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Case Report

Re-evaluation of retested nucleic acid-positive cases in recovered COVID-19 patients: Report from a designated transfer hospital in Chongqing, China

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ABSTRACT

Since the outbreak of coronavirus disease 2019 (COVID-19) in Wuhan, Hubei Province, China [1], a large number of confirmed cases met the discharge criteria (one of which is two consecutive negative nucleic acid tests with an interval of at least 24 h) [2]. Previous studies have paid more attention to the epidemic situation of COVID-19 and patient diagnosis and treatment. Close attention also should be paid to the discharged patients. Surprisingly, a previous follow-up reported that some patients' nucleic acid retest results were positive again after discharge [3]. Factors impacting these follow-up test results should be further investigated. Since the first confirmed case was diagnosed in our hospital (Chongqing Emergency Medical Center, the designated transfer hospital) on February 4th, we confirmed a total of 17 cases. All patients infected with the novel coronavirus were transferred to a designated hospital in Southwest China's Chongqing by ambulance with an inbuilt negative-pressure chamber [4]. In the follow-up examination of these patients, RT-PCR tests were conducted again 3 days after discharged from the designated hospital. Four patients showed recurrence of positive results after a few days of discharge. Thus, we examined these cases herein, aiming to provide information for policy formulation and modification of discharge plans.

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Methods

Data were collected from the medical records of these patients with novel coronavirus pneumonia confirmed by Chongqing Emergency Medical Center. Their families, the Center for Disease Control and Prevention of Yuzhong District, Chongqing, and the designated hospital were contacted directly. We further analyzed the epidemiological history, clinical symptoms and multiple RT-PCR

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test results of virus nucleic acids after diagnosis and recovery.

All of the cases reported were confirmed in our hospital by the trial version 5 of the new coronavirus pneumonia diagnosis and treatment program [5]. The patients were then transferred to the designated hospital to undergo treatment until they met the discharge criteria [4,5]. The discharge decisions were made by a panel of experts on COVID-19. The patients were quarantined sequentially, and the nucleic acid test was conducted 3 days after discharge. All patients were followed up by telephone.

This study was approved by the medical ethics committee of the Chongqing Emergency Medical Center (No. 2020-06). Written informed consent was waived for emergency medical rescue of public health emergencies in accordance with the relevant provisions of national medical ethics.

Table 1
COVID-19 nucleic acid detection results of the cases 1 in different samples.

Case 1	2.1	2.11	2.13	2.15	2.17 (Our hospital)	2.20	2.29	3.2	3.5	3.30 (Our hospital)
Oropharyngeal swabs (Ct of N/1ab)	+	–	–	Discharge	33.15/Negative	–	–	–	–	ND
Nasopharyngeal swab (Ct of N/1ab)	NA	–	–		32.77/33.83	–	–	–	–	–
Anal swab (Ct of N/1ab)	NA	–	NA		35.77/Negative	–	–	–	–	ND

Table 2
COVID-19 nucleic acid detection results of the cases 2 in different samples.

Case 2	2.2	2.11	2.13	2.16	2.18 (Our hospital)	2.20	2.29	3.2	3.5 (Our hospital)	3.30 (Our hospital)
Oropharyngeal swabs (Ct of N/1ab)	+	–	–	Discharge	36/Negative	–	–	–	–	–
Nasopharyngeal swab (Ct of N/1ab)	NA	–	–		ND	–	–	–	ND	ND
Anal swab (Ct of N/1ab)	NA	NA	NA		36.76/35.42	–	NA	NA	ND	ND

Results

Two patients showed positive nasopharyngeal swabs three days after discharge. The remaining patients showed positive anal swab results three days after discharge. However, the symptoms and CT manifestations of the disease were not exacerbated for the latter patient. Therefore, the former three patients returned to the designated hospital to be quarantined again. Two patients were discharged again from the hospital on March 2, 2020, and the nucleic acid was still negative after discharge. The other patient (case 4) is still under medical observation. Case 3 was quarantined in our hospital due to positive anal swab results.

Case 1

A 29-year-old male, He is working in the service industry. The specific exposure history is unknown. This patient may represent the first case of a family cluster with the COVID-19. He lives with his parents, who were also confirmed to be infected with the novel coronavirus. He had symptoms of fever and cough at onset on January 27, and presented to our hospital 3 days later. Due to a positive nucleic acid test, he was confirmed as having novel coronavirus disease. After 14 days of treatment, he met the discharge criteria on February 15. The nasopharyngeal swab was positive 3 days after discharge, but it was subsequently negative for four times until March 5th, 2020.

Case 2

A 49-year-old female (the mother of case 1) was exposed to her infected son. She had symptoms of cough and the confirmation test was made by a combination of exposure history and a positive nucleic acid test. She also received antiviral treatment for 14 days, until discharge on February 16th. Three days after discharge, the nasopharyngeal swab test result was positive. Four subsequent results were negative until March 5th, 2020.

Table 3
COVID-19 nucleic acid detection results of the cases 3 in different samples.

Case 3	2.5	2.21	2.22	2.23	2.26 (Our hospital)	2.28 (Our hospital)	3.4 (Our hospital)	4.1 (Our hospital)
Oropharyngeal swabs (Ct of N/1ab)	+	–	–	Discharge	ND	–	ND	ND
Nasopharyngeal swab (Ct of N/1ab)	NA	–	–		–	ND	–	–
Anal swab (Ct of N/1ab)	NA	NA	NA		35.56/36.64	33.7/32.25	–	ND

Case 3

A 12-year-old female was exposed to her infected mother. Thus, she was asked to visit our hospital to undergo oropharyngeal swabs for the RT-PCR test and to undergo a chest computed tomography (CT) examination. Mild COVID-19 was diagnosed due to positive RT-PCR tests results. Antiviral treatment with arbidol, interferon and traditional Chinese medicine was conducted in the designated hospital over the next 15 days. Then, she was met the discharge criteria (2 negative RT-PCR test results at least 1 day apart). In addition, she was asymptomatic, and the CT scan was negative. The nucleic acid test of anal swab was positive three days after discharge. It remained positive at the next two tests before March 5th, 2020 (Table 1).

Case 4

A 38-year-old male was exposed when dining with his friends who had traveled to Wuhan. Three of the tables were infected with COVID-19. He presented with fever, fatigue, and cough for 8 days. He was diagnosed with novel coronavirus pneumonia on January 30, 2020, according to typical respiratory symptoms, positive oropharyngeal swab results and radiological ground-glass opacification. He was transferred to the designated hospital, and was treated for 27 days. The nasopharyngeal swab was positive 3 days after discharge, but became negative 2 days later on March 4th, 2020 (Table 2).

Discussion

With the intensive surveillance measures that have been taken to prevent and control epidemics by the Chinese government, a good impact has been achieved on the spread and treatment of COVID-19 in Wuhan and the whole country. However, according to a report in JAMA, a follow-up of the recovered patients showed a recurrence of RT-PCR positivity in some patients [3] (Table 3).

Table 4
COVID-19 nucleic acid detection results of the cases 4 in different samples.

Case4	1.30	2.24	2.26	2.28	3.1 (Our hospital)	3.4	4.7 (Our hospital)
Oropharyngeal swabs (Ct of N/1ab)	+	–	–	Discharge	ND	NA	ND
Nasopharyngeal swab (Ct of N/1ab)	NA	–	–		40.35/40.67	–	38.54/>40
Anal swab (Ct of N/1ab)	NA	NA	NA		sputum(-)	–	ND

+ = positive, – = negative, NA = Not available, ND = not do.

Why does this happen? In general, specimens such as alveolar lavage fluid deposited deep in the lungs have a higher positive rate than that of oropharyngeal swabs [2] and turn negative more slowly. If the patient is discharged after two negative results of oropharyngeal swab test separated by at least 24 h, there may still be a persistent virus in the lung. When patient immunity declines, the RT-PCR test of oropharyngeal swabs may be positive again. Thus it is recommended that saliva should be collected if possible, and it has been emphasized that specimens of the lower respiratory tract (saliva or airway extract) provide more accurate RT-PCR tests [2]. In addition, virus-free cells may be collected due to improper sites and insufficient depth [6], which will also cause “false negatives”. This phenomenon may also be due to the biological characteristics of the novel coronavirus [7] (Table 4).

Positive results of the anal swab nucleic acid test do not mean that there is live virus in the stool of the patient. Second, the removal rate of viral RNA in the stool of the patient is slower than that of the oropharyngeal swab. Therefore the duration of positive anal swabs or stool samples during recovery is relatively long [8].

There are several limitations in our observation. Virus nucleic acids of different samples were tested in the two hospitals and at the CDC, and samples were collected by different medical professionals in the above mentioned settings. Furthermore, as we were facing to a new virus, different batches of kits from different manufacturers were used, which might increase bias.

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Competing interests

None declared.

Ethical approval

Not required.

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