral load had increased (2.37×10^4 copies/mL). We started on ART (bictegravir/emtricitabine/tenofovir alafenamide fumarate) and he has had no particular problems for the next 2 months (Figure 1).

This is a case report of COVID-19 in an untreated HIV patient.

Neither our case nor the previous untreated HIV cases[3-5] required invasive mechanical ventilation although all cases had $CD4^+$ T lymphocyte counts under 200 at the first visit (Table 1). Respiratory viral infections may become severe and prolonged in HIV patients.[5] $CD4^+$ T lymphocyte counts may not affect the severity of COVID-19 or delay SARS-CoV-2 clearance in the nasopharynx (Table 1).

In our case, ART was not given during the hospitalization because there can be a risk of developing immune reconstitution inflammatory syndrome (IRIS). *P. jirovecii* and *Mycobacterium* spp. are the pathogens causing IRIS in pneumonia in HIV patients.[6] The latest guideline recommends starting ART as soon as possible, except in cases of tuberculous meningitis. However, we did not administer ART to the patient during the acute phase for the following three reasons. First, SARS-CoV-2 exists more frequently in sputum than in the nasopharynx or oropharynx.[7] Second, a decrease in $CD4^+$ T lymphocytes can slow SARS-CoV clearance.[8] Finally, a relationship between COVID-19 pneumonia and cytokine storms has been suggested.[9]

The HIV-1 viral load was significantly reduced on admission compared with the last visit 2 years prior. It is possible that the HIV-1 virus was reduced by SARS-CoV-2 interference. Moss et al[10] reported that HIV replication is suppressed during acute measles.

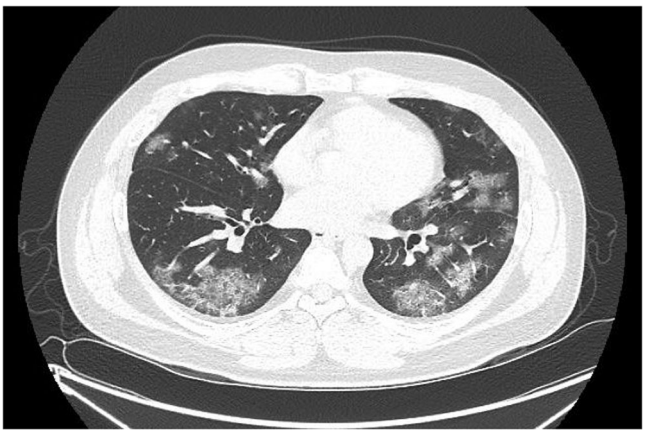

FIGURE 1 Thoracic computed tomography image on admission

TABLE 1 Comparison of previous cases and our case

Characteristics	Chinese case	Turkish case	Spanish case	Our case
Age (years)	61	34	31	28
Sex	Male	Male	Transgender	Male
Underlying condition	Diabetes, Smoker	HBV infecition, Bipolar disorder	none	Smoker, Drinker, HBV infection
Day of illness admission	8	not available	7	8
Saturation on admission (%)	80	not available	<90%	97
CT findings on admission	multiple GGO	multiple GGO	not available	multiple GGO
Lymphocyte counts (/μL)	560	360	900	981
$CD4^+$ lymphocyte counts (/μL)	26.6	2.8	13	194
HIV-1 viral load (copies/mL)	not available	434,782	45,500	100
Lactate dehydrogenase (U/L)	not available	308	1,149	529
C reactive protein (mg/dL)	not available	0	40	10.97
Maximum oxygen supply (L/min)	5	0	not available	0.6
Possible anti SARS-CoV-2 agents	Lopinavir/ritonavir γ-globlin	Lopinavir/ritonavir Azithromycin	Darunavir/cobicistat Hydroxychloroquine Interferon beta-1b Azithromycin	Hydroxychloroquine
Mechanical ventilation	none	none	non-invasive	none
Day of SARS-CoV-2 negativity from admission	11	not available	not available	8

GGO = ground-glass opacities.

Here, we describe a case of COVID-19 pneumonia with untreated HIV infection. COVID-19 pneumonia in untreated HIV patients requires careful follow-up for IRIS with ART.

ACKNOWLEDGMENTS

The authors would like to thank Editage (http://www.editage.com) for English language editing. This study was partly supported by funding research grants from the Emerging/Re-emerging Infectious Diseases Project of Japan from the Japan Agency for Medical Research and Development, AMED (20fk0108116h0001).

Takato Nakamoto MD[1]
Satoshi Kutsuna PhD[1]
Yasuaki Yanagawa[2]
Kouhei Kanda[1]
Ayako Okuhama[1]
Yutaro Akiyama[1]
Yusuke Miyazato[1]
Satoshi Ide[1]
Keiji Nakamura[1]
Kei Yamamoto[1]
Norio Ohmagari[1]

[1]*Disease Control and Prevention Center, National Center for Global Health and Medicine, Tokyo, Japan*
[2]*AIDS Clinical Center, National Center for Global Health and Medicine, Tokyo, Japan*

Correspondence
Satoshi Kutsuna, Department of Infectious Diseases, Disease Control and Prevention Center, National Center for Global Health and Medicine, 1-21-1 Toyama, Shinjuku-ku, Tokyo 162-8655, Japan.
Email: skutuna@hosp.ncgm.go.jp

ORCID

Takato Nakamoto https://orcid.org/0000-0002-0547-1026
Satoshi Kutsuna https://orcid.org/0000-0002-6929-8955

REFERENCES

1. Bedford J, Enria D, Giesecke J, et al. COVID-19: towards controlling of a pandemic. *Lancet*. 2020;395:1015-1018.
2. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med*. 2020:e200994. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2763184
3. Zhu F, Cao Y, Xu S, Zhou M. Co-infection of SARS-CoV-2 and HIV in a patient in Wuhan city, China. *J Med Virol*. 2020;92:529-530.

4. Aydin OA, Karaosmanoglu HK, Yasar KK. HIV/SARS-CoV-2 co-infected patients in Istanbul, Turky. *J Med Virol*. 2020. https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25955
5. Blanco JL, Ambrosioni J, Garcia F, et al. COVID-19 in patients with HIV: clinical case series. *Lancet HIV*. 2020;7(5):e314-e315.
6. King JC Jr. Community respiratory viruses in individuals with human immunodeficiency virus infection. *Am J Med*. 1997;102(3):19-24.
7. Yu F, Yan L, Wang N, et al. Quantitative detection and viral load analysis of SARS-CoV-2 in infected patients. *Clin Infect Dis*. 2020: ciaa345. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa345/5812997
8. Li G, Fan Y, Lai Y, et al. Coronavirus infections and immune responses. *J Med Virol*. 2020;92(4):424-432.
9. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395(10229):1033-1034.
10. Moss WJ, Ryon JJ, Monze M, Cutts F, Quinn TC, Griffin DE. Suppression of human immunodeficiency virus replication furring acute measles. *J Infect Dis*. 2002;185(8):1035-1042.