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SARS-CoV-2 turned positive in a discharged patient with COVID-19 arouses concern regarding the present standard for discharge

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Abstract:

An outbreak of COVID-19 in Wuhan, China caused by SARS-CoV-2 has led to a serious epidemic in China and other countries, resulting in worldwide concern. With the active efforts from prevention and control, the quantity of discharged patients is escalating. How to manage these patients normatively is still challenging. We hereby reported an asymptomatic discharged patient with COVID-19 who was retested positive for SARS-CoV-2, which arouses concern regarding the present discharge standard of COVID-19.

Since December, 2019, an outbreak of coronavirus disease (COVID-19) in Wuhan, Hubei, China caused by a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to a serious epidemic in China and other countries, resulting in worldwide concern.¹ Because of the seriousness of this outbreak, WHO declared it a public health emergency of international concern on Jan 30, 2020. As of February 21, 2020, a total of 75,569 COVID-19 cases have been confirmed in China. Notably, 1200 confirmed cases have been reported in 26 other countries beyond China.²

Since the outbreak, China has taken unprecedented measures to contain the spread of the virus within China. Though the number of cases outside China has remained relatively small, it's very challenging that some of the cases did not have clear epidemiological link, and some asymptomatic carriers with SARS-CoV-2 might be a new potential source of infection. It's very worrisome that South Korea and Italian now have the most confirmed cases outside China.

With the huge efforts from medical professionals to treat patients, substantial public health prevention measures, and accelerated research, the quantity of discharged patients is escalating.² How to manage these patients normatively is still challenging. We hereby reported an asymptomatic discharged patient with COVID-19 who was retested positive for SARS-CoV-2, which arouses us to rethink the present discharge standard of COVID-19.

A 54-year-old man had a close contact with a person from Wuhan at a meeting on January 12, 2020. He felt fatigue and mild myalgia on January 17. And on January 20, he began to have a fever of 37.5°C, so he went to a fever clinic of a tertiary hospital. Chest CT scan on January 20 showed multiple and scattered ground-glass opacities in the sub-pleural area of bilateral lungs. Immediately he was diagnosed as suspected case of COVID-19 and isolated at an observation unit. On January 21, throat swab sample tested positive for SARS-CoV-2 by real-time reverse transcription polymerase chain reaction assay, so he was diagnosed as a confirmed COVID-19 case. Gradually, he had a mild to moderate dyspnea, and a fever of 38.3 °C on January 24. Followed chest CT scan demonstrated increasing area and number of ground-glass opacities in bilateral lungs on January 24. He received supplemental oxygen at a rate of 5 liters per minute, and took antiviral drugs (0.2g of arbidol hydrochloride tablet orally taken three times a day) and low-dose hormone since January 24. However, the symptoms weren't improved at all. On January 27 he was transferred to a COVID-19-designated hospital and given antiviral treatment in an isolated ward (0.2g of arbidol hydrochloride tablet orally taken three times a day and 0.5g of chloroquine hydrochloride tablet orally taken

twice a day). On February 2, his fever, cough and other symptoms disappeared. Chest CT follow-up showed bilateral pulmonary lesions obviously resolved. Throat swab samples tested negative for SARS-CoV-2 on February 2 and February 4, respectively (Figure 1, 2).

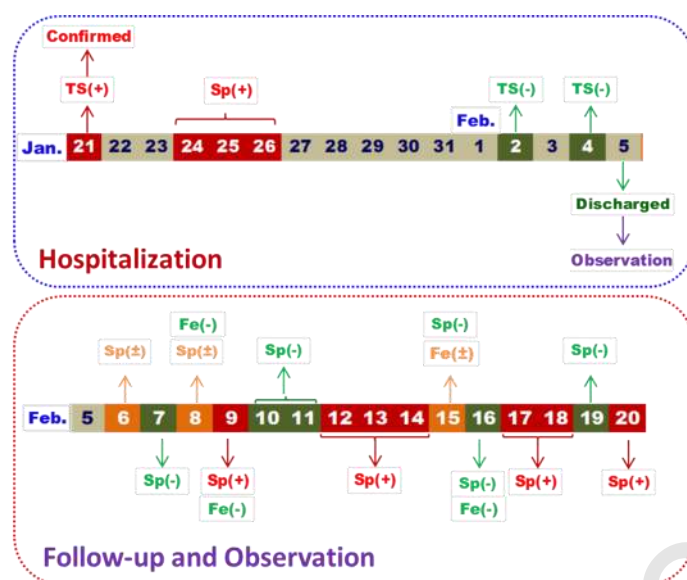


Figure 1. Chronological changes of SARS-CoV-2 gene nucleic acid detection of a 54-year-old man with confirmed COVID-19.

The time point in the upper blue dotted frame refers to changes of SARS-CoV-2 gene nucleic acid detection during the hospitalization, and the time point in the lower red dotted frame means changes of SARS-CoV-2 gene nucleic acid testing after discharge and followed up at a designated medical unit.

TS, sample of throat swab
Sp, sample of sputum
Fe, sample of feces
+ refers to positive
- refers to negative
± refers to weakly positive, which should be concerned and followed up.

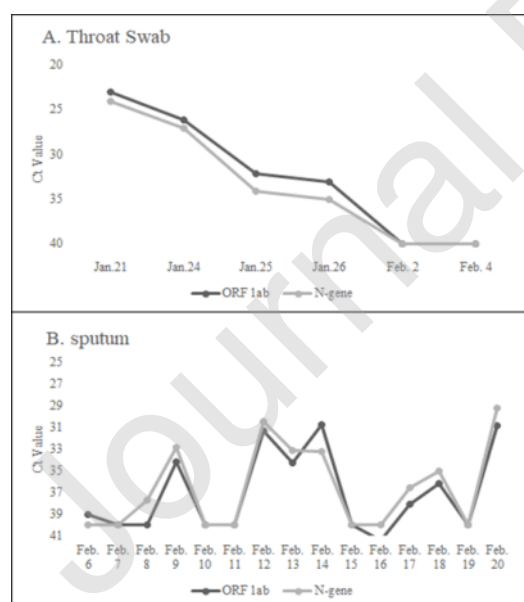


Figure 2. The same patient as Figure 1. Dynamic changes of SARS-CoV-2 viral load detection in sputum and throats swabs.

Ct value ≤ 37 refers to positive (+)

Ct value > 40 refers to negative (-)

$37 < \text{Ct value} \leq 40$ refers weakly positive (\pm), which should be concerned and followed up.

According to the discharge standards as following: (1) the body temperature returned to normal for more than 3 days, (2) respiratory symptoms improved significantly, (3) inflammation of the lungs showed obvious signs of absorption, and (4)

respiratory nucleic acid was negative for two consecutive times (24 hours sampling time interval at least), which is from the guideline proposed by the National Health Commission of China, the patient can be discharged and released from isolation.^{3, 4}

However, it remained unclear about viral clearance pattern after the SARS-CoV-2 infection. For the caution and safety, the committee of prevention and control of COVID-19 in our hospital proposed a local guideline to manage the discharged patients. All discharged COVID-19 patients are transferred to a designated medical unit for extra 14 days' quarantine and observation. As shown in **Figure 1** and **Figure 2**, after discharge on February 5, the patient was transferred to a designated medical unit for isolation and monitoring. Unfortunately, nucleic acid detection for SARS-CoV-2 displayed positive again. This arouses us to rethink the present discharge standards, and whether persistent asymptomatic carriers of SARS-CoV-2 exist and to reach an accurate definition of when a patient can be considered cured.

Actually, nucleic acid detection has a certain possibilities of false negative, which could mainly depend on the following situations: (1) the source of samples collected; (2) the method of samples collected; (3) antiviral drugs or hormone taken; (4) the sensitivity of nucleic acid test kit.^{5, 6}

Notably, the virus was found in the loose stool of a patient in the USA, suggesting potential transmission through the fecal-oral route.⁷ Similarly, our patient was found weakly positive for stool sample testing only once during the period under observation. Accordingly, our hospital implemented the standards for discharge, both

nasopharyngeal swab or sputum, and fecal virus nucleic acid detection were negative for more than 2 consecutive times (the interval was greater than 24 hours).

As mentioned above, an asymptomatic discharged patient with SARS-CoV-2 nucleic acid retested positive arouses concern regarding the discharge standard of COVID-19. Up to now, although no evidence demonstrated that a discharged patient who had repeated SARS-CoV-2 nucleic acid positive could be infectious to others, the patient reported by us showed high viral load for SARS-CoV-2 nucleic acid after discharge. If any of these individuals was contagious and released from quarantine, he or she might be a potential and mobile infectious source.⁸

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Ethical Approval: This study was approved by Ethics Committee of our hospital.

Contributors: JFZ and TC designed the study, KY collected the data, HHY and JL analyzed the data, JFZ and JJZ wrote this article.

Conflict of Interest: None.

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