

Positive stool test suggests that the discharge standard of COVID-19 needs to be improved

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Summary

We report a hospitalized patient with COVID-19 whose fecal samples turned negative 22 days later than the respiratory samples. It highlights that the duration of virus release from patients is longer than previously expected. Current clinical examinations for treatment and discharge standard are limited to respiratory samples. However, we believe that nucleic acid testing of both respiratory and fecal samples is necessary for discharged patients. Further studies are needed to confirm the potential for fecal-oral transmission or fecal-respiratory transmission via aerosols.

Since the outbreak of 2019 novel coronavirus disease (COVID-19) in Wuhan, it has evolved into a global pandemic in three months. By 19 April 2020, 2241,778 patients and 152,551 deaths have been reported (1, 2). China, the first country of the COVID-19 epidemic, after more than 84,000 confirmed cases and 4642 deaths, has successfully controlled the epidemic and accumulated extensive experience in clinical diagnosis and treatment. However, the understanding of the virus is still limited. Here, we report a hospitalized patient with COVID-19 whose fecal samples turned negative 22 days later than the respiratory samples.

Respiratory samples were collected for influenza A and B viruses test using the Xpert Xpress Flu/RSV assay (GeneXpert System, Cepheid, Sunnyvale, CA, USA) according to the manufacturer's instructions. The nucleic acid testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was run by real-time RT-PCR. After mixing and centrifuging, the respiratory and fecal samples were added with nucleic acid releaser for releasing the nucleic acid. Then added the PCR reaction solution to the samples and tested them on the PCR instrument. The novel coronavirus ORF1ab and the specific conserved sequences encoding nucleocapsid protein N gene were detected by multiplex rapid fluorescent PCR. The cycle threshold (Ct) reference value of the target gene detected by the kit was 40. Typical S-type amplification curve was detected in

FAM channel, and $Ct \leq 40$, indicating positive detection. If not, or $Ct > 40$, it was negative. Test kit was from Zhuo Cheng Hui Sheng Biotechnology Co., Ltd and Berger Medical Technology Co., Ltd.

A 55-year-old woman, who visited Wuhan from 28 December 2019 to 22 January 2020, showed mild symptoms of throat discomfort on January 16. After simple treatment in a community clinic in Wuhan, the symptoms eased. Then, she went to Jiaying on January 22.

On January 25, she began to have a fever (37.8°C), fatigue and inappetence, and went immediately to a fever clinic (During the outbreak of SARS in 2003, most hospitals in China have set up fever clinics for early detection of cases, and they were maintained afterward as a regular clinic check. After the outbreak of COVID-19 in Wuhan, the fever clinic started testing of COVID-19 for suspected patients). Pre-admission examinations showed a body temperature of 38.0°C , leukocyte count of $5.3 \times 10^9 /\text{L}$ (normal range 3.9-9.9), and lymphocyte count of $1.1 \times 10^9 /\text{L}$ (normal range 1.1-3.6). CT scan showed inflammation in the lower left lung. She was isolated as a suspected COVID-19 case in the same fever clinic based on her travel history and clinical symptoms. The results showed that influenza A and B were negative while SARS-CoV-2 was positive. She was diagnosed as a COVID-19 patient on January 26.

The patient received treatment for 4 days following the Novel Coronavirus Pneumonia Diagnosis and Treatment Plan (Provisional 5th Edition) guidelines (3): TREATMENT DESCRIPTION. The second chest CT examination on January 30 showed progressing lung shadow. She was transferred to the COVID-19 designated hospital on February 1, where she was diagnosed as moderate pneumonia. The symptoms gradually alleviated after a series of antivirals (lopinavir/ritonavir, arbidol) and supportive treatment. On February 3, the patient's temperature returned to normal and

breathing was stable. Respiratory samples for SARS-CoV-2 test were negative. On February 6, CT follow-up showed that the left lung inflammation was significantly absorbed, and respiratory samples were negative. The patient met the discharge standard defined by the guidelines (3): 1) continuous normal body temperature for more than 3 days, 2) significant improvement of respiratory symptoms, 3) significant absorption of pulmonary inflammation, 4) nucleic acid testing of respiratory tract samples being negative for 2 consecutive times (24 hours interval).

However, the fecal samples on February 7 were tested positive for SARS-CoV-2. Considering the unclear transmission mechanism, after discussion among clinicians and the patient, we decided to keep the patient in the hospital for further treatment and continuous nucleic acid testing of respiratory and fecal samples every 1-2 days. On February 25, the fecal samples turned negative for SARS-CoV-2. Based on double the negatives of respiratory and fecal samples on February 26, the patient was discharged on the same day and did not test re-positive during her follow-up on March 4 and 11 (Fig.1).

At present, it has been confirmed that SARS-CoV-2 can be transmitted by respiratory tract and close contact (4, 5). Some studies had isolated infectious viruses from patients' feces (6-7). In addition, the latest research showed that the virus can replicate in human intestinal organs. It may infect the host intestinal cells (8). All of these indicated that fecal-oral transmission or fecal-respiratory transmission might occur through aerosols. A follow-up study of 401 patients found that most of the patients' clinical symptoms had disappeared at 3 to 5 weeks of the course, and all indicators met the discharge standard. However, 12% of the patients still tested positive for SARS-CoV-2 in their feces (9). It was showing that they were not completely free of viruses, and the current discharge standard based on the disappearance of clinical symptoms and negative respiratory samples might be of concern. In our case report, clinical symptoms and nucleic acid

testing results showed that the virus could survive for a long time in the patient and continue to be discharged out of body. The respiratory samples were negative after antiviral treatment, which might be related to the decrease of virus load (10). After 8 days of treatment, the symptoms disappeared, and the respiratory samples turned negative. Nevertheless, the fecal samples remained positive in the next 21 days.

In summary, we believe that false recovery is a new challenge for global prevention and control of COVID-19 (11, 12). We suggest that the discharge standard of COVID-19 should be improved. It is necessary to strengthen fecal management for convalescent patients. The results of both respiratory and fecal samples should be used to evaluate the rehabilitations and transmission of patients with COVID-19.

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Conflict of interest

No potential conflict of interest was reported by the author(s).

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Figure legend

Figure 1. Timeline for course of disease and detection of SARS-CoV-2 by RT-PCR, + refers to positive, - refers to negative.

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Figure 1

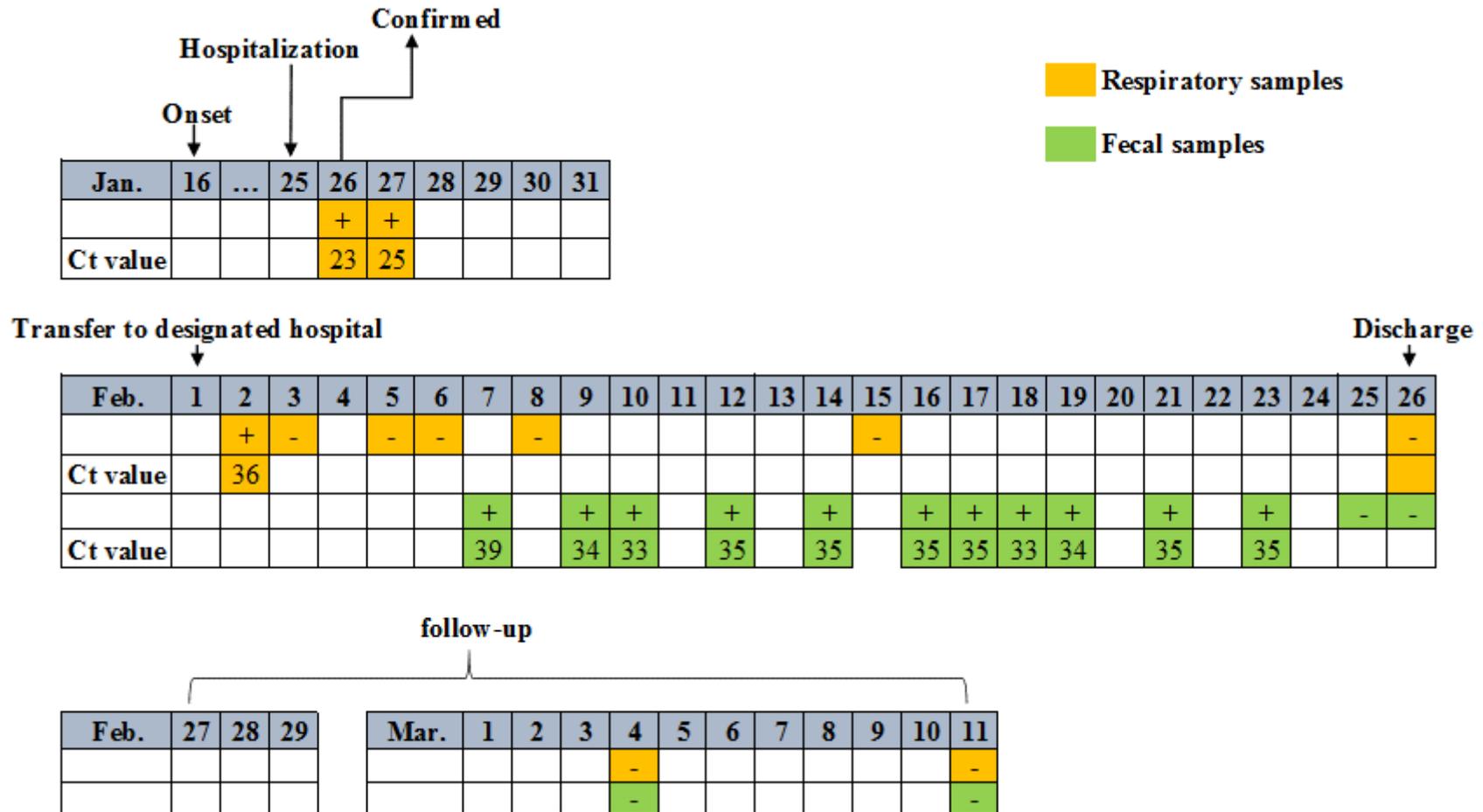


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