A COVID-19 Patient Discharged According to Strict Discharge Standards: Viral Negativity in Both Nasopharynx and Feces

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Abstract

Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) currently has spread all over the world. However, the dynamic characteristics of SARS-CoV-2 infections have not previously been described in detail. Here, we report a cured patient in West China Hospital, and describe the dynamic detection of SARS-CoV-2-RNA in different specimens and viral specific IgM and IgG antibodies in blood. The findings suggest that the faecal SARS-CoV-2-RNA negativity may be considered as a new standard for discharge. Serum IgM and IgG antibodies detection were helpful for early diagnosis of SARS-CoV-2 infection and judgment of patients in recovery stage, respectively.

Keywords: Feces; IgG antibody; IgM antibody; SARS-CoV-2; Viral RNA

Introduction

Coronavirus disease 2019 (COVID-19) is an acute infectious disease caused by a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] At present, the detection of viral-RNA in respiratory tract (mainly in the nasopharynx and oropharynx) and blood specimens is recommended as the standard for the diagnosis of SARS-CoV-2 infection.[2] Recently, the distribution of SARS-CoV-2 in specimens from other parts of patients has attracted much attention, such as in urine and feces.[3] Here, we report a cured patient with dynamic viral-RNA detection in different specimens such as nasopharynx swabs, sputum, blood, urine and feces. In addition, serum specific anti-SARS-CoV-2 IgM and IgG antibodies were also dynamically observed.

Case presentation

On January 22, 2020, a 19-year-old female university student was admitted to West China Hospital of Sichuan University with a 2-day history of dry cough. She disclosed that she had returned to Chengdu on January 21 from Wuhan. After admission, she felt intermittent fever (maximum temperature 37.8°C) accompanied by headache for 4days until February 1, 2020. On January 22, the laboratory examination only indicated a slight increase of monocytes, and chest high-resolution CT (HRCT) showed no evidence of obvious pneumonia, but Centers for Disease Control and Prevention (CDC) and the hospital both confirmed that the patient’s nasopharyngeal swabs detected positive SARS-CoV-2 by real-time RT-PCR assay. According to guidelines issued by the National Health Commission,[2] lopinavir and ritonavir (two tablets twice a day, oral administration, from January 29 to February 18), interferon alfa (5 million units twice a day, atomized inhalation, from February 20 to 24) as well as Arbidol (200mg three times a day, oral administration, February 19 to 27) were successively prescribed [Figure 1]. In the later stage of lopinavir/ritonavir treatment, there was just a slight increase of serum alanine aminotransferase, but quickly recovered to the normal range after adjusting antiviral drugs. During her hospitalization, no deterioration of pneumonia was found by dynamic detection of chest HRCT [Figure 2]. Before February 20, nasopharyngeal swab specimens tested persistently positive for SARS-CoV-2, whereas the serum and urine remained negative for SARS-CoV-2. On February 21, nasopharyngeal swab (nasopharynx and oropharynx) was tested negative. Sputum cannot be obtained, thus SARS-CoV-2 in sputum is unclear for this patient.

Unlike in serum and urine, SARS-CoV-2 tested positive in feces for many times. The feces were first tested positive for SARS-CoV-2 on February 9 and lasted for nearly 2weeks thereafter, then turned negative on February 24. In addition, serum IgM (1:1) antibody and IgG (1:1) antibody turned positive on January 28 and February 3, respectively. On February 20, serum IgM titer increased to 1:20, but dropped to 1:10 on February 24. On the contrary, the serum IgG titer increased gradually and reached its peak (1:20) on February 24.

On February 27, she was afebrile and all respiratory symptoms had resolved for more than 3weeks, and SARS-CoV-2 was negative in both nasopharynx swabs and feces. Thus, she was discharged and asked to observe at home for 2weeks.

The detailed clinical information was shown in Figure 1 and dynamic chest HRCT imaging was shown in Figure 2.
Discussion
According to recommendations issued by the National Health Commission of PRC, viral-RNA negative in two consecutive respiratory samples at least 24 hours apart is an important evaluation criteria for terminating isolation of SARS-CoV-2 pneumonia. As SARS-CoV-2 pneumonia is mainly transmitted through the respiratory tract, nasopharynx swab or sputum specimens negative for SARS-CoV-2 is important and indispensable criterion for assessing the reliability of de isolation or discharge. For this patient, nasopharynx swab negative for SARS-CoV-2 had lasted for at least 4 days, thereby reducing or eliminating her potential as a source of infection. Inducing sputum method was considered as the patient could not provide reliable sputum. But it was not implemented as the high risk of aerosol pollution in the ward. To ensure the accuracy of upper respiratory tract specimen detection, both nasopharynx and oropharynx swabs were collected at the same time, which also minimized the risk of inadequate collection of specimens.

Recently, Chinese scientists have isolated SARS-CoV-2 strains from samples of critically ill patients’ feces. Therefore, some experts worry patients whose feces are continuously positive for SARS-CoV-2 may become long-term carriers of the virus.

Figure 1: The symptoms, antiviral therapy and dynamic viral-RNA and antibodies detections. The RNA of SARS-CoV-2 was detected by real-time RT-PCR and serum IgM and IgG antibodies were detected by multiple dilution method. The primers and probe targeting to ORF1ab and N gene were used. Lower Ct values indicate higher viral loads, and Ct values more than 40 indicate undeterminate. Ct: Cycle threshold; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

Figure 2: Dynamic chest HRCT imaging throughout the course of treatment. There was no deterioration of pneumonia during the patient’s hospitalization. HRCT: High resolution computed tomography.
Recent structural analysis suggests that SARS-CoV-2 might be able to bind to the angiotensin-converting enzyme 2 (ACE2) receptor in humans. According to PubMed database, the RNA SEQ analysis of 27 different tissue samples from 95 persons showed ACE2 (functional receptor for SARS Coronavirus) protein was highly expressed in the small intestine and duodenum. In fact, the surface expression of ACE2 protein on enterocytes of the small intestine has already been reported as early as 2004. Importantly, SARS-CoV-2 infection can be manifested as diarrhea with an incidence of 10.1%, and this may be explained by the high ACE2 expression in intestinal tissue. Thus, if conditions permit, it is better to achieve a negativity of SARS-CoV-2 in feces before de isolation.

Due to the relatively high false negative rate of PCR detection method, the detection of serum IgM and IgG antibodies against SARS-CoV-2 were eagerly awaited. For this patient, the serum specific IgG and IgM antibodies were detected with multiple dilution method. And the finding suggested that the serum IgM antibody could appear in the early stages of the disease, and its titer increased first and then decreased, while serum IgG antibody appeared later than IgM antibody, and its titer gradually increased. Thus, it was not hard to see that the dynamic detection of serum IgM and IgG antibodies was extremely helpful for early diagnosis as well as evaluation in recovery stage.

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Author Contributions
Enqiang Chen, Ping Feng and Hong Tang conceived and designed the manuscript. Enqiang Chen, Lichun Wang, Guangming Tang, Menglan Wang and Yachao Tao acquired and interpreted the data. Enqiang Chen drafted the manuscript. All authors read, revised, and approved the manuscript.

Conflicts of Interest
None.

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