

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

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Case Report

Keywords: Coronavirus disease 2019, SARS-CoV-2, Recurrence

Posted Date: November 3rd, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-23197/v2>

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Abstract

Background: Coronavirus disease 2019 (COVID-19) is a highly infectious disease. A small proportion of discharged patients became positive again for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA, even though they met 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. He was discharged from hospital when meeting the discharge criteria. He tested positive for SARS-CoV-2 RNA twice during the quarantine and was hospitalized again. He was asymptomatic then, but IgG and IgM anti-SARS-CoV-2 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 tested positive once again on the 3rd and 4th days after the second discharge. Two days later, the SARS-CoV-2 RNA results became negative in three consecutive retests, and he was finally discharged.

Conclusion: This case suggests that convalescent patients may become positive again for SARS-CoV-2 RNA after discharge due to prolonged nucleic acid transition. However, the potential infectivity of these patients needs to be further confirmed in future research.

Introduction

The outbreak of coronavirus disease 2019 (COVID-19) has posed great threats to public health around the world. Most studies have focused on the epidemiological, clinical, and imaging features of confirmed COVID-19 cases.^{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 its spread. Recently, several studies found that a small proportion of discharged patients became positive again for SARS-CoV-2 RNA, even though they met the discharge criteria including two consecutive negative results.³⁻⁵ However, the cause of recurrence of SARS-CoV-2 RNA positivity and the infectivity of these patients remain controversial. Here, we report a rare COVID-19 patient with recurrent recurrence of SARS-CoV-2 RNA positivity during quarantine after discharge.

Case Report

A 68-year-old man was admitted due to fever, muscle pain, and fatigue over 8 days. On January 27, 2020, the patient and his wife had a family dinner with his niece and son-in-law, who were later diagnosed with COVID-19. On January 30, he had a fever of 38.0 °C with muscle pain and fatigue, and self-medicated for 4 days. His temperature returned to normal, and his symptoms were relieved. However, he had a fever again on February 6. The next day, he was taken to a local hospital. A routine blood test showed decreased lymphocyte counts and lymphocyte percentages. His blood was negative for common influenza virus antigens (including influenza A virus, influenza B virus, and parainfluenza virus). However,

chest computed 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 using nasopharyngeal swabs were positive (cycle threshold [Ct] of 22.80 and 19.79, respectively) on February 8 and 9, respectively (*Figure 1*). The Ct value of the reference gene was ≤ 38 according to the kit instruction (Shanghai BioGerm Medical Biotechnology Co., Ltd). 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 period.

On February 13, he experienced fever complicated by cough, expectoration, chest distress and asthma. Chest CT reexamination suggested that more shadows on both lungs and also larger shadows. 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+ cells was decreased and that the ratio of CD4+/CD8+ cells was increased. The level of cytokine interleukin-6 (IL-6) was also elevated (*Figure 2, Table 1*). He was eventually diagnosed with severe COVID-19 with atrial fibrillation and cardiac insufficiency. After oxygen inhalation, antiviral treatment with lopinavir/ritonavir, and symptomatic treatment, his respiratory symptoms improved, and his temperature returned to normal. Chest CT on February 20 showed remarkable absorption of the shadows in both lungs. On February 21 and 22, he tested negative for SARS-CoV-2 RNA and was discharged without any symptom 1 week later (*Figure 1*).

On March 2, he tested positive for SARS-CoV-2 RNA (Ct of 36.41) at the quarantine station, but he had no symptoms. On March 5, the retest result for SARS-CoV-2 RNA was still positive (Ct of 31.67), and he was hospitalized at the infectious disease hospital. During this quarantine period, the patient did not contact other COVID-19 patients. Chest CT the next day showed marked lesion absorption. IgG and IgM anti-SARS-CoV-2 were both positive. He continued to receive antiviral treatment. From March 9 to 12, he tested negative for SARS-CoV-2 RNA in four consecutive tests and was 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 (Ct of 30.41 and 29.69, respectively). He was admitted to our hospital on March 17. IgG and IgM anti-SARS-CoV-2 were still positive on March 18. However, three consecutive RT-PCR test results for SARS-CoV-2 RNA were negative from March 18 to 20. He was discharged on March 21 and was under quarantine (*Figure 1*).

The requirement for ethics approval to publish this case report was waived by the Institutional Review Board of the Affiliated Hefei Hospital of Anhui Medical University. Written informed consent to publish the case was provided by the patient.

Discussion

Although some convalescent COVID-19 patients became positive again for SARS-CoV-2 RNA, the cause of recurrence of SARS-CoV-2 RNA positivity and the infectivity of these recurrently positive patients remain controversial. Based on previous studies, recurrence of SARS-CoV-2 RNA positivity may be

related to the biological characteristics of SARS-CoV-2, underlying diseases, clinical status, host immune function, sampling and sample processing and detection.⁵⁻⁸ However, reinfection cannot be ruled out.

First, in this case, four consecutive negative SARS-CoV-2 results during the second hospitalization might have greatly reduced the possibility of false-negative results. Second, the patient was under single isolation after discharge from the hospital, and his range of daily activities was restricted during the so-called after-hospital quarantine. These measures made the chance of reinfection from a potential source of infection extremely low and make the inference of two recurrences of SARS-CoV-2 RNA positivity more convincing. Recurrent recurrence of positive SARS-CoV-2 RNA might be related to his venerable age, many concomitant diseases, severe pneumonia and immune deficiency. The decreased level of T-lymphocytes and increased CD4+/CD8+ ratio with persistent positive IgM also support this point, and the duration of RNA detection may be related to host cell immunity.^{6,7,9} It is supposed that the “virus repository” of the lungs may detoxify intermittently or that virus in the lower respiratory tract is continuously and slowly released.⁹ Although the clinical symptoms disappear in these patients, the virus has not been completely cleared and they may still be virus carriers and infectious, especially in patients with immunodeficiency. However, the condition of a few patients with recurrence of SARS-CoV-2 RNA positivity was worse than before, especially among elderly patients.¹⁰ In our hospital, we also interviewed an elderly patient with the recurrence of SARS-CoV-2 RNA positivity after discharge, and his clinical symptoms and lung lesions were significantly worse than before.

All of the above findings suggest the complexity of infectivity in patients with recurrence of SARS-CoV-2 RNA positivity. Several reasons might contribute to such situations. First, it has been shown that SARS-CoV-2 RNA positivity after a hospital stay may be due to false-negative RT-PCR test results.^{8,11} Second, prolonged nucleic acid conversion and viral reactivation, which are more frequently observed in elderly patients with a relatively weak immune response, would cause recurrence and render their secretions contagious.^{10,12,13} Taken together, from a public health perspective, more caution should be paid to the period after release from the hospital, as patients should still receive regular RNA detection with monitoring for recurrence.

According to the dynamic evolution of Ct value of SARS-CoV-2 RNA positive results and the lack of clinical symptoms, the two recurrences of SARS-CoV-2 RNA positivity in this patient might be attributed to prolonged nucleic acid transition. Of course, viral reactivation was not completely excluded. Regardless, whether these patients are infectious remains controversial. Virus isolation and cell culture test may help to determine whether the virus has infectious activity. In addition, it was rare for this patient to repeatedly become positive for SARS-CoV-2 RNA after two discharges, with a long period of 47 days from onset to the last positive result based on respiratory samples due to two recurrences. In a recent study, the longest time from onset to the last positive SARS-CoV-2 RNA result was 31 days for respiratory samples and 47 days for faecal samples.¹⁴

Given the possibility of recurrent SARS-CoV-2 RNA positivity, especially in immunocompromised patients, and the uncertainty of infectivity of recurrently positive patients, discharged patients should

continue to be quarantined for at least 14 days or more and repeatedly monitored for SARS-CoV-2 RNA and be aware of the possibility of being a virus carrier and thereby spreading the virus to others.

Conclusions

This case suggests that convalescent patients may become positive again for SARS-CoV-2 RNA after discharge due to prolonged nucleic acid transition. However, the potential infectivity of these patients needs to be further confirmed in future research.

Declarations

Consent for publication

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

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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Figures

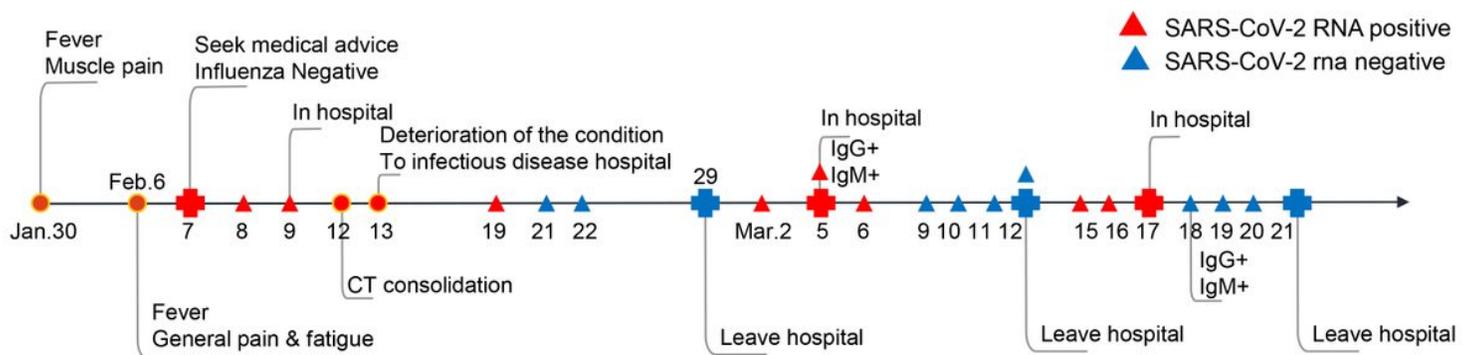


Figure 1

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

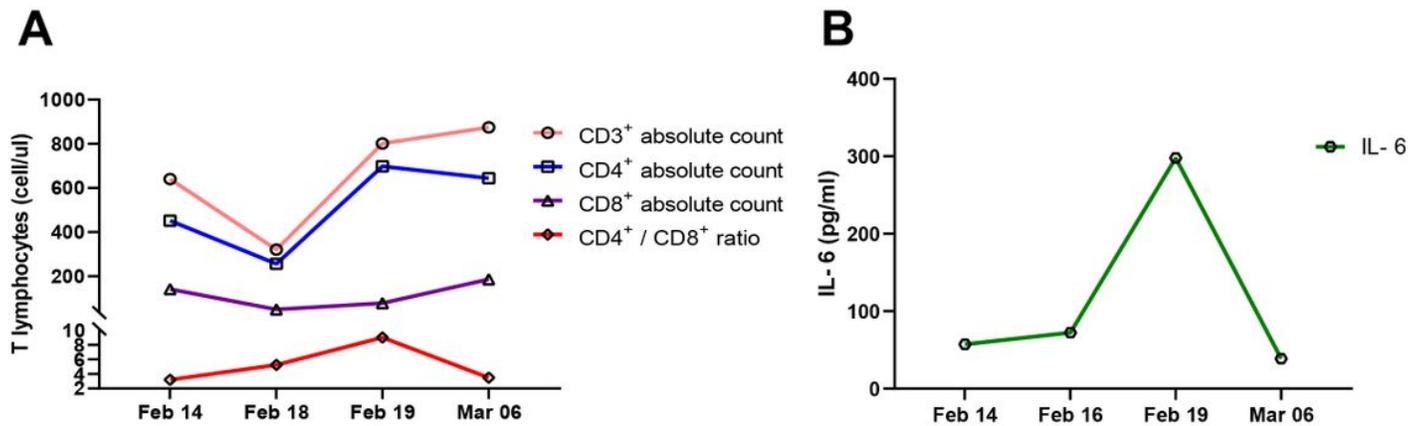


Figure 2

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