

Recurrent recurrence of positive SARS-CoV-2 RNA in a COVID-19 patient

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Case Report

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is a highly infectious disease. A small proportion of discharged patients may become positive again for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA, even if they meet the discharge criteria. Herein, we report a rare COVID-19 patient with recurrent recurrence of positive SARS-CoV-2 RNA.

Case presentation: A 68-year-old man was admitted due to fever, muscle pain, and fatigue. He was initially diagnosed with COVID-19 according to two consecutive positive results for SARS-CoV-2 RNA plus clinical symptoms and chest CT findings, and was discharged from hospital when meeting the discharge criteria, including two consecutive negative results. He was tested positive for SARS-CoV-2 RNA twice during the quarantine and was hospitalized again. He was asymptomatic then, but IgG and IgM were both positive. He was discharged in the context of four consecutive negative test results for SARS-CoV-2 RNA after antiviral treatment. However, he was tested positive once again on the 3rd and 4th day after the second discharge, although still asymptomatic. IgG and IgM were still positive. After antiviral treatment, the results of SARS-CoV-2 RNA were negative in three consecutive retests, and he was finally discharged and quarantined for further surveillance.

Conclusion: This case suggests that a small proportion of convalescent patients may become positive again for SARS-CoV-2 RNA and be a virus carrier.

Background

The outbreak of coronavirus disease 2019 (COVID-19) has posed great threats to public health around the world. Most studies focused on epidemiological, clinical, and imaging features of confirmed COVID-19 patients [1,2]. The early detection of asymptomatic virus carrier provides an opportunity to further study the different transmission ways of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and thereby block the spread of SARS-CoV-2. Recently, several studies found that a small proportion of discharged patients turned positive again for SARS-CoV-2 RNA, even if they met the discharge criteria, including two consecutive negative results and were usually asymptomatic then [3,5]. However, it remains controversial regarding the cause of recurrence of positive SARS-CoV-2 RNA, and the infectivity of these patients. Herein, we report a rare COVID-19 patient with recurrent recurrence of positive SARS-CoV-2 RNA.

Case Presentation

A 68-year-old man was admitted due to fever, muscle pain, and fatigue for 8 day. On January 27, 2020, the patient and his wife had a family dinner with his niece and son-in-law, who were first diagnosed as COVID-19 later. On January 30, he got a fever of 38.0 °C with muscle pain and fatigue, and took some medicine himself for 4 days. His temperature returned to normal and the symptoms were relieved. However, he had a fever again on February 6. The next day, he was taken to a local hospital. The routine blood test showed decreased lymphocyte counts and lymphocyte percentage. The common influenza

virus antigenes (including influenza A virus, influenza B virus, and parainfluenza virus) were tested negative. But the chest computerized topography (CT) showed patchy areas of ground-glass shadows in both lungs. The results of two consecutive real-time reverse transcription-polymerase chain reaction (RT-PCR) tests for SARS-CoV-2 RNA were both positive through throat swabs, on February 8 and 9, respectively (**Figure 1**). He had a history of hypertension, diabetes and coronary heart disease. His wife and daughter, as close contacts, were also diagnosed with COVID-19 during the quarantine.

Although he received antiviral treatment with lopinavir/ritonavir and interferon- α and symptomatic treatment, he still suffered from fever, complicated with cough, expectoration, chest distress and asthma. The chest CT reexamination suggested that the shadows of both lungs were larger and more than before. He was transferred to an infectious disease hospital. The results of T lymphocyte subtype detection showed that the absolute count of CD3⁺, CD4⁺ and CD8⁺ cell decreased, and the ratio of CD4⁺ / CD8⁺ cell increased. Cytokine interleukin-6 (IL-6) was also elevated (**Figure 2, Table 1**). He was eventually diagnosed as severe COVID-19 with atrial fibrillation and cardiac insufficiency. After oxygen inhalation, antiviral treatment and symptomatic treatment, the respiratory symptoms improved and the temperature returned to normal. The chest CT on February 20 showed the remarkable absorption of the shadows in both lungs. On February 21 and 22, he was tested negative for SARS-CoV-2 RNA and discharged without any symptom 1 week later (**Figure 1**).

Table 1 The dynamics of lymphocyte subtypes and cytokine IL-6 in the COVID-19 patient

	Feb 14	Feb 16	Feb 18	Feb 19	Mar 06
CD3 ⁺ absolute count, cell/ul	640	/	320	801	874
CD4 ⁺ absolute count, cell/ul	451	/	256	698	644
CD8 ⁺ absolute count, cell/ul	140.94	/	48.95	77.56	185.59
CD4 ⁺ / CD8 ⁺ ratio, %	3.2	/	5.23	9	3.47
CD19 ⁺ cell, %	/	/	28	36	19
NK cell, %	/	/	10	2	6
IL-6, pg/ml	57.14	72.31	/	297.7	38.8

NK: natural killer; IL-6: interleukin-6

On March 2, he was tested positive for SARS-CoV-2 RNA at the quarantine station, but he had not any symptom then. On March 5, the retest result for SARS-CoV-2 RNA was still positive, and he was hospitalized at the infectious disease hospital. During this quarantine period, the patient did not contact with any COVID-19 patient. The chest CT the next day showed the marked lesion absorption than before. IgG and IgM were both positive. He continued to receive antiviral treatment. From March 9 to 12, he was tested negative for SARS-CoV-2 RNA in four consecutive detections and discharged on March 12. However, the RT-PCR tests were repeated for surveillance on March 15 and 16, and the results became

positive once again. He was admitted to our hospital, although asymptomatic. IgG and IgM were still positive. After antiviral treatment, the three consecutive RT-PCR test results of SARS-CoV-2 RNA were negative from March 18 to 20. He was discharged on March 21 and was under quarantine (**Figure 1**).

Discussion

Although a small proportion of discharged COVID-19 patients became positive again for SARS-CoV-2 RNA, it remains controversial regarding the cause of recurrence of positive SARS-CoV-2 RNA and the infectivity of these recurrently positive patients. The recurrence of SARS-CoV-2 RNA positivity may be related to the biological characteristics of SARS-CoV-2, underlying diseases, clinical status, immune function, and sampling, processing and detecting of samples [5-7]. In addition, re-infection or false negativity sometimes for nasopharyngeal test cannot be ruled out [8].

The patient reported here repeatedly became positive for SARS-CoV-2 RNA after two consecutive discharge, even if he met the discharge criteria. Even in the context of four consecutive negative RT-PCR test results plus absence of clinical symptoms in the second hospitalization, he was still tested positive on the 3rd and 4th day after discharge, suggesting that at least a proportion of convalescent patients may become positive again. Recurrent recurrence of positive SARS-CoV-2 RNA might be related to his age, many concomitant diseases, severe pneumonia and immune deficiency in this patient. The decreased T-lymphocytes and increased CD4+/CD8+ ratio with persistent positive IgM also endorsed this point, and the duration of RNA detection may relate to the host cell immunity [6,7,9]. It is supposed that the "virus repository" of the lungs may detoxify intermittently or the virus of the lower respiratory tract is continuously and slowly released [9]. Although the clinical symptoms disappeared in these patients, the virus had not been completely cleared. They may still be virus carriers, but it is not clear if they are infectious. However, also a few patients with the recurrence of positive SARS-CoV-2 RNA were worse than before, suggesting that these patients might be still infectious.

In addition, it was rare for the present patient to have a period of 47 days from onset to the last positive result in respiratory samples due to recurrent recurrence of positive SARS-CoV-2 RNA. In a recent study, the longest time from onset to the last positive SARS-CoV-2 RNA was 31 days in respiratory samples and 47 days in faecal samples [10]. The time remaining positive for SARS-CoV-2 RNA after onset in faecal samples was 11.2 days longer than that in respiratory samples, which indicated whether these patients were true-negative and whether they were infectious remain to be further discussed [10]. Therefore, further follow-up and virus detection are still needed after discharge and discontinuation of quarantine.

Given the possibility of recurrently positive SARS-CoV-2 RNA, especially in immunocompromised patients, and the uncertainty of infectivity of recurrently positive patients, the discharged patients should continue to be quarantined for at least 14 days and monitored for SARS-CoV-2 RNA repeatedly, and be wary of becoming a virus carrier and thereby spreading the virus to others.

Conclusions

This case suggests that a small proportion of convalescent patients may become positive again for SARS-CoV-2 RNA and be a virus carrier, which need to be vigilant.

Abbreviations

COVID-19: Coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; CT: computerized topography; RT-PCR: reverse transcription-polymerase chain reaction; L-6: Cytokine interleukin-6

Declarations

Ethics approval and consent to participate

All authors' institutions did not require ethical approval for publication of a single case report.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying data. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors have no conflicts of interest to declare.

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Authors' contributions

CS,WA, LJ, and LY contributed to data collection and interpretation. CS and WA wrote the initial draft of the manuscript. LY assisted in the preparation of the manuscript. WJ and XM reviewed the manuscript. The authors read and approved the final manuscript.

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Figures

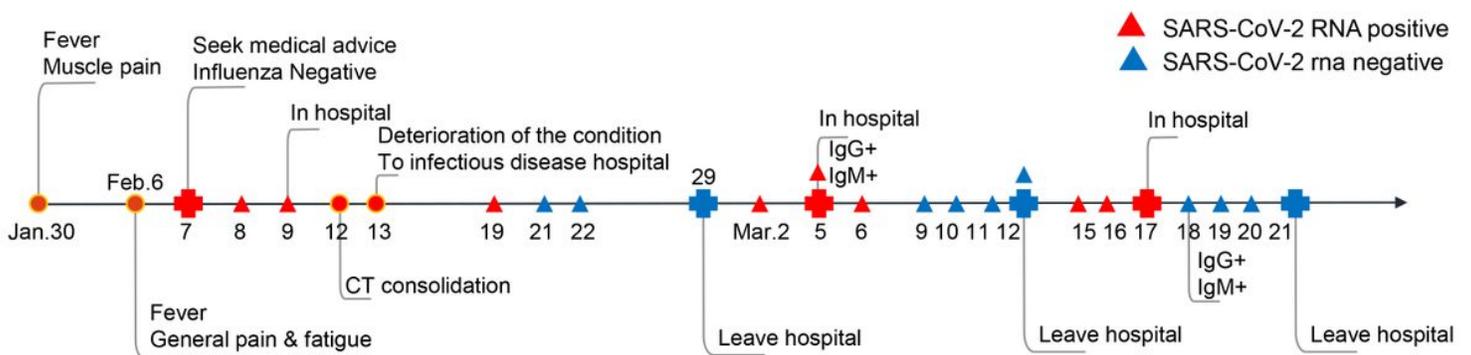


Figure 1

The disease evolution and dynamics of SARS-CoV-2 RNA on RT-PCR in the COVID-19 patient.

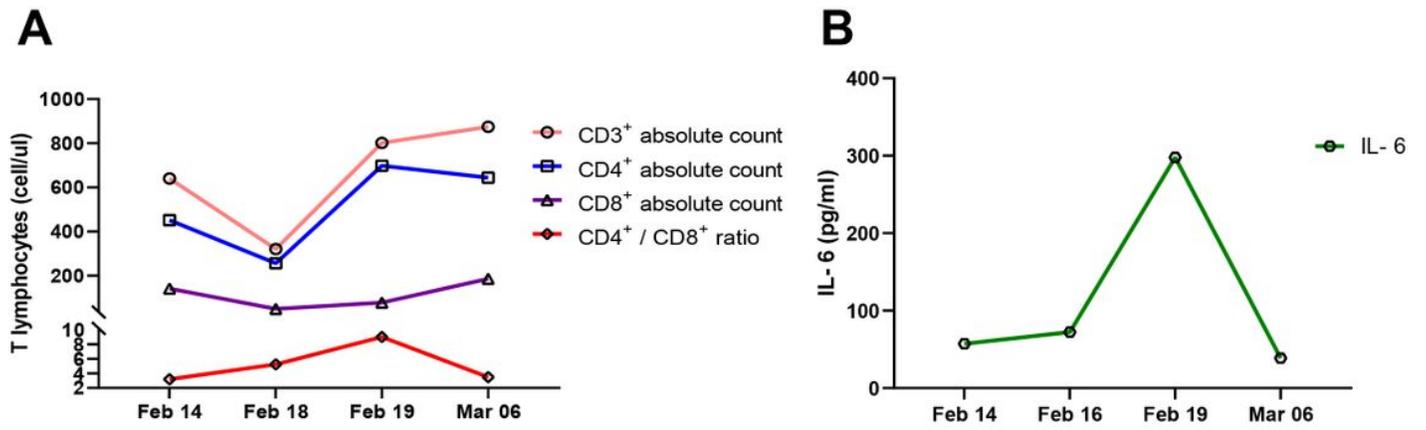


Figure 2

A: The dynamics of B lymphocyte subtypes in the COVID-19 patient. B: The dynamics of cytokine IL-6 in the COVID-19 patient.