

Positive RT-PCR Test Results in Discharged COVID-19 Patients: Reinfection or Residual?

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Case Report

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Abstract

Background: The coronavirus disease-19 (COVID-19) is a highly infectious disease. Moreover, 14% of the discharged patients tested virus positive again. However, the underlying clinical mechanisms are still under investigation.

Case presentation: The current study summarized the clinical course, radiological features and laboratory test results of two COVID-19 patients who tested positive again during the quarantine after hospital discharge. We found that while all symptoms were relieved, their lesions in lungs were not fully recovered, and both of them had slight coughs. In addition, when the lesions were further recovered and the cough symptoms were further remitted, they tested virus negative again.

Conclusions: These results implied that the positive result is unlikely caused by the reinfection from others or the remained virus. Rather, it may derive from the remained virus transferred from the lower respiratory tract to the throat or nose with coughs. Accordingly, we proposed some suggestions regarding the discharge management. This study enhances our knowledge of the progress of COVID-19 and benefit the control of this disease.

Background

An outbreak of coronavirus disease-19 (COVID-19) infection began in Wuhan, Hubei province of China, and rapidly spread to the whole country and around the world. Up to date (11: 17 on March 6, 2020), this virus has resulted in 97205 cases in 81 countries with 3327 deaths [1]. Many COVID-19 studies have been conducted regarding its epidemiological, clinical and radiological features [2-9].

Several cities have reported that the patients exhibit positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test results again several days after discharging from the hospital [9-10]. According to Caixin magazine's report [10], approximately 14% of discharged patients in Guangdong province are readmitted after testing positive again. However, the clinical mechanisms underlying this phenomenon remain obscure.

Wenzhou, a city in the southeast of China, has the largest number of cases (504 to date) in China outside Hubei Province. The First Affiliated Hospital of Wenzhou Medical University, one of the designated hospitals for treating COVID-19, received two patients who tested positive again after hospital discharge. Here, we summarized the clinical course, radiological features and laboratory test results of these two patients. This study was approved by the ethical committee of the First Hospital Affiliated to Wenzhou Medical University and written informed consent was waived for this retrospective study.

Case Presentation

Case 1

Case 1 was admitted to the hospital on January 26, 2020. She was a 39-year-old woman and had a 6-day history of intermittent coughs, nasal congestion, runny nose, and slight sore throat. She returned from Wuhan to Wenzhou on January 20 and stayed with a friend confirmed with COVID-19 before January 22. She had no history of hypertension, coronary heart disease, diabetes and surgical operations. Her body temperature was elevated to 37.6°C without abnormal pulmonary auscultation on admission. In addition, she had a blood pressure of 112/68 mmHg, pulse of 88 beats per minute and respiratory rate of 20 breaths per minute. Laboratory information (Table 1) showed a normal white-cell count of $4.38 \times 10^9/L$ (normal range, $3.5-9.5 \times 10^9/L$), 71.7% neutrophils (normal range, 40.0%–75.0%), and a decreased absolute value of lymphocytes of $0.87 \times 10^9/L$ (normal range, $1.1-3.2 \times 10^9/L$) and 19.9% lymphocytes (normal range, 20.0%–50.0%). Her C-reactive protein was less than 0.499mg/L (normal range, 0–8mg/L). On admission, non-enhanced chest computed tomography (CT) was performed (Figure 1F), which showed multiple bilateral mixed pattern of ground-glass opacities and consolidation in lungs, including inferior lingual segment of left upper lobe, dorsal segment of left lower lobe, lateral basal segment of left lower lobe, lateral segment of right middle lobe, lateral basal segment of right lower lobe and posterior basal segment of right lower lobe. This patient tested positive RT-PCR nucleic acid 3 days after hospitalization.

Table 1. Laboratory test results of Case1 during the first and second admission

Measure	Normal range	First admission					Readmission		
		day 1	day 3	day 8	day 10	day 13	day 1	day 2	day 5
white-cell count (X10 ⁹ /L)	3.5-9.5	4.38	2.41*	4.83	3.02*	6	4.1	4.1	5.38
percentage of neutrophils (%)	40.0%–75.0%	71.70	34.00*	57.20	42.80	50.20	56.40	52.90	58.70
absolute neutrophils count (X10 ⁹ /L)	1.8-6.3	3.14	0.82*	2.76	1.29*	3.01	2.31	2.17	3.16
percentage of lymphocyte (%)	20.0%–50.0%	19.9*	55.2#	27.7	38.7	37.2	34.1	38.3	29.4
absolute lymphocyte count (X10 ⁹ /L)	1.1-3.2	0.87*	1.33	1.34	1.17	2.23	1.4	1.57	1.58
C-reactive protein (turbidimetry, mg/L)	0.0-0.8	<0.499	<3.14	<3.14	-	-	<0.499	<5.0	<5.0

Note: *means the value abnormally decreased. #means the value abnormally increased.

After 13 days of treatment, including interferon inhalation, antiviral therapy of lopinavir/ritonavir tablets and symptomatic supportive care, the patient's symptoms were remitted and her body temperature became normal. At day 14, chest CT showed decreased ground-glass opacities (Figure 1G). RT-PCR of the patient's pharyngeal swab became negative in two consecutive tests with one day interval combined with negative stool nucleic acid test. Eighteen days after the hospitalization, the patient met hospital discharge criteria and was discharged. According to the diagnosis and treatment of COVID-19 in China (trial sixth Edition), the criteria for hospital discharge are as follows: (1) normal body temperature lasts for longer than three days, (2) significantly remission in respiratory symptoms, (3) substantially relieved acute exudative lesions on chest CT, and (4) consecutive negative two RT-PCR tests results with at least one day interval [12]. In addition, our hospital also require that the patient's stool nucleic acid test should be negative.

Case 2

Case 2 was admitted to the hospital on January 30, 2020. He was a 50-year-old man and had a 2-day history of subjective fever accompanied by sore throat, coughs and expectoration. He had no recent Wuhan travelling history. This patient reported a history of smoking for 25 years, 30 cigarettes per day and drinking for 30 years, 500ml of beer daily. However, he had given up smoking for three years. On admission, his highest body temperature reached to 38.2°C. Meanwhile, his lung auscultation was normal and his blood pressure was 133 /94 mmHg, with a pulse of 82 beats per minute, and a respiratory rate of 20 breaths per minute. Laboratory test results showed a normal white-cell count of $4.91 \times 10^9/L$ (normal range, $3.5-9.5 \times 10^9/L$), a little increased count of 75.2% neutrophils (normal range, 40.0%–75.0%), a decreased absolute value of lymphoid count of $0.9 \times 10^9/L$ (normal range, $1.1-3.2 \times 10^9/L$) and 18.3% lymphocytes (normal range, 20.0%–50.0%). Meanwhile, his C-reactive protein was elevated to 15.6mg/L (normal range, 0–10mg/L). In addition, his chest CT on admission (Figure 2E) showed multiple bilateral and peripheral ground-glass opacities in both lungs, including the superior lingual segment of left upper lobe, dorsal segment, lateral basal segment, posterior basal segment of left lower lobe, anterior and posterior segment of right upper lobe, lateral segment of right middle lobe, dorsal segment, lateral and posterior basal segment of right lower lobe. The patient showed positive RT-PCR nucleic acid results for two times on admission and 8 day after hospitalization.

Table 2. Laboratory test results of Case 2 during the first and second admission

Measure	Normal range	First admission				Readmission		
		day 1	day 4	day 5	day 7	day 13	day 2	day 5
white-cell count ($\times 10^9/L$)	3.5-9.5	4.91	6.52	6.03	4.82	4.61	5.68	4.9
percentage of neutrophils (%)	40.0%–75.0%	75.2#	66.2	65.2	64.5	59.1	62.3	54.2
absolute neutrophils count ($\times 10^9/L$)	1.8-6.3	3.69	4.32	3.93	3.11	2.72	3.54	2.66
percentage of lymphocyte (%)	20.0%–50.0%	18.3*	25	25.5	24.3	32.5	27.8	32.9
absolute lymphocyte count ($\times 10^9/L$)	1.1-3.2	0.9*	1.63	1.54	1.17	1.5	1.58	1.61
C-reactive protein (mg/L)	0.0-0.10	15.6#	32.7#	32.9#	17.1#	1.54	<5.0	<5.0

Note: *means the value abnormally decreased. #means the value abnormally increased.

After 12 days of treatment, including interferon inhalation, antiviral therapy of lopinavir/ritonavir tablets, oral administration of abidor granules, moxifloxacin hydrochloride injection for anti-infection, and other symptomatic supportive care, the patient's symptoms were relieved and his body temperature became normal. The follow-up chest CT on day 14 showed decreasing ground-glass opacities (Figure 2G). On day 16, the patient met the discharge criteria and was discharged.

Follow-up

After hospital discharge, the two patients were quarantined. They were required to monitor their temperature and symptoms by themselves and return to hospital after one week, two weeks, and four weeks, respectively. Six days after the discharge, both of them were found virus positive again and were readmitted to the hospital. On readmission, they both had no fever but slight coughs, and none of them showed renewed symptoms. Laboratory test results (Table 1) of Case 1 were normal on readmission. Except for a decreased albumin (38 g/L; normal range, 40.0–55.0 g/L), an increased alanine aminotransferase (138 U/L; normal range, 9–50U/L) and aspartate aminotransferase (65 U/L; normal range, 15–40 U/L), other laboratory test results (Table 2) of Case 2 were normal on readmission. Note that for both patients, the follow-up chest CT showed no evidence of renewed infiltrating lesions and the residual ground-glass opacities were almost resolved after readmission. Meanwhile, both of them had no cough. They were discharged again after 2 consecutive negative RT-PCR test results.

Discussion And Conclusion

Since the patients were quarantined after hospital discharge, they were unlikely to be infected by others. Since the follow-up CT scans showed that the lesions were not fully recovered, it is reasonable to assume that these discharged patients might still carry the virus [13]. However, all the symptoms were remitted, which rule out the possibility of the reinfection of the upper respiratory tract from the lower respiratory tract. Interestingly, both of them exhibited mild coughs on the first admission and readmission. It is well known that cough is a common symptom of the respiratory tract which is caused by inflammation of the trachea and bronchial mucosa, and cough has the protective effect of removing foreign bodies and secretions from the respiratory tract. Therefore, it is possible that the positive result is more a detection of the remained virus transferred from the lower respiratory tract to the throat or nose with coughs, rather than an indicator of the reinfection of the upper respiratory tract.

Accordingly, it is suggested that the specimen detection of bronchoalveolar lavage fluid from the lower respiratory tract should be used as the discharge criteria. Meanwhile, since previous studies had reported false-negative RT-PCR nucleic acid test results [7, 14], more consecutive nucleic acid tests for more tissues should be performed before discharge. We also suggest that the patients should not be discharged until their cough symptoms are largely recovered. We estimated that this may costed two weeks more quarantine time in the hospital. Even if the above suggestion cannot be fully adopted due to the limited health care resource, the discharged patients should wear masks and be retested one week,

two weeks and four weeks, respectively after discharged, in order to reduce the risk of reinfection and further transmission.

Further, we put forward some directions for future studies. First, the infectious of the remained virus need to be investigated. For example, can the upper respiratory tract be reinfected by the remained virus in the lower respiratory tract? Can other people be infected by the remained virus? Second, how long it takes for the complete elimination of the virus. Finally, how sensitive of the virus in different tissue to the treatment. These issues can be addressed with larger sample size and more case-control studies.

The current study described the clinical information and radiological features of two COVID–19 patients who tested positive again after hospital discharge. The results imply the progress trajectories of this disease. Therefore, we suggest that the hospital discharge criteria should be revised and the management of discharged patients should be strengthened. In summary, our study provides a better understanding of the progress of this disease, and provides some direction for future studies. It also benefits the public health by making policies accordingly.

Abbreviations

COVID–19: corona virus disease 2019; RT-PCR: real-time reverse transcriptase–polymerase chain reaction; CT: computed tomography.

Declarations

Ethics approval and consent to participate

This study was approved by the ethical committee of the First Hospital Affiliated to Wenzhou Medical University.

Consent for publication

Written informed consent was waived for this retrospective study.

Availability of data and materials

All original (de-identified) data and materials are available upon request from the corresponding author.

Competing Interests

The authors have declared that no competing interest exists.

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Authors' contributions

Contributed data: YY, MW. Analyze images: HS, GF, LL, GC, JT. Analyzed the data: JT, SC, JL, PP and AQ. Wrote the paper: JT, ZH, and MW.

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Figures

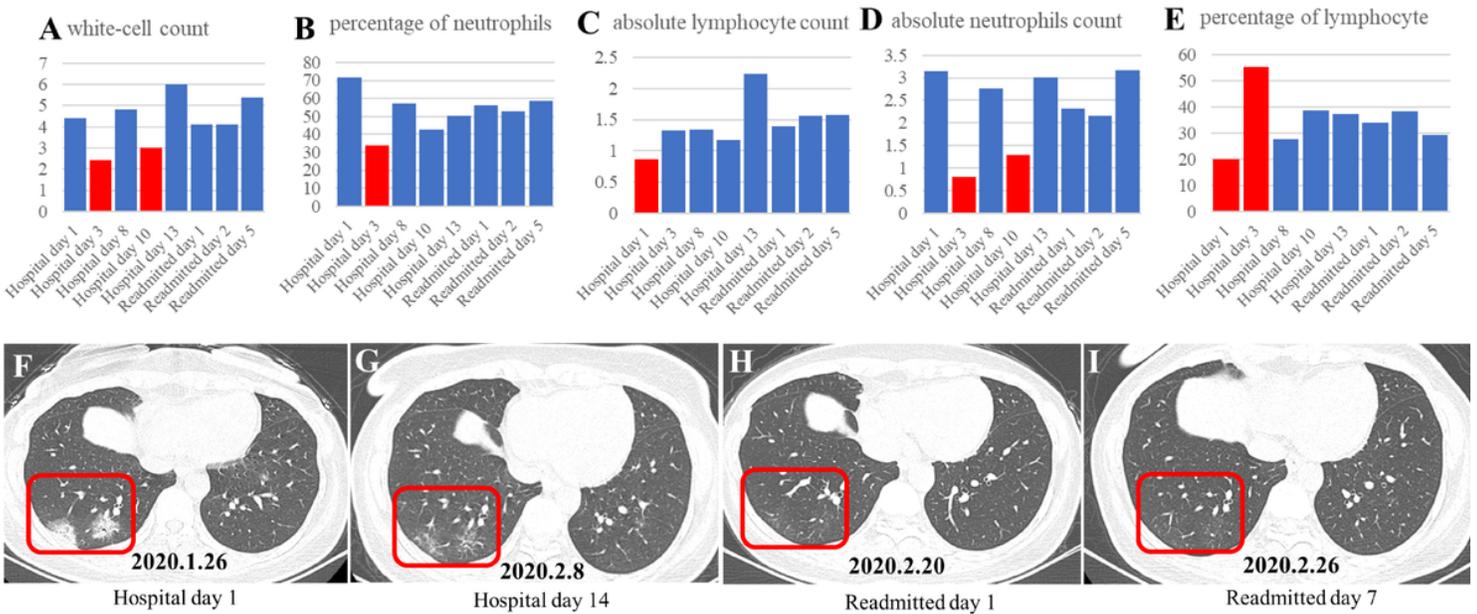


Figure 1

Laboratory test results and CT scans (slice thickness = 1.25 mm) for Case 1. (A~E) The laboratory test results in different stages. Only those exhibited at least one abnormal value were displayed. The red bars represent abnormal values and the blues ones represent normal values. (F) Chest CT on day 1 at admission shows multiple bilateral mixed pattern of ground-glass opacities and consolidation in both lungs. (G) Follow-up CT scan on day 14 at admission shows recovering of the consolidations and ground-glass opacities. (H) CT scan on day 1 at readmission shows absorbing and dissipating of the ground-glass opacities. (I) CT scan on day 7 at readmission shows almost complete resolution. The red rectangles highlight the progress of the relatively larger lesions.

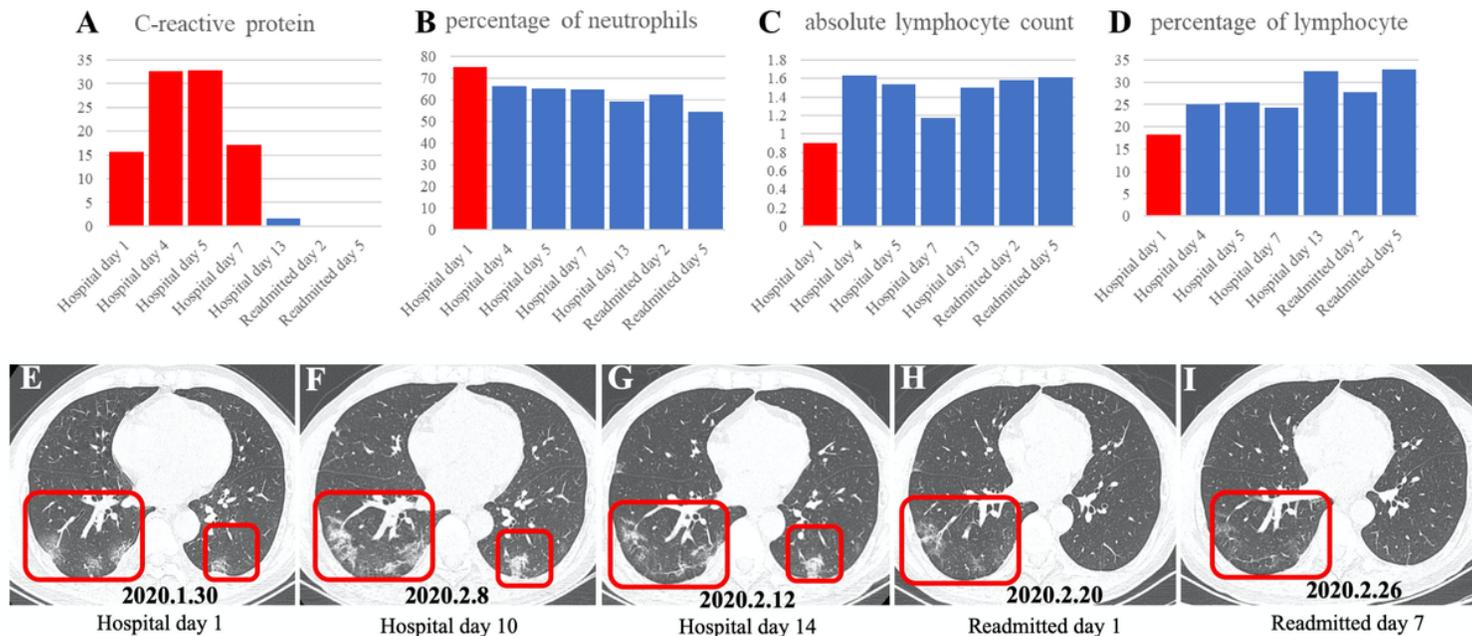


Figure 2

Laboratory test results and CT scans (slice thickness =1.25 mm) for Case 2. (A~D) The laboratory test results in different stages. Only those exhibited at least one abnormal value were displayed. The red bars represent abnormal values and the blues ones represent normal values. (E) Chest CT obtained on day 1 at admission shows multiple bilateral and peripheral ground-glass opacities in both lungs. (F) Follow-up CT scan obtained on day 10 at admission shows progressive lesions of mixed patterns of ground-glass opacities and consolidation. (G) CT scan on day 14 at admission shows exudative lesions decrease and ground-glass opacities are partly resolved in both lung lobes. (H) CT scan on day 1 at readmission shows absorbing and dissipating of the consolidations and ground-glass opacities continuously. (I) CT scan on day 7 at readmission shows almost complete resolution. The red rectangles highlight the progress of the relatively larger lesions.