The host immune response of a discharged COVID-19 patient with twice reemergence of SARS-CoV-2: a case report

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Abstract

Background: The coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a global pandemic. There have been reports that long-term SARS-CoV-2 RNA shedding and re-infection of COVID-19 patients existed. However, the specific mechanism, diagnosis, and treatment of COVID-19 are still unclarified.

Case presentation: In this case, we reported a 64-year-old patient who had a long-term course of COVID-19 for 174 days with two retests of SARS-CoV-2 RNA positive after discharging from the hospital. The patient’s serum immunoglobulin G (IgG) of SARS-CoV-2 tested positive after the initial infection. And during treatment, the CD4+ T cell count and ratio to peripheral blood mononuclear cell (PBMC) were in dynamic change.

Conclusions: Our results suggested that the host immune system responded with IgG production after SARS-CoV-2 infection, but was not protective enough for the patient. The reemergence of SARS-CoV-2 could be related to the cell count and proportion of CD4+ T cells in PBMC. And the increase of CD4+ T cells after treatment may help to clear the virus.

Keywords: SARS-CoV-2, COVID-19, Reemergence, RNA test, Host immune response

Background

The quantitative real-time polymerase chain reaction (qRT-PCR) was used generally to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with samples of the nasopharynx, pharynx, bronchoalveolar lavage fluid, feces, and blood [1]. And there has been a patient with long-term SARS-CoV-2 RNA shedding for up to 105 days after initial diagnosis as coronavirus disease 2019 (COVID-19) [2]. Additionally, there were some symptomatic and asymptomatic cases who had RNA test positive again for SARS-CoV-2 following a period of negative testing exited [3]. Thus, it’s been a hotspot that whether it is long term viral persistence, sampling issues, or re-infection for ‘recovered’ patients with re-tested SARS-CoV-2 RNA positive [4–6]. However, the exact mechanism for SARS-CoV-2 reemergence is still unclear, and high-level vigilance remains required for this kind of reemergence. Here, we reported a case of COVID-19, who was twice-time reemergence and had a long-term course of SARS-CoV-2 for 174 days.

Case presentation

The patient was a 64-year-old Chinese man who had baseline comorbidities including coronary atherosclerotic heart disease, high blood pressure, and diabetes. The epidemiological history of the patient: no history of travel in Wuhan and surrounding areas, the patient’s
son-in-law and the mother of the patient's son-in-law were both diagnosed with COVID-19 on February 12, 2020. The medications he takes daily include Aspirin, Atorvastatin, Bisoprolol, and Acarbose. As shown in the time axis of Fig. 1A, he developed a fever up to 38 °C on February 6th with a dry cough and mild fatigue but had no treatment. Four days later, he developed a more severe dry cough and his body temperature rose to 40 °C, and then he went to the Peking University Third Hospital. The chest computed tomography (CT) scan showed a symmetrical thoracic cage, centered trachea, no displacement of the mediastinum, and multiple ground-glass opacity under the pleura of both lungs (Fig. 1B). The sera alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBIL) were slightly increased. The following nasal swab sample of the SARS-CoV-2 test...
was positive with the qRT-PCR assay targeting ORF1ab and N genes of the virus genome (day 0). The patient was then transferred to the Beijing Youan hospital.

At admission, the patient's physical condition was examined and, the oxygen saturation (SaO2%) was 95%-98%. And the CT result showed severe inflammation in his lungs. Then, the patient received treatment including Methylprednisolone (40 mg, day 2), Bicyclol piece, and Silybin glutamine tablets for liver protection. After treatment, the patient's liver enzymes returned to normal, cough and other symptoms gradually decreased. The qRT-PCR examination for SARS-CoV-2 of the patient was performed on days 11 and 12, and both tests were negative. Since the discharge criteria of the COVID-19 is two consecutive negative SARS-CoV-2 RNA tests, the patient was then discharged from the hospital and was instructed to receive a quarantine at home. Besides, there was no new infection of SARS-CoV-2 confirmed among his family and close contact.

First-time reemergence: On day 31, the patient was tested positive for SARS-CoV-2 when he returned to the hospital for a follow-up. He complained of no symptoms, including fever, cough, sputum, chest tightness, and dysphoria. However, the serum immunoglobulin G (IgG) of SARS-CoV-2 was positive, and the serum immunoglobulin M (IgM) of SARS-CoV-2 was negative. These results suggesting that the adaptive immune responded after the first infection, and this temporal reemergence might not be due to re-infection but re-activation of the virus [7]. A chest CT scan of the patient on day 31 showed grinding glass shadow of both lungs was absorbed more than before. Subsequently, the patient was treated with Chloroquine phosphate tablet (500 mg, twice a day, day 52–59). However, upon completion of the treatment, the patient still failed to meet the discharge criteria. The patient was then prescribed Thymalfasin (1.6 mg, hypo-dermic injection, day 59–69) for injection of the next 20 days. During this stage of treatment, the patient took traditional Chinese medicine (TCM) decoction, which consisted mainly of Honeysuckle, Forsythia, Scutellaria, Angelica, Radix achyranthes, Honeysuckle. After TCM formula were: Ginseng, Bupleurum, Radix scutellariae, Angelica, Radix achyranthes, Honeysuckle. After the treatment, the SARS-CoV-2 RNA tests of the patient were both negative. The detailed SARS-CoV-2 RNA test results of the patient were in Table 1.

Discussion and conclusions

Like previous reports, our observations also offered evidence for long-term shedding of SARS-CoV-2. The viral load result in a sample may fluctuate and be restricted by testing methods [8], where false-negative results occur during the disease process. On the other side, temporal but inadequate immune response and drug intervention could temporarily suppress the virus; however, once the drug is discontinued or immune function compromised, the re-activation of SARS-CoV-2 occurs. It is not clear whether this positive finding is associated with disease transmission potential. Thus, giving the disastrous consequences of transmission, a prolonged
observation and multiple dimensions of virological assessment should be considered for such patients.

Furthermore, the study showed that the balance between regulatory and cytotoxic SARS-CoV-2-reactive CD4+ T cells in COVID-19 patients was broken, and a reduced proportion of regulatory CD4+ T cells was observed [9]. And the T-cell subset counts including CD8+ and CD4+ T cells in peripheral blood could be used as discriminatory biomarkers for diagnosis and severity prediction of COVID-19 [10]. Our results further suggested that the reemergence of SARS-CoV-2 could be related to the cell count and proportion of CD4+ T cells, and the increase of CD4+ T cells after treatment may help the host immune to clear the viral infection. What is noteworthy is that the researchers found that six months after infection, the neutralizing antibodies in COVID-19 patients were significantly lower than during the acute phase, which increased the risk of re-infection for patients presenting compatible symptoms of COVID-19 [11]. In our report, the patient had recurrent COVID-19 while his serum-IgG was positive, indicating that a low antibody level may not provide sufficient protection against SARS-CoV-2 re-infection. However, it needs more evidence to prove.

### Abbreviations
COVID-19: Coronavirus disease 2019; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; qRT-PCR: Quantitative real-time polymerase chain reaction; CT: Computed tomography; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TBIL: Total bilirubin; PBMC: Peripheral blood mononuclear cell; IgG: Immunoglobulin G; IgM: Immunoglobulin M.

### Acknowledgements
The authors would like to thank all the medical workers participate in the study.

### Authors’ contributions
ZXB and ZY wrote the manuscript, contributed equally to this work. YYA and LXK initiated and designed the project. LYJ and CX collected the data. CHN performed the data analyses. ZXB prepared Table and Figure. All authors read and approved the final manuscript.

### Funding
This study was founded by Research Fund of Institute of Liver Diseases, Beijing University of Chinese Medicine (No. 2016-173-05) and Scientific research and innovation team project of Beijing University of Chinese Medicine (No. 2019-JYB-TD-009).

### Availability of data and materials
Not applicable (no datasets were generated or analyzed during the current report).

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**Table 1** The SARS-CoV-2 RNA tests of the patient from 2/11/2020 to 8/3/2020

| Date  | Test | Date  | Test | Date  | Test | Date  | Test | Date  | Test | Date  | Test | Date  | Test |
|-------|------|-------|------|-------|------|-------|------|-------|------|-------|------|-------|------|
| 2/11  | +    | 3/13  | +    | 4/9   | +    | 5/16  | +    | 6/1   | +    | 7/1   | +    | 8/2   | -    |
| 2/22  | -    | 3/22  | +    | 4/30  | +    | 5/21  | +    | 6/5   | +    | 7/6   | -    | 5/17  | +    |
| 2/23  | -    |       |      |       |      |       |      |       |      |       |      | 5/19  | +    |
| 2/24  | +    | 6/9   | +    | 7/11  | +    | 5/25  | +    | 6/10  | +    | 7/12  | -    | 5/26  | +    |
| 2/27  | +    | 6/12  | +    | 7/28  | +    | 5/28  | +    | 6/13  | +    | 7/29  | +    | 5/29  | +    |
| 5/30  | +    | 6/18  | +    | 8/2   | -    | 5/31  | +    | 6/19  | +    | 8/2   | -    | 6/21  | -    |
| 6/22  | -    |       |      |       |      |       |      |       |      |       |      | 6/23  | +    |
| 6/24  | -    |       |      |       |      |       |      |       |      |       |      | 6/25  | +    |
| 6/26  | -    |       |      |       |      |       |      |       |      |       |      | 6/27  | +    |
| 6/28  | -    |       |      |       |      |       |      |       |      |       |      | 6/29  | +    |

+, test positive; -, test negative
Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent for publication of their clinical details and images was obtained from the patient.

Competing interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Received: 24 April 2021 Accepted: 9 September 2021
Published online: 23 September 2021

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