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LETTER TO THE EDITOR

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Clinical features and outcomes of four HIV patients with COVID-19 in Wuhan, China

To the Editor,

Severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) is the coronavirus that has been identified as the pathogen causing coronavirus disease 2019 (COVID-19).[1] Human immunodeficiency virus (HIV) attacks the immune system and leads to acquired immune deficiency syndrome (AIDS) in the late stage of disease. Concerns have been raised on HIV as a risk factor for COVID-19. However, little is known about the clinical features and outcomes of HIV patients with COVID-19, especially those who have the AIDS stage of the disease. Here, we described four patients with COVID-19 at different time points of the spectrum of HIV infection.

Patient A was a 38-year-old man. In April 2019, his HIV antibody test was positive. He reported a history of walking by Huanan Seafood market[2] every day in early January. On 10 January, he started to develop dry cough and further developed spiking fever and dyspnea, and chest computed tomography (CT) abnormalities showing ground-glass opacities (GGOs) predominantly involving perihilar and midzones on 30 January; see Figures 1(1A) and 1(1D). On 31 January, he was admitted for inpatient care, and on 11 February, he was further admitted to COVID-ward. On the 10th day, SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test was for the first positive. His respiratory symptoms changed minimally during the stay. He was transferred to Jinyintan Hospital after revelation of his past HIV test result. Chest CT showed a mixed pattern of GGOs, reticulations, consolidation, and cystic airspaces 1 week after transfer; see Figures 1(1B) and 1(1E). On 22 March, pneumocystis jirovecii DNA from sputum sample was identified and pneumocystis pneumonia (PCP) was additionally diagnosed. His symptoms gradually improved during the stay. Chest CT showed partial resolution of lesions after 3 weeks; Figures 1(1C) and 1(1F). At the last time of data collection, the patient reported moderately improved exercise tolerance and his SpO_2 was 96% at rest with oxygen support (5 L/min).

Patient B was a 25-year-old man. In 2019, he had a positive HIV antibody test. On 8 February, he developed high fever, cough, and dyspnea. He was immediately admitted for inpatient care and SARS-CoV-2 RT-PCR test was positive. His symptoms did not improve after 10 days and he was admitted to COVID-19 ward. Upon admission, his chest CT scan revealed diffuse irregular GGOs with subpleural and peripheral involvement; see Figures 1(2A) and 1(2D). He further developed sore throat and dysphagia. The patient mentioned his previous HIV test after further query and HIV status was confirmed by the antibody test. After transfer to Jinyintan Hospital, chest CT showed confluence of peripheral lesions in the left upper lung and a mixed pattern of GGOs and reticular opacities in the lower lung bilaterally; see Figures 1(2B) and 1(2E). His symptoms significantly improved during the stay. His SpO_2 was 98% at rest without oxygen supply, and chest CT showed wide resolution of lesions before discharge to observation site; Figures 1(2C) and 1(2F).

Patient C was a 46-year-old man. He had 5 years history of HIV infection and was on highly active antiretroviral therapy (HAART). On 1 February, he developed mild fever and cough. RT-PCR test for SARS-CoV-2 was positive and he was admitted for inpatient care. RT-PCR test remained positive after 2 weeks and chest CT scan showed irregular GGOs at the periphery of the lower lung bilaterally; Figures 1(3A) and 1(3D). He was transferred to Jinyintan Hospital due to HIV history. Chest CT showed enlargement of GGOs (Figures 1(3B) and 1(3E)) and resolution of lesions (Figures 1(3C) and 1(3F)) 2 and 3 weeks after transfer, respectively. The patient was free of symptom before discharge to the observation site.

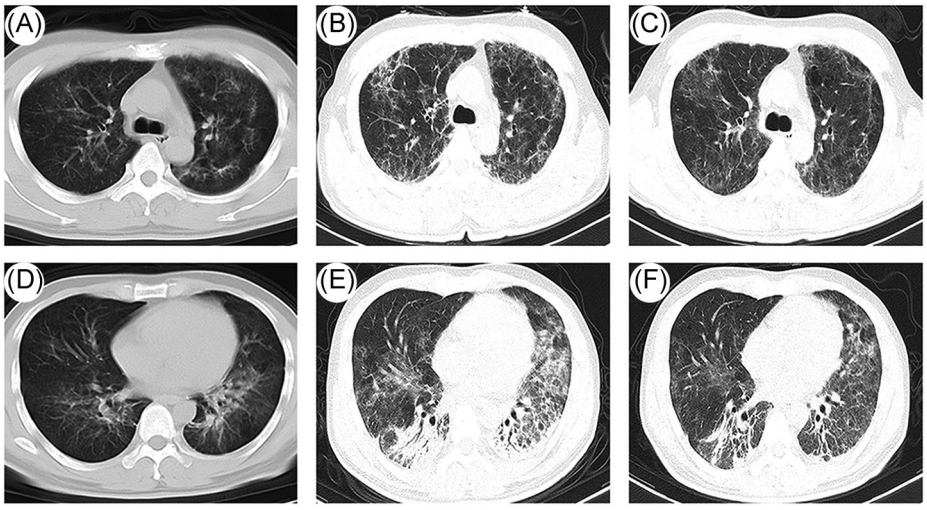
Patient D was a 54-year-old man. He had 4 years history of HIV infection and was on HAART. He also had hypertension, diabetes, and coronary heart disease and took Aspirin, Atorvastatin, Ezetimibe, Bisoprolol, and Trimetazidine regularly. He had a history of close contact with his wife who was a confirmed case of COVID-19 1 week before he developed fever, cough, and dyspnea. Upon symptom onset, chest CT showed wedge-shaped GGOs in the upper lung bilaterally; Figures 1(4A) and 1(4D). He was admitted for inpatient care and furthered transferred to Jinyintan Hospital due to HIV history. After transfer, chest CT initially showed enlarging areas of GGOs bilaterally with formation of reticulation and consolidation (Figures 1(4B) and 1(4E)), but partial resolution of lesions (Figures 1(4C) and 1(4F)) after 2 weeks. The patient was symptom-free before discharge to the observation site.

For details of medical care timeline, patient demographic data, and laboratory testing results, please refer to the Supplementary Information Material.

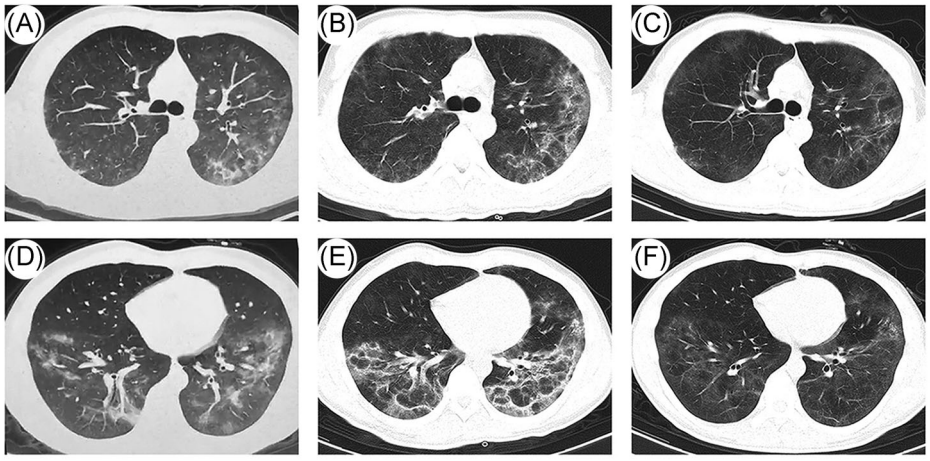
DISCUSSION

We described distinct clinical courses of COVID-19 in four patients with underlying HIV infection. Fever, cough, and dyspnea were common symptoms as those of large groups of patients.[3] It is to note that patient A had one time fever 3 days after transfer and 2 days of fever for the second time 2 weeks after transfer, and patient B had

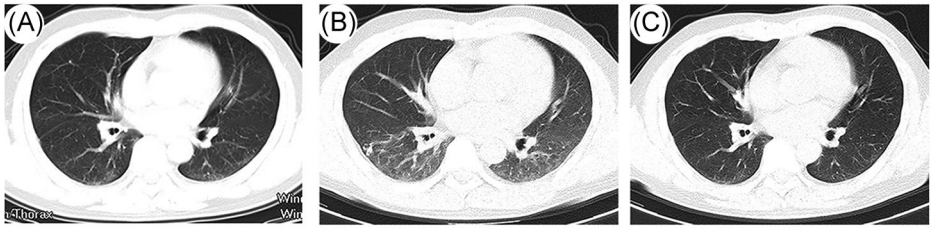
(1) Patient A



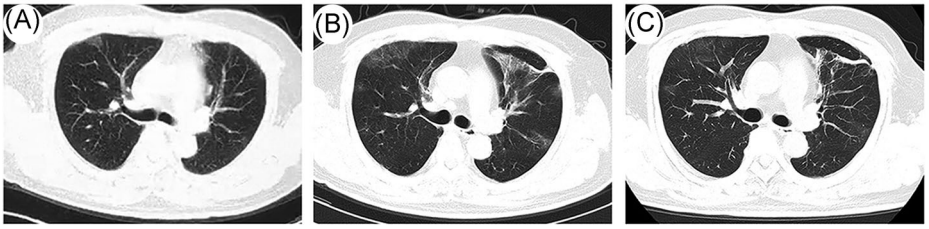
(2) Patient B



(3) Patient C



(4) Patient D



3 days of fever 1 week after transfer. This might be explained by a protracted disease course complicated by AIDS-defining opportunistic infections (pneumocystis pneumonia for patient A and pharyngeal or esophageal infection for patient B). In addition, we could only assume that these two patients with severe form of COVID-19 were having significant clinical symptoms and high interleukin-6 level, due to which Tocilizumab was initiated.

Overall, patients A and B, who were in the stage of AIDS, underwent a more complicated clinical course than patients C and D, who had asymptomatic HIV infection.[4] For patient A, chest CT performed around 3 weeks after symptom onset showed mainly diffuse bilateral predominantly involving perihilar and midzones with relative subpleural sparing (Figures 1(1A) and 1(1D)), which were not typical radiological features of COVID-19.[5] Taken together, the history of intermittent fever and progressive respiratory symptoms refractory to supportive care, finding of pneumocystis jirovecii DNA in the sputum, response to HAART and antifungal medications,[6,7] and the early stage radiological features favor an initial diagnosis of PCP rather than COVID-19.[8]

Patients C and D had moderate clinical symptoms of COVID-19. Notably, patient C had multiple positive RT-PCR tests until around 6 weeks after symptom onset. In contrast, multiple RT-PCR tests for patient D were negative even 4 weeks after symptom onset, but only confirmed Envelope gene segment of SARS-CoV-2 in stool sample (test repeated) at 5 weeks. However, clinical data including close contact history with a confirmed COVID-19 case and the dynamic radiological features (Figure 1(3)) that were in accordance with the published study[5] support a diagnosis of COVID-19.

As to adaptive immune response, patients A and B who had CD4+ T-cell less than 50 cells/μL seemed to have insufficient or delayed immunoglobulin M (IgM) and/or IgG production.[9] Patient A had positive IgM and negative IgG 3 weeks after the initial positive RT-PCR result; however, IgM turned negative and IgG remained negative after another 3 weeks. By contrast, patient B has negative IgM and IgG twice more than 6 weeks after the initial positive RT-PCR result. Zhao et al[10] suggested that low CD4+ T-cell count might partly explain the early incomplete viral clearance and delayed humoral responses towards SARS-CoV-2.

In summary, our paper highlights the importance of differential diagnoses for COVID-19 especially in patients with HIV infection based on dynamic clinical symptoms and radiological data. Large cohorts are required to further characterize the relationship between viral replication, immune response, and clinical progression of COVID-19, and to evaluate potential prophylactic and therapeutic options for patients with HIV infection.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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FIGURE 1 Serial chest computed tomography scans of four patients since symptom onset. (1) Patient A: (A and D) diffuse bilateral ground-glass opacities (GGOs) predominantly involving perihilar and midzones with relative subpleural sparing at 3 weeks after symptom onset. (B and E) A mixed pattern of GGOs, reticulation and air space consolidation, cystic airspaces, decreased lung volume, and compensatory increased anterior-posterior chest diameter at 9 weeks. (C and F) Partial resolution of various lesions at 12 weeks. (2) Patient B: (A and D) diffuse irregular GGOs mainly with subpleural and peripheral involvement 10 days after symptom onset. (B and E) Confluence of peripheral lesions in the left upper lung and a mixed pattern of ground-glass and reticular opacities in the lower lung bilaterally at six weeks. (C and F) Lesion resolution with some remnant GGOs at 8 weeks. (3) Patient C: (A) irregular GGOs at the periphery of the lower lung bilaterally 4 weeks after symptom onset. (B) Enlarged areas of GGOs bilaterally and an irregular nodule in the right lower lung at 6 weeks. (C) minimal residual opaque lesions at eight weeks. (4) Patient D: (A) wedge-shaped GGOs at the periphery of the right upper lung and the left upper lung medially 2 days after symptom onset. (B) Enlarging area of GGOs bilaterally with reticulation and consolidation in the left lung at three weeks. (C) Partial resolution of GGOs at 5 weeks

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.