Early virus clearance and delayed antibody response in a case of COVID-19 with a history of co-infection with HIV-1 and HCV

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Abstract

The effect of host immune status on SARS-CoV-2 infection remains unknown. Here, we report the first case of COVID-19 with HIV-1 and HCV co-infection, who showed a persistently negative SARS-CoV-2 RNA test, but delayed antibody response in the plasma. This case highlights the influence of HIV-1-induced immune dysfunction on the early SARS-CoV-2 clearance.

Background

In late December, 2019, the outbreak of coronavirus disease 2019 (COVID-19) caused by a novel coronavirus (named SARS-CoV-2) started in Wuhan, China, which has quickly spread to many countries in the world[1]. Clinical manifestations of COVID-19 have been shown to vary widely, from asymptomatic clinical presentation to acute respiratory distress syndrome (ARDS)[2-4]. It remains unknown what host factors may affect the clinical presentation of COVID-19. Our recent studies indicated that monocyte-derived FCN1+ macrophages in bronchoalveolar lavage fluid (BALF) overwhelmed in the severely damaged lungs, while the formation of tissue resident with highly expanded clonal CD8+ T cells in mildly symptomatic patients suggested a robust adaptive immune response associated with better control of COVID-19[5]. Moreover, a higher titer of antibody in the plasma was independently associated with disease severity in patients with COVID-19[6]. These data suggest that the host immune status, to some extent, may affect the outcomes of SARS-CoV-2 infection. However, there is lack of direct evidence for immune influence on the acute infection of SARS-CoV-2. Here, we report a unique case of COVID-19 with preexisting immune dysfunction from previous co-infection of HIV and HCV, who showed persistently negative SARS-CoV-2 RNA test but delayed antibody response in the plasma.

Case presentation

A 38-year-old man was admitted for fever to the Shenzhen Third People's Hospital in Shenzhen, China on January 25, 2020. He reported a travel history to Wuhan, China before January 16, 2020, where the outbreak of COVID-19 started. He had repeated fever accompanied by muscle aches since January 20, 2020, without other symptoms

such as nasal congestion, runny nose, cough, expectoration, chest tightness, palpitation and abdominal distension. He was admitted to the hospital with a low fever of 37.2 ℃ and normal pulse, breath and blood pressure. A chest CT showed right lower pneumonia. He was treated with oseltamivir and IFN-α inhalation. His body temperature rose to 38.3℃on January 26, 2020. With oral fluid supplementation and physical cooling, his body temperature became normal. On January 30, 2020 he was discharged with the resolution of right lower pneumonia and three times of negative test of SARS-CoV-2 RNA from nasopharyngeal swabs by the hospital and Shenzhen CDC. During the hospital course, he had normal laboratory tests, including white blood cell counts, lymphocyte counts, platelet, except that he had slightly elevated plasma CRP on January 26, 2020. This study was reviewed and approved by the Medical Ethical Committee of Shenzhen Third People's Hospital (2020-0110). Written informed consent was obtained from the patient.

Because the patient had a history of co-infection with HIV-1 and HCV four years earlier, on March 2, 2020, 42 days from the onset of his illness, his immune response was evaluated by testing the plasma total antibody (Ab) and IgM Abs specific for SARS-CoV-2 using chemiluminescence kits supplied by Beijing Wantai Biological Pharmacy Enterprise Co., Ltd., China, according to the manufacturer's instructions. The specificity of the assays for total Ab and IgM was determined as 99.1% (211/213) and 98.6% (210/213) by testing of samples collected from healthy individuals before the outbreak of SARS-CoV-2. This test showed total Ab of 13.2 COI and IgM of 49.5 COI, which were significantly lower and higher, respectively, than those in patients with COVID-19 who had recovered from the illness. At this time, his SARS-CoV-2 RNA

test was still negative from nasopharyngeal and anal swabs. Also, RNAs of influenza A and B and respiratory syncytial virus were all negative. One week later, 49 days from the onset of illness, his plasma total Ab rose to 523.8 COI while IgM remained at similar levels with 54 COI (Table 1).

Retrospectively, the patient had been previously co-infected with HIV-1 and HCV through homosexual transmission. After he was diagnosed with co-infection of HIV-1 and HCV in 2016 when his CD4 T cell count was 84 cells/μl, he had been taking lamivudine, tenofovir and efavirenz until today. In 2017, he took antiviral agents (DAA) against HCV for 3 months by himself, and HCV became persistently negative. During the past two years, his CD4 T cell counts have been fluctuating between 250-300 cells/μl. On March 2, 2020, his CD4 and CD8 T cell counts in peripheral blood were 216 and 584, respectively. On March 9, 2020 his CD4 and CD8 T cell counts were slightly increased and plasma HIV-1 and HCV were both tested negative (Table 1). Since the onset of COVID illness in this patient, his close contact partner, an HIV-1-infected person currently taking lopinavir and ritonavir, was tested to be negative for SARS-CoV-2.

Discussion

This patient had a travel history to the epicenter of COVID-19, Wuhan, China and displayed clinical presentation of COVID-19, such as fever and typical pneumonia on CT. Although the test of SARS-CoV-2 RNA was persistently negative on different specimen samplings at various times, plasma anti-SARS-CoV-2 antibody was positive, which, together with the typical clinical presentation, confirmed the diagnosis of SARS-CoV-2 infection. The

reasons/mechanisms underlying the undetectable RNA of SARS-CoV-2 in this case are unclear. One potential explanation is that he was taking anti-HIV-1 agents which had been reported to have anti-SARS-CoV-2 effects.[7] His close contact partner with HIV-1 infection, who was also taking anti-HIV agents, was also tested negative for SARS-CoV-2 RNA. These data are consistent with the notion that some anti-HIV-1 agents may have preventive and/or therapeutic effects against SARS-CoV-2. Another possibility is that the activated type I interferon (IFN-I) may help suppress SARS-CoV-2. Previous study has shown that HIV-1 infection may induce high levels of IFN-I[8], which may to some extent clear SARS-CoV-2 infection, thus leading to persistently undetectable RNA. Future studies are needed to prove these possibilities.

Notably, the SARS-CoV-2-specific total antibody titer was low and IgM was high even after 42 days of illness, which was significantly different from antibody levels in other patients who have recovered from COVID-19 at the similar time points of the illness. Importantly, the total Ab level was largely increased and IgM remained at the peak level one week later, suggesting that the antibody responses against SARS-CoV-2 in this HIV-1-infected case were delayed. It is possible that there was early incomplete clearance of the virus that induced the subsequently delayed antibody response. Future studies are needed to address the mechanism underlying this delayed antibody response to SARS-CoV-2 with a history of co-infection of HIV-1 infection and HCV, even with the latter being cleared in this case.

In summary, we report for the first time a case of COVID-19 with a history of co-infection of HIV-1 and HCV that showed delayed antibody response. This case highlights the possible influence of HIV-1-induced immune dysfunction on the immune responses to and clearance of SARS-CoV-2.

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Table 1. The events and timeline of the disease course in a case of COVID-19 with a history of co-infection of HIV-1 and HCV

(January 25 – March 9, 2020)

Date	Jan 25	Jan 26	Jan 27	Jan 28	Jan 29	Jan 30	Mar 2	Mar 9
Fever (℃)	37.2	38.3	< 37					
Right low pneumonia	yes	yes	yes	yes	yes	no		
Oseltamivir	yes	yes	yes	yes	yes	no		
IFN-α inhalation	yes	yes	yes	yes	yes	no		
Nasopharyngeal swabs	–	–					–	
Anal swab							–	
WBC counts (10^9/L)	2.8	3.1					3.77	
Lymphocyte (10^9/L)		1.48					1.38	
Platelet (10^{12}/L)		170					238	
CRP (mg/L)		16.6					< 5	
IgM (COI)							49 (4.6, 0.5-9.4)[a]	54(1.4, 0.15-11.2)[d]

TotalAb (COI)	13.2 (530, 183-1190)[b]	523.8(207, 8-812)[e]
CD4 T cell (/μL)	216 (250-300)[c]	250
CD8 T cell (/μL)	584	701
HIV-1 RNA (copies/ml)	< 500	< 500
HCV RNA (copies/ml)		< 500

a, The median and range of plasma IgM titers in 8 patients who recovered from COVID-19 with similar illness dates.

b, The median and range of plasma total antibody titers in 8 patients who recovered from COVID-19 with similar illness dates.

c, The range of CD4 T cell counts in recent two years.

d, The median and range of plasma IgM titers in 12 patients who recovered from COVID-19 with similar illness dates.

e, The median and range of plasma total antibody titers in 12 patients who recovered from COVID-19 with similar illness dates.