Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Patients Living with Human Immunodeficiency Virus: Case Reports and Review of the Literature

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Case Report

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Abstract

Background: Novel coronavirus pneumonia (COVID-19) outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread over the globe. The knowledge about SARS-CoV-2 infection in immunocompromised patients was limited.

Case presentation: We presented here two human immunodeficiency virus (HIV)-infected cases with laboratory confirmed COVID-19 and clinically confirmed COVID-19, respectively. The patients both presented with fever at illness onset and patchy shadows in radiological images of lungs. Laboratory findings revealed leukopenia, lymphopenia and positive anti-HIV antibody. The younger case had a moderate course and was discharged after a 28-day hospitalization. However, the elder case with multiple comorbidities developed dyspnea and died on the fourth day after admission.

Conclusions: Combining our data with two case reports, we summarize that disease course varies in HIV-infected patients with COVID-19. More attention should be paid to the management of these patients. Whether there is any difference about clinical characteristics and prognosis of COVID-19 between HIV-infected and non-HIV infected patients, remains to be further investigated.

Background

First reported in December 2019 in Wuhan City, China, an emerging outbreak of novel coronavirus pneumonia (COVID-19) has rapidly spread over the globe. The etiology was identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1, 2]. The symptoms of COVID-19 include fever, cough, shortness of breath and dyspnea [3]. Radiological findings show multiple ground glass opacities (GGOs) and patchy shadows, sometimes lung consolidation [4]. Epidemiology evidence revealed populations were generally susceptible [5]. However, the knowledge about SARS-CoV-2 infection in immunocompromised patients was limited. Here we present two human immunodeficiency virus (HIV)-infected cases with laboratory confirmed COVID-19 and clinically confirmed COVID-19, respectively.

Case Presentations

Case 1 (laboratory confirmed COVID-19)

On 23 January 2020, a 27-year-old male of Wuhan native presented with fever and dry cough for one day and visited a local hospital. Chest computed tomography (CT) images showed viral pneumonia. SARS-CoV-2 RNA was tested positive. The patient's fever was not controlled with administration of antiviral drug and oral antibiotics. Subsequently, he developed chest distress and shortness of breath. On 3 February, he was transferred to Tongji Hospital, Wuhan, a tertiary hospital designated for quarantine and treatment of COVID-19.

On admission, physical examination revealed vital signs within normal range. However, he had a recurrent fever of 40.3 °C after 8 hours. He denied history of hypertension, diabetes, surgery, trauma, drug abuse and blood transfusion. Serological tests showed leukopenia (2.75×10^9/L) and lymphopenia (0.77×10^9/L), elevated lactic dehydrogenase (345 U/L), and elevated C-reactive protein (CRP) of 85.9 mg/L. Acid-fast bacilli was negative in sputum specimen. Common pathogens tests of blood-transmitted diseases found the patient was positive of HIV. The result was confirmed by centers for disease control (CDC). The patient provided that he was diagnosed with HIV infection 5 years ago when his HIV-RNA was 2.3×10^5 IU/ml and CD4+ T cell count was 295×10^6/L. He received cocktail treatment (zidovudine, lamivudine and efavirenz) regularly at CDC and plasma HIV was tested negative six months later. Although he used to have sexual life and tattoos, the transmission routes remain to be identified. The patient continued to visit local CDC every six months for monitor and treatment.

The antiviral treatment strategy for the patient included lopinavir/ritonavir 400/100 mg per dose twice daily for 20 days, arbidol and inhaled interferon. Glucocorticoid was given at a daily dose of 0.9 mg/kg through intravenous injection. Other treatments included moxifloxacin, γ-globulin and Chinese traditional medicine. On the fourth day after medication therapy, the patient didn't have a fever again. His cough improved markedly within 12 days after hospitalization. On 11 February, he firstly tested negative for SARS-CoV-2, and continuously tested negative for 3 times. Consistently, the patient showed a remarkable radiological improvement (Fig. 1). Furthermore, abnormal laboratory findings almost got back to normal. The patient was discharged on 1 March 2020 and quarantined for another 14 days. A follow-up CT showed lung lesions has completely gone. He felt well after one month from discharge and retested negative for SARS-CoV-2 RNA.

Case 2 (clinically confirmed COVID-19)

A 56-year-old male patient of Wuhan native was sent to emergency department of Tongji Hospital by ambulance on 20 February 2020. He had repeated fever at the beginning of February 2020 without other respiratory symptoms. However, he aggravated with dyspnea, facial cyanosis and headache two days before admission. Chest CT showed there were multiple GGOs, patchy shadows, and pleural effusions in

bilateral lungs. For diagnosed with clinically confirmed COVID-19 according to Chinese guidance on novel coronavirus pneumonia prevention and control program (fifth edition) (http://www.nhc.gov.cn/yzygj/s7653p/202002/3b09b894ac9b4204a79db5b8912d4440/files/7260301a393845fc87fcf6dd52965ecb.pdf. Accessed 5 February 2020), the patient was admitted to quarantine ward. He was in complex condition with history of diabetes, hypertension, coronary heart disease, and post-surgery of cerebral hemorrhage. Additionally, he was diagnosed with acquired immunodeficiency syndrome (AIDS) and received anti-HIV therapy in the past. Monitoring of vital signs showed respiratory rate of 32 breaths per minute, oxygen saturation of 77% at rest, pulse 140 beats per minute. Gas analysis revealed respiratory failure. High-flow nasal cannula oxygen therapy was rapidly performed to ameliorate hypoxemia. Routine tests showed antibodies of treponema pallidum and HIV were both positive, confirmed by CDC, either. Other common respiratory pathogens were tested negative. There were lots of disturbed laboratory parameters in the patient, such as increased inflammatory cytokines (interleukin 2 receptor, interleukin 8, tumor necrosis factor α), elevated liver enzymes, lactic dehydrogenase, and CRP, reduced albumin, increased cardiac troponin and N-terminal pro-brain natriuretic peptide, leukopenia (2.44×10^9/L) and lymphopenia (0.22×10^9/L). On the second day, the patient got worse and was transferred to intensive care unit. Besides mechanical ventilation, comprehensive measures such as controlling inflammation and infection, regulating blood glucose and pressure, anticoagulation, early dehydration, and hepatic protection were adopted to treat both primary pulmonary diseases and comorbidities. Although the oxygen saturation turned better, it was followed with severe conditions of extremely high blood glucose, acidosis, and tachyarrhythmia. On 24 February 2020, the patient with multiple organs dysfunction died of cardiac arrest. The duration from symptoms onset to fatality was 24 days.

Discussion And Conclusions

To date, there is no specific drug available for COVID-19. To protect vulnerable groups is a crucial approach to epidemic. Those people living with HIV were believed to usually be in immunocompromised status. Hence, information on SARS-CoV-2 infection in people with HIV is of great concern. There were rare publications on this topic [6, 7]. Herein we reported cases of co-infection with SARS-CoV-2 and HIV, demonstrating clinical characteristics, laboratory findings and prognosis in these patients.

Both patients in our study had repeated fever at illness onset. With similar laboratory findings to reported cases of COVID-19 [3], leukocytes and lymphocytes were decreased in our cases, while more dramatically in Case 2. Case 1 had a moderate disease course. In contrast, Case 2 was severely ill and dead shortly after admission. Our study indicated SARS-CoV-2 infection might lead to different outcomes in people with HIV. Previous studies demonstrated age, dyspnea, underlying health condition, and lymphocytopenia were risk factors involved in severity and fatality of COVID-19 [8, 9].

Since first reported in 1981, AIDS has already spread in many areas of the world [10]. Loss of CD4+ T cells is a representative feature of AIDS, leading to aberrant immune response [11]. Especially, count of CD4+ T cells and CD8+ T cells were also decreased in severe COVID-19 [12], which indicates there is possible a double-whammy to immune system in patients co-infected with HIV and SARS-CoV-2. HIV-infected patients are prone to secondary and opportunistic infections. Evidence showed that HIV-infected patients were more susceptible to influenza infection and at higher risk for severe influenza than non-HIV-infected patients [13]. However, it's controversial because similar clinical outcomes were reported between two groups [14]. It's possibly elucidated by different immune status of patients included. With non-severely immunosuppressed HIV-infection, these patients had a mild disease course similar to non-HIV infected patients, even milder due to a lack of "inflammation storm". However, severely immunosuppressed HIV-infected patients with influenza had a poorer outcome than patients with influenza only [13, 15]. Attacking respiratory tracts as common targets, SARS-CoV-2 shares partial pathogenesis in stimulating dysregulated immune response with influenza virus [16, 17]. Consequently, it remains a question whether there were different outcomes between HIV infected patients and non-HIV infected patients after SARS-CoV-2 infection.

As no SARS-CoV-2 infection occurred among HIV-infected patients in Thailand, Joob B assumed that HIV-infected patients receiving antiretroviral therapy might not have increased risk, but the possibility of a lower risk for COVID-19 [18]. Lopinavir/ ritonavir, a HIV-1 protease inhibitor, is a major therapeutic drug of AIDS [19]. In vitro studies demonstrated that lopinavir/ritonavir could inhibit SARS-CoV and Middle East respiratory syndrome coronavirus [20, 21]. Lopinavir/ritonavir was recommended as an off-label medicine for COVID-19 in Chinese guidance on novel coronavirus pneumonia prevention and control program (fourth edition) (http://www.nhc.gov.cn/yzygj/s7653p/202001/4294563ed35b43209b31739bd0785e67/files/7a9309111267475a99d4306962c8bf78.pdf. Accessed 27 January 2020). Some studies with small samples described lopinavir/ritonavir was effective in treating COVID-19 [22, 23]. Case 1 recovered after lopinavir/ritonavir therapy concomitant with other drugs. However, a trial of 199 patients with severe COVID-19 found that lopinavir/ritonavir was not beneficial compared with standard care alone [24]. Theoretically, we assumed the effect of lopinavir/ritonavir on patients co-infected with SARS-CoV-2 and HIV might be superior to non-HIV infected patients.

To our best knowledge, only 2 cases of co-infection with SARS-CoV-2 and HIV have been described previously. The first reported patient presented with decreased CD4+ T cells and total lymphocytes. He received lopinavir/ritonavir therapy similar to case 1, however, it cost only 14 days for him to meet discharge criteria [7]. More recently, Zhao and colleagues has reported a case of COVID-19 with co-infection with HIV-1 and hepatitis C virus, whose SARS-CoV-2 RNA were persistently negative while anti-SARS-CoV-2 IgM antibody was positive even after 42 days. The possible explanations by authors were that anti-HIV treatment had anti-SARS-CoV-2 effects, and early incomplete clearance of virus contributed to delay antibody response [6]. However, a potentially high false negative rate of nucleic acid detection of SARS-CoV-2 was reported in the early stage [25]. It should be noticed there was possibility of false negative results in the study. Instead, persistent existence of IgM antibody indicated that impaired immune system in the HIV-infected patient resulted in delay of viral shedding. In fact, HIV-infected patients showed a poor response of specific antibodies and reduced ability of clearance of influenza virus [26].

In summary, there are SARS-CoV-2 and HIV co-infections in the outbreak. Disease course varies in HIV-infected patients with COVID-19. More attention should be paid to the management of these patients. Whether there is any difference about clinical characteristics and prognosis of COVID-19 between HIV-infected and non-HIV infected patients, remains to be further investigated.

Abbreviations

COVID-19: novel coronavirus pneumonia; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; HIV: human immunodeficiency virus; GGO: ground glass opacity; CT: computed tomography; CRP: C-reactive protein; CDC: center for disease control; AIDS: acquired immunodeficiency syndrome

Declarations

Ethics approval and consent to participate

The institutional review boards at Tongji Hospital approved the study protocol.

Consent to publish

A written consent for publication was obtained from himself for the case one, and a written consent for publication was obtained from the patient's wife for the second case. The written consents are available for the journal upon request.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study. If readers would like additional information about the radiological images, he or she should contact the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LC1 and GW drafted the manuscript. FX, LC2, ZZ and QD analyzed the clinical data. MX and YW performed figure preparation. WY, DT and GW revised the manuscript. All authors read and approved the final manuscript.

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Figures

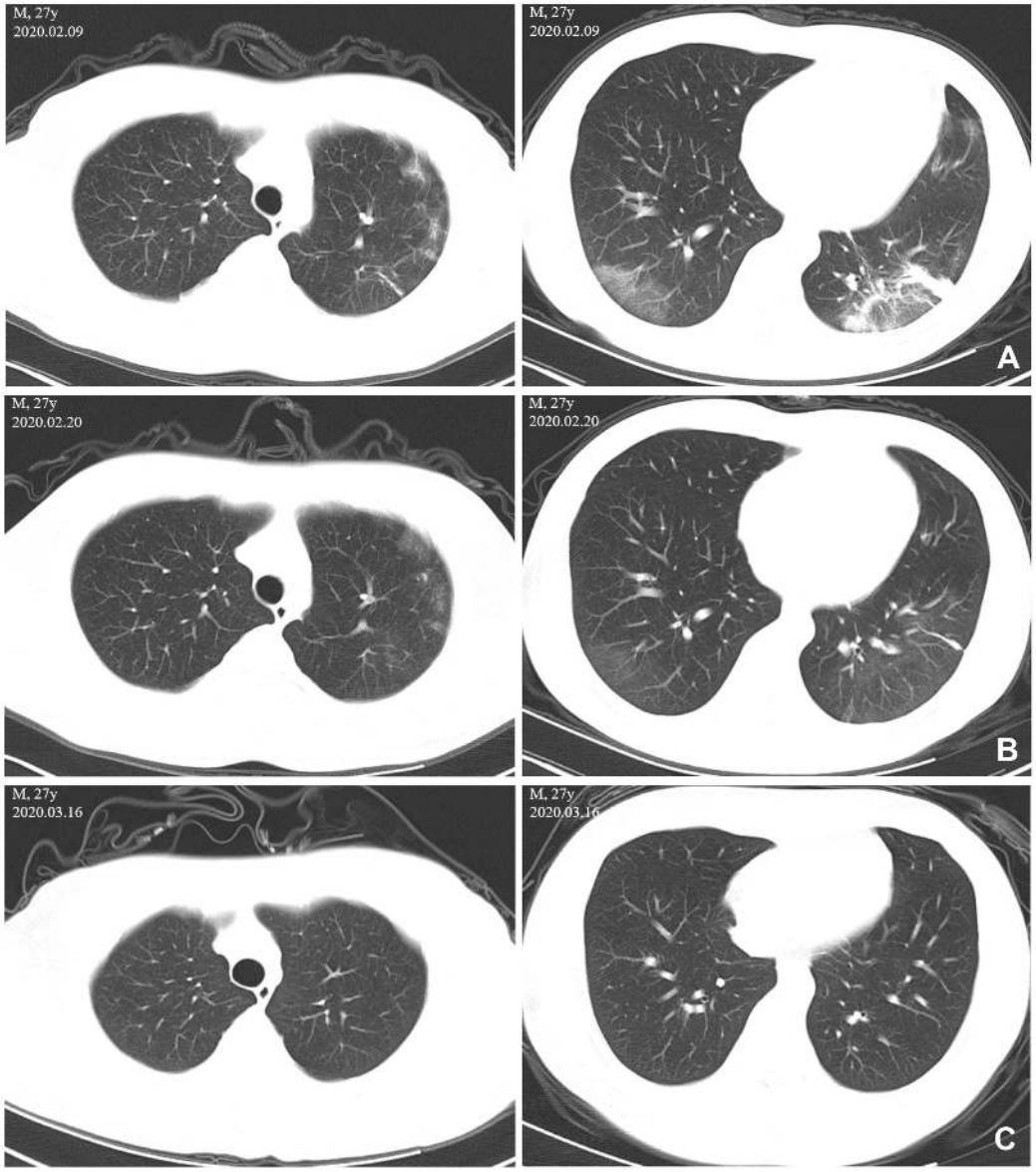

Figure 1

Representative chest axial computed tomography images in lung window of Case 1. The images revealed bilateral multiple ground glass opacities and solid patches on day 17 after symptom onset (A), resolved bilateral multiple ground glass opacities and solid patches on day 28 after symptom onset (B), and nearly normal presentation on day 53 after symptom onset (C).

Supplementary Files

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