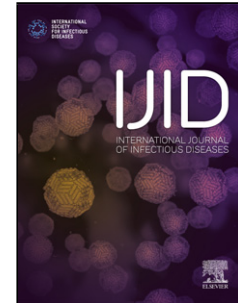


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Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report

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Highlights

- People with positive SARS-CoV-2 RNA of respiratory tract specimen are infectious source of COVID-19.
- SARS-CoV-2 RNA of respiratory tract specimen may be persistent or recurrent positive during the course.
- Dynamic surveillance of SARS-CoV-2 RNA should be performed for infectivity assessment.

Abstract

The ongoing outbreak of COVID-19 that began in Wuhan, China, has constituted a Public Health Emergency of International Concern, with cases confirmed in multiple countries. Currently patients are the main source of infection. We report a confirmed case of COVID-19 whose oropharyngeal swab test of SARS-CoV-2 RNA turned positive in convalescence. This case highlights the

importance of dynamic surveillance of SARS-CoV-2 RNA for infectivity assessment.

Keywords

COVID-19; SARS-CoV-2; novel coronavirus; NCP; infectivity

Introduction

Since December 2019, SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2; previously known as 2019-nCoV) has generated over 70000 cases of COVID-19 (Corona Virus Disease 2019, previously known as Novel Coronavirus Pneumonia, NCP) in China, including 1870 deaths, as of 17 February 2020 (National Health Commission of the People's Republic of China, 2020). The epidemic has been spreading to other 25 countries with 794 confirmed cases and 5 deaths (World Health Organization, 2020). Respiratory droplets and contact are considered as the main routes of transmission. Currently the COVID-19 patients remain as the main source of infection (Chan JF et al., 2020; General Office of National Health Commission, 2020; Special Expert Group for Control of the Epidemic of Novel Coronavirus Pneumonia of the Chinese Preventive Medicine Association, 2020). We reported a case of COVID-19 with recurrently positive SARS-CoV-2 ribonucleic acid (RNA) of oropharyngeal swab test.

Case presentation

A 46-year-old woman got a fever of 38.3°C with no other obvious symptoms on 17 January 2020. After taking two-day oral antibiotics, the temperature returned normal. On 23 January, she suffered from sore throat, cough and chest distress, with a body temperature of 37.3°C. The next day, she

came to the fever clinic of the Third Affiliated Hospital of Sun Yat-sen University.

She disclosed that she had been travelling in Wuhan with a friend from 11 to 13 January, who had been diagnosed as a confirmed case of COVID-19 on 19 January. She denied of exposure to the Huanan seafood market or wild animals.

A high-resolution computed tomography (HRCT) of the chest was performed immediately, images of which reported multiple patchy ground glass opacities in bilateral subpleural areas (Figure 1). Given the travel history and chest HRCT findings, she was admitted an airborne-isolation unit as a suspected case of COVID-19.

On admission, Physical examination revealed normal vital signs with oxygen saturation of 98% while the patient was breathing ambient air. Lung auscultation revealed no rhonchi. Arterial blood gas analysis indicated no abnormality with arterial oxygen tension (PaO₂) of 105mmHg and oxygenation index of 499 mmHg. Blood routine, liver function, renal function, myocardial enzymes, electrolyte, serum procalcitonin were normal. Antigen test for influenza A and B was negative. IgM test for influenza A and B, parainfluenza, respiratory syncytial virus, adenovirus, Mycoplasma pneumoniae, Chlamydia pneumoniae, Rickettsia burneti, Legionella pneumophila was negative. On 24 January, the Centers for Disease Control (CDC) confirmed that the patient's oropharyngeal swab test of SARS-CoV-2 by qualitative real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay was positive. According to the diagnostic criteria in China (General Office of National Health Commission, 2020), she was confirmed as a COVID-19 patient.

The patient's respiratory symptoms improved and maintained normal body temperature after symptomatic treatment and antimicrobial therapy including oseltamivir, arbidol, Lopinavir/ritonavir and moxifloxacin. Oropharyngeal swab tests of SARS-CoV-2 RNA were performed repeatedly for

surveillance (Table. 1). Exceptionally, the result was positive on 2 February, with a viral load of 4.56×10^2 copies/mL detected by quantitative real-time PCR. The dynamics of chest HRCT revealed gradual absorption of lung lesions. On 9 February, she was discharged and suggested home quarantine for at least 14 days. SARS-CoV-2 RNA of oropharyngeal swab remained negative in her follow-up visit on 17 February.

Discussion

World Health Organization (WHO) Director-General has declared that the outbreak of COVID-19 constitutes a Public Health Emergency of International Concern on 30 January 2020. The spectrum of this disease ranges from mild to life-threatening. Some cases might progress rapidly to acute respiratory distress syndrome (ARDS) and/or multiple organ function failure. The epidemiological survey has indicated that the general population is susceptible to SARS-CoV-2. Respiratory droplets and contact are considered as the main routes of transmission. The COVID-19 patients currently remain as the main source of infection. Asymptomatic carriers and those in the incubation period may also be infectious (General Office of National Health Commission, 2020; Rothe C et al., 2020; Special Expert Group for Control of the Epidemic of Novel Coronavirus Pneumonia of the Chinese Preventive Medicine Association, 2020; Yu P et al., 2020). Recognition, quarantine and treatment of the confirmed patients is critically important.

People with positive SARS-CoV-2 RNA of respiratory tract specimen are probably infectious source of COVID-19. According to the guideline in China, patients should be isolated until two consecutive SARS-CoV-2 RNA tests of respiratory tract specimens are both negative, with the interval of at least 24 hours (General Office of National Health Commission, 2020).

However, the patient we reported in this article presented an inconsistent situation. The oropharyngeal swab test for SARS-CoV-2 RNA on 2 February became positive again after two consecutively negative results on 28 January and 30 January, while her respiratory symptoms had already improved and had no fever. In other words, she was still possible to transfer the virus to other people, if she was relived or discharged right after the second negative test.

We speculate the reasons why the results of SARS-CoV-2 RNA tests in this case were fluctuant. First of all, by now no research has accurately proved the contagious period of COVID-19. Besides patients and asymptomatic carriers, those in convalescence may also be infectious. SARS-CoV-2 RNA of respiratory tract specimen may be persistent or recurrent positive during the course. Furthermore, Angiotensin converting enzyme-2 (ACE-2), identified as the cell entry receptor of SARS-CoV-2, was highly expressed in lungs rather than upper respiratory tract (Lu R et al., 2020; Zhou P et al., 2020). The result of SARS-CoV-2 RNA test probably depends on the viral load of the specimen. Therefore, it could be false negative sometimes for oropharyngeal or nasopharyngeal swabs test, affected by the site of sample, the experience of operator, and the actual quantity of virus. Bronchoalveolar lavage fluid (BALF) specimen test is considered more accurate but with higher exposure risk. As well as the above specimens, SARS-CoV-2 RNA can be detected in patient's sputum, blood or stool swab by RT-PCR assay. Running multiple tests and collecting combined different specimens would be effective approaches to maximize the sensitivity. Combination with SARS-CoV-2 RNA test and other detective methods such as specific antigen, IgM antibody or the next generation sequencing, is also conducive to diagnosis.

Given the possibility of recurrently positive SARS-CoV-2 RNA in clinical course and to reduce the risk of transmission in other COVID-19 cases, we suggest that: (1) both nasopharyngeal and

oropharyngeal swabs test of SARS-CoV-2 RNA should be performed to reduce the false negative rate. More tests, more specimens, and more methods could be considered. (2) Patients in convalescence should also be regularly tested for infectivity assessment. And all the discharged patients should take home quarantine for at least 14 days.

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Ethical approval

Informed consent was obtained from the patient for publication of this case report and accompanying image.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Figure Legend

Figure 1. Chest HRCT images on 23 January 2020, showing multiple patchy ground glass opacities in bilateral subpleural areas (red arrows). HRCT, high-resolution computed tomography

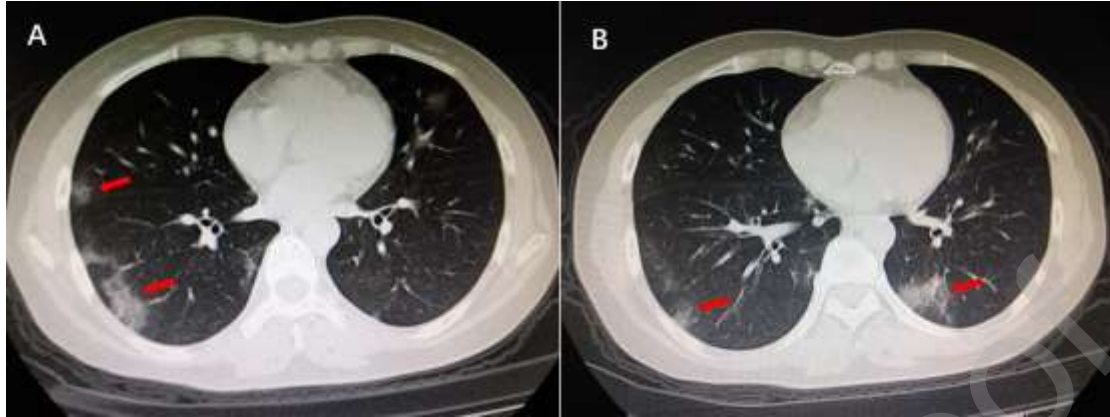


Table 1. The dynamics of oropharyngeal swab test of SARS-CoV-2 RNA

Date	1-24	1-28	1-30	2-2	2-5	2-7	2-17
Day after onset	Day 8	Day 12	Day 14	Day 17	Day 20	Day 22	Day 32
SARS-CoV-2 RNA (copies/mL)	Positive	Negative	Negative	4.56x10 ²	Negative	Negative	Negative
Body temperature	normal	normal	normal	normal	normal	normal	normal
SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; RNA, ribonucleic acid							