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Case Report

A case report of moderate COVID-19 with an extremely long-term viral shedding period

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Abstract: Background: COVID-19 is caused by infection with a new form of coronavirus (SARS-CoV-2). The WHO raised the COVID-19 alert to the highest level. The virus is a highly contagious via human-to-human transmission. The median duration of viral shedding is 20.0 days. We report a long duration of viral shedding that was 32.0 days from illness onset in a patient with moderate COVID-19 admitted to Qianjiang Central Hospital. Case report: A 37-year-old patient sought medical advice while suffering from fever, dry cough, fatigue, dizziness, runny nose and diarrhoea. Five days before the visit, he had a history of travel from affected geographic areas. The patient had a positive RT-PCR test, and chest CT images showed multiple nodules and mixed ground-glass opacification with consolidation in bilaterally in the lungs. Laboratory findings showed that the lymphocyte and $CD4^+$ counts were below the normal range. The patient was given antiviral treatment, including arbidol, lopinavir, IFN-α, and traditional Chinese medicine, and other necessary supportive care. All clinical symptoms and CT imaging manifestation abnormalities resolved during the course of therapy. Conclusion: Although the positive RT-PCR tests were verified in consecutive upper respiratory specimens, the patient's clinical symptoms, CT imaging findings, $CD4^+$ lymphocyte counts, and IgG antibody levels had obviously improved. Positive tests may be detecting pieces of inactive viruses, which would not be transmissible in individual cases.

Keywords: COVID-19, IgG antibody, viral shedding, RT-PCR, $CD4^+$ count

Introduction

Since the outbreak of coronavirus disease in 2019 (COVID-19, previously known as SARS-CoV-2), the causative pathogen has rapidly spread throughout the world in a relatively short period of time. This is a positive-sense single-stranded RNA virus belonging to the family Coronaviridae, which is distributed broadly among humans, other mammals, and birds. Most coronaviruses cause a range of mild upper respiratory infections, inducing fever, fatigue, and dry cough. Some patients may present with nasal congestion, runny nose, diarrhoea and shortness of breath [1]. In some cases, they even exhibit severe acute respiratory syndrome (SARS), coagulation disorders and metabolic acidosis [2].

As of March 7, 2020, the cumulative incidence in mainland China, Hong Kong, and Macau was 80,735 cases, of which 67,592 cases were diagnosed in Hubei. Additionally, 3,045 deaths have been linked to the outbreak, and 19,903 cases have been reported in South Korea, Iran, Italy, France, Japan, the United States and other countries [3].

Chinese health authorities posted the full COVID-19 genome sequence on January 10, 2020, and the Chinese Center for Disease Control and Prevention (CDC) approved a real-time RT-PCR test that could diagnose COVID-19 clinical respiratory specimens [4], including upper (nasopharyngeal and throat swabs) and lower (sputum and bronchial lavage fluid) respiratory tract specimens, anal swabs and faecal samples. Hence, real-time reverse transcriptase-polymerase chain reaction (RT-PCR) is widely deployed in the diagnosis of COVID-19. According to the Chinese management guidelines for COVID-19 (standard version 6) [5], neg-

Table 1. Primer sequence and probe for amplifying target genes in SARS-CoV-2

Target gene	Primer	Primer sequence	Probe
ORF1ab	ORF1ab-F	CCCTGTGGGTTTTACACTTAA	5'-FAM-CCGTCTGCGGTATGTGGAAAGGTTATGG-BHQ1-3'
	ORF1ab-R	ACGATTGTGCATCAGCTGA	
N	N-F	GGGGAACTTCTCCTGCTAGAAT	5'-ROX-TTGCTGCTGCTTGACAGATT-TAMRA-3'
	N-R	CAGACATTTTGCTCTCAAGCTG	

ative RT-PCR results from at least 2 consecutive sets of specimens collected at least 24 hours apart, in a patient with COVID-19 indicate release from quarantine. Thus far, the onset and viral shedding duration of COVID-19 are not yet completely known. We report here a rare case in which consecutively positive RT-PCR test results were separated by more than one month.

Case report

A 37-year-old male had a history of travel from affected geographic areas (Wuhan) on January 26, 2020 and then presented with fever (38.5°C), dry cough, fatigue, dizziness, runny nose and diarrhoea 5 days later. Physical examination revealed increased respiratory (25/min) and heart rates (115/min), and lung auscultation revealed a few moist rales in the right lower lobe. On admission, the patient had positive RT-PCR test results, and chest computed tomography (CT) images showed multiple nodules and mixed ground-glass opacification with consolidation in both lungs. The presence of SARS-CoV-2 in respiratory specimens was detected by real-time RT-PCR. Total RNA of SARS-CoV-2 was extracted within 20 minutes using an RNA isolation kit (Liferiver, Wuhan, China) from the throat and nasopharyngeal swab samples. The RT-PCR was performed using a SARS-CoV-2 nucleic acid detection kit according to the manufacturer's protocol (Sansure Biotech, Hunan, China). Two target genes were tested during the real-time RT-PCR assay, namely, open reading frame 1ab (ORF1ab) and nucleocapsid protein (N) (**Table 1**). Laboratory findings showed that the patient's lymphocyte and $CD4^+$ (cluster of differentiation 4) counts were below the normal range. Blood gas analysis and neutrophil enumeration revealed no obvious abnormities.

In this case, the hospitalized patient with COVID-19 was treated at Qianjiang Central Hospital, Chongqing, which was a designated hospital for COVID-19 pneumonia and Public Health Clinical Center, from February 2, 2020, to March 6, 2020, and was evaluated with consecutive RT-PCR tests for COVID-19 nucleic acid. The patient was diagnosed with moderate COVID-19 pneumonia according to the China Health Authority's interim criteria. Informed consent for the therapeutic regimen was obtained from the patient before treatment.

The patient received antiviral treatment, including arbidol (0.2 g, tid, po), Kaletra (lopinavir 400 mg/ritonavir 100 mg, q12h, po), IFN-α (interferon-α 50 μg, q12h, hypo), and traditional Chinese medicine. He accepted supplemental oxygen by nasal cannula after admission to the hospital. The duration of antiviral treatment was 9 days and IFN-α was 13 days, separately (**Figure 1**). Routine blood analysis showed an increased lymphocyte count, indicating recovery and restoration of immune function. Arterial blood gas analysis showed no hypoxia. The fever, fatigue, diarrhea and rhinorrhea disappeared after four days of treatment. The cough lasted for 25 days from the illness onset. A CT scan on February 7 showed that bilateral pneumonia remained, but the appearance of the left lower lobe mildly worsened. On February 28, a chest CT scan demonstrated bilateral multiple nodules and mixed ground-glass opacification with consolidation, which were improved compared with those observed on February 4, 2020 (**Figure 2**). Throat and nasopharyngeal swab nucleic acid testing, COVID-19-specific antibody detection (IgG and IgM), and $CD4^+$ lymphocyte counts were evaluated regularly during the period of hospitalization (**Figure 3**). The results of two continuous COVID-19 virus tests were negative for throat swabs and nasopharyngeal swabs, and the patient was thus discharged on March 6, 2020. The nucleic acid test was negative from the throat-swab follow-up for two weeks.

Discussion

We report here a rare case with COVID-19, for which the longest duration of viral shedding

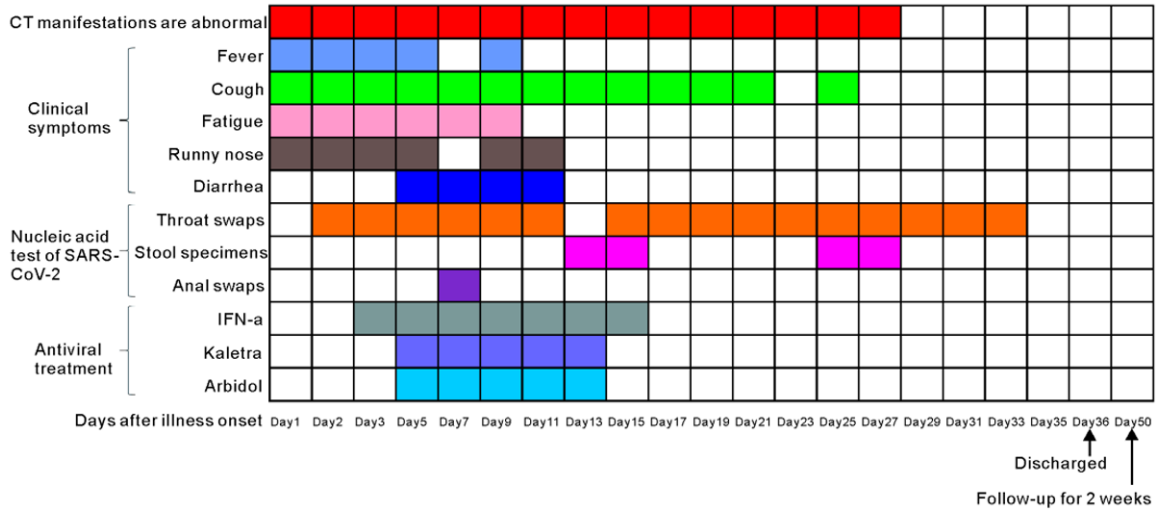

Figure 1. Clinical courses of CT scan of results, clinical symptoms, nucleic acid test of SARS-CoV-2, antiviral treatments and outcomes and duration of viral shedding from illness onset to follow up two weeks in this patient with COVID-19. (CT: computed tomography, SARS-CoV-2: novel coronavirus, IFNα: interferon-α, Kaletra: lopinavir/ritonavir).

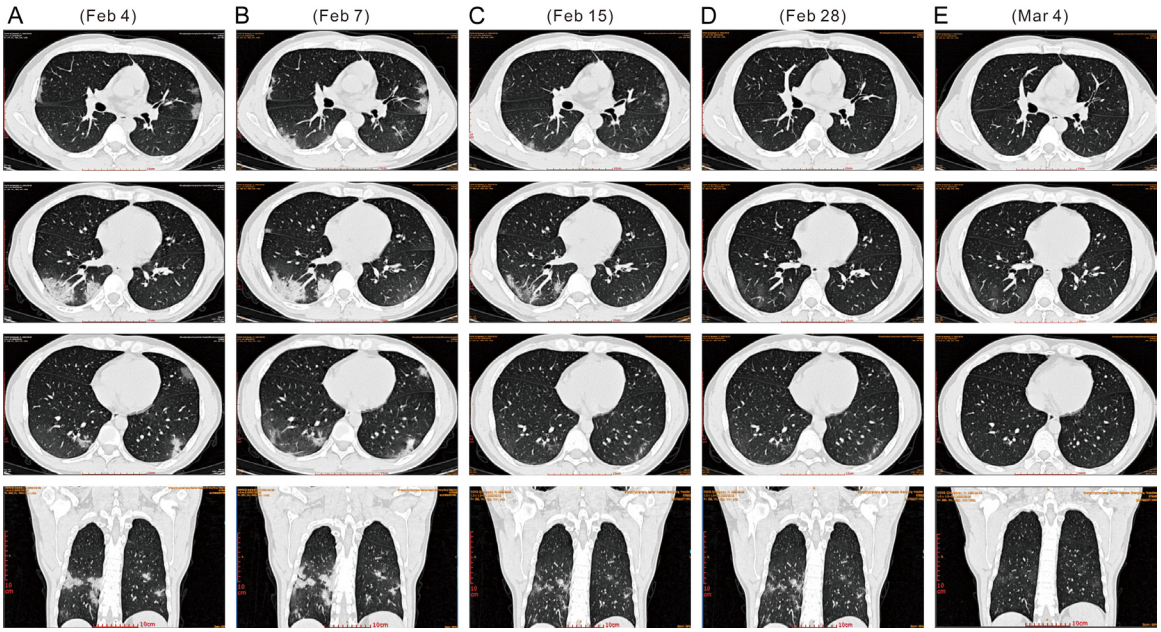

Figure 2. Chest CTs of the patient with COVID-19 obtained on February 4 (A), February 7 (B), February 15 (C), February 28 (D), March 4 (E).

was 32.0 days from illness onset with moderate COVID-19 pneumonia. The time from symptom onset to recovery was 36 days. Feiz et al. [6] reported that the median duration of viral shedding was 20.0 days (IQR 17.0-24.0 days) in survivors, but the COVID-19 virus was detectable in patients who unfortunately died, and the longest shedding time was 37 days. That study showed that the duration of viral shedding was affected by the severity of the disease and noted that all patients in the study were hospitalized. Furthermore, prolonged viral shedding suggests that patients may still be able to transmit the new coronavirus, and prolonged shedding of the virus has important guiding significance for isolation prevention measures. Hence, non-symptomatic infected persons or recovered patients should be in in-

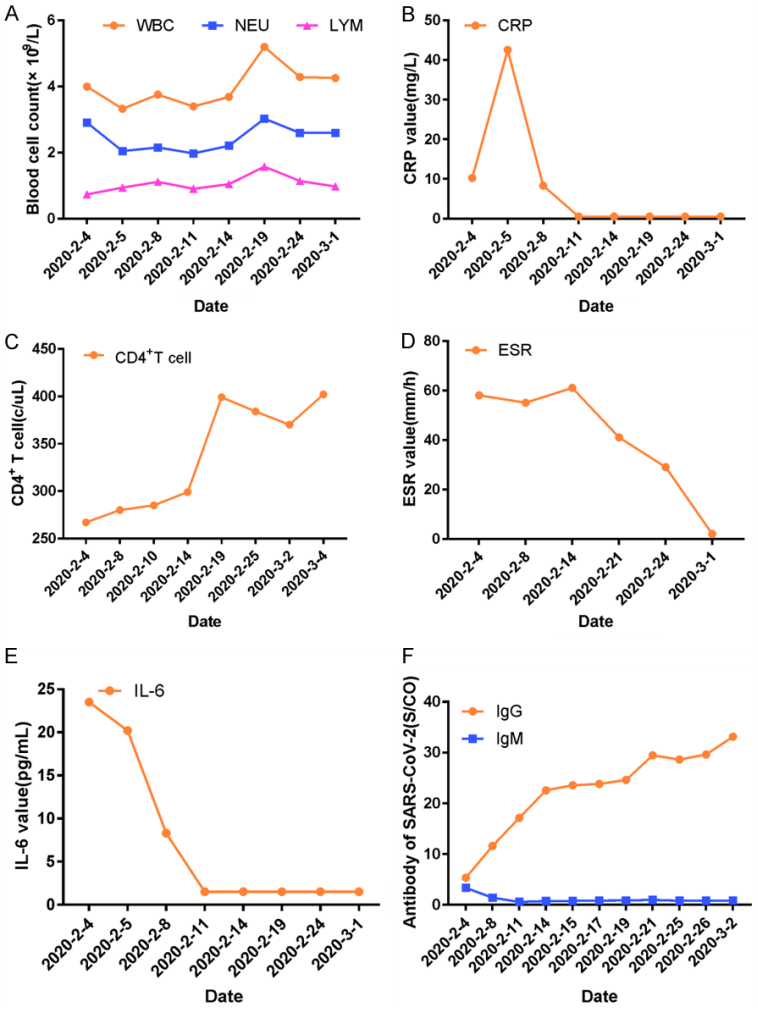

Figure 3. Temporal changes in laboratory markers from illness onset in this patient hospitalized with COVID-19. It shows temporal changes in blood cell count (A), CRP value (B), CD4⁺ lymphocytes' count (C), ESR value (D), IL-6 value (E), antibody of SARS-CoV-2 (F). CRP: C-Reactive Protein, CD4: Cluster of differentiation, ESR: Erythrocyte Sedimentation Rate, IL-6: Interleukin-6, WBC: White blood cell, NEU: Neutrophil, LYM: Lymphocyte. The increased of CRP on February 5 was related to the aggravation of the pneumonia.

home quarantine for an extended time of more than 14 days.

Recently, many cases were positive upon RT-PCR retesting during quarantine and observation after discharge [7]. These findings indicated that some recovered patients may still be virus carriers. However, Nancy Knight, an officer of the CDC's Division of Global Health Protection, said that it is possible that the oral and nasal swab positive tests detected pieces of the dead virus, that would not be transmissible [8]. In the present case, consecutively positive RT-PCR tests were verified for the upper respiratory tract. The lymphocyte count from routine blood testing and CD4⁺ count from the peripheral blood increased gradually. IgM and IgG antibodies are known to be important indicators of current, recent and past infection [9]. New coronavirus-specific IgG and IgM antibody levels changed in this case throughout the entire course of infection and recovery period. The recovery period of IgG antibodies was 3 times longer than that of the acute period. Therefore, the patient's upper respiratory tract swab positive test may have been caused by a piece of the inactive virus.

The therapeutic procedure for this COVID-19 patient consisted of comprehensive therapy. The antiviral treatment regimen included arbidol, lopinavir/ritonavir, and interferon-α1b. The combination of therapeutic strategies is currently recommended in the latest version of China's National Health Commission-issued (version 7) official guidance. Aralen (chloroquine phosphate) is an effective antimalarial drug used to treat and prevent malaria [10]. Aralen demonstrated effectiveness against COVID-19 in a randomized multicentre controlled clinical trial (ChiCTR2000029559) [11].

In conclusion, the patient was given combination medical treatment. All clinical symptoms and CT imaging manifestation abnormalities resolved during the course of therapy. The new coronavirus-specific IgG antibody levels significantly increased by more than 3 times above those at illness onset, which were accompanied by decreased IgM levels. Even though the positive RT-PCR tests were verified in the upper respiratory specimens, SARS-CoV-2 may have changed from active to inactive, at which point it is not easily transmissible among humans and moderate COVID-19 patients. However, the shedding period of the virus is not clear in severely or extremely ill COVID-19

patients. The results warrant further independent verification in future studies; if confirmed, this information can reduce hospital bed occupancy and save medical resources.

Acknowledgements

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Disclosure of conflict of interest

None.

Abbreviations

WHO, world health organization; COVID-19, coronavirus disease 2019; ARDS, severe acute respiratory syndrome; CDC, Center for Disease Control and Prevention; RT-PCR, real-time reverse transcriptase-polymerase chain reaction; CD4, cluster of differentiation 4; CT, computed tomography.

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