Persistent infection with SARS-CoV-2 – first direct evidence

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Short report

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Abstract

Whether persistent infections with SARS-CoV-2 exist is still unknown. This study reported a case with COVID-19 who still got positive RT-PCR test results for SARS-CoV-2 in his throat swabs about 4 months post symptom onset. This case is potentially the first direct evidence of persistent infection with SARS-CoV-2.

Introduction

Coronavirus disease in 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] It has spread widely across the world. Whether persistent infections with SARS-CoV-2 exist is still unknown. This study reported a case with COVID-19 who still got positive time reverse-transcriptase polymerase chain reaction (RT-PCR) test results for SARS-CoV-2 in his throat swabs about 4 months post symptom onset.

Methods

The study was approved by the institutional ethics board at Zhongnan Hospital of Wuhan University and requirement for written informed consent was waived by the institutional ethics board for emerging infectious disease. One 30-year old male patient is a physician with no preexisting conditions. He had prior close contact with patients with respiratory infections in December 2019 and lived close to Huanan Seafood Market. He still got positive RT-PCR test results for SARS-CoV-2 in his throat swabs about 4 months post symptoms onset.

Results

The patient started to show typical symptoms of COVID-19 on January 3, 2020 (disease course see Fig. 1). These symptoms include intermittent fever, occasional dry cough, general fatigue, malaise, poor appetite, and poor sleep. He took oral azithromycin by himself. He went to the fever clinic at Zhongnan Hospital of Wuhan University on January 7, 2020. He received intravenous infusion of amoxicillin/Clavulanate and his symptoms were improved. The chest CT images on January 8, 2020 showed infections in both lungs (viral pneumonia suspected) and he was admitted to the hospital. He received antivirals (oseltamivir, ganciclovir), antibiotics (yapenem, linezolid, moxifloxacin, ceftriaxone/tazobactam), and corticosteroids (methylprednisolone) treatment and low-flow oxygen in the hospital. Antibody test and nuclear acid test for common respiratory pathogens (adenovirus, parainfluenza virus, influenza virus type A and B, H7 avian influenza, Legionella, mycoplasma, and chlamydia) all were negative. Blood culture for aerobic and anerobic bacteria both came negative. After his symptoms were alleviated (no fever or cough) and lung infections got better as shown on chest CT images (January 9 and 14), he was discharged on January 15, 2020 with a diagnosis of COVID-19 (clinical diagnosis).

The patient was followed up at the outpatient clinic after discharge. RT-PCR tests for SARS-CoV-2 in the throat swabs were negative on January 28, positive on February 10 and 15, negative on February 17, 19, and 21 and March 4, positive on March 7, negative on March 11, 13, 14, and 24, positive on April 3, negative on April 8, and positive on April 14, 17, and 19, 2020. The results of IgM/IgG test for antibodies to SARS-CoV-2 (spike protein and nucleocapsid protein) were 1.37 AU/ml for IgM (negative) and 48.19 AU/ml for IgG (positive) on March 16, 2020 and 1.14 AU/ml for IgM (negative) and 49.65 AU/ml for IgG (positive) on April 3, 2020. His chest CT images showed continuous improvements in lung infections (Fig. 2).

Discussion

This case is potentially the first direct evidence of persistent infection with SARS-CoV-2. After infected with SARS-CoV-2 (several days before symptom onset on January 3, 2020), the patient was still tested positive for the virus in the throat swab about 4 months later on April 24, 2020. To our observation, this patient was strictly self-quarantined after hospital discharge and unlikely to be reinfected after another exposure. The negative IgM and positive IgG to SARS-CoV-2 and continuous improvements in lung infections (chest CT images) would also help rule out reinfection. After seroconversion, a rapid decline in viral load is not necessarily followed.[2] Infections with some viruses, such as HIV, do not illicit robust protective immunity[3]. Infections with SARS-CoV-2 might be a similar case. SARS-CoV-2 detected in the throat swabs of this patient is most likely residual RNA fragments rather than viable virus. Live virus SARS-CoV-2 can be isolated from the throat in the early disease course[2], but unlikely to be isolated two or three months post infection. Live virus was never isolated from the upper respiratory track in patients infected with SARS, and unlike SARS-CoV-2, viral load in the throat in patients infected with SARS rapidly declined to undetectable range.[2] Live SARS-CoV-2 was found in pulmonary tissues of a patient with three-consecutive negative RT-PCR tests for SARS-CoV-2.[4] COVID-19 is a systemic disease involving many organs that express angiotensin-converting enzyme 2 (ACE2), the cell receptor for viral entry of SARS-CoV-2. Live SARS-CoV-2 may be found in the lung or other organs in the late phase of the disease. Negative RT-PCR tests for SARS-CoV-2 are usually due to the low viral load in the clinical specimen and low sensitivity of RT-PCR test (lower limit of detection ~ 500 copies/ml). More sensitive test methods, such as SHERLOCK (lower limit of detection ~ 100 copies/ml)[5], may detect the virus in clinical samples with low viral load that might have an otherwise negative RT-PCR test result. This may partly explain the intermittently positive RT-PCR test results for SARS-CoV-2 in throat swabs in our patient. The National Health Commission of China reported over 30 cases of patients infected with SARS-CoV-2 who were still tested positive for the virus 2–3 months after initial infection.[6] Whether these patients are still infectious needs close monitoring. The proportion of persistent infections among all infected patients is also not known. Persistent infections (chronic infection and latent infection) are observed in a wide variety of viruses after primary infection, such as HIV, HBV, HCV, HSV, VZV, CMV, HPV, EBV, etc. It seems that SARS-CoV-2 may join the list of viruses that can cause persistent infections.

Conclusion

This case is potentially the first direct evidence of persistent infection with SARS-CoV-2.

Abbreviations

COVID-19: Coronavirus disease in 2019;

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2;

RT-PCR: time reverse-transcriptase polymerase chain reaction;

Declarations

Ethics approval and consent to participate

The study was approved by the institutional ethics board at Zhongnan Hospital of Wuhan University. Requirement for written informed consent was waived by the institutional ethics board for emerging infectious diseases.

Consent for publication

Not applicable.

Availability of data and material

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Dr. X. Wang, Tao Liu,and T. Liu had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Tao Liu, H. Tao and J. Peng contributed equally to the study. Drs Tao Liu, F. Zhou, T. Liu and X. Wang contributed equally as senior authors. Concept and design: T. Liu and X. Wang.

Acquisition, analysis, or interpretation of data: Tao Liu, H. Tao, J. Peng and F. Zhou. Drafting of the manuscript: Tao Liu, H. Tao, J. Peng. Critical revision of the manuscript for important intellectual content: T. Liu, X. Wang.

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