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RESEARCH ARTICLE

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Prolonged fecal shedding of SARS-CoV-2 in a young immunocompetent COVID-19 patient: A case report and literature overview

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Abstract

Clinicians are facing several challenges in tackling coronavirus disease 2019 (COVID-19); one issue is prolonged detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA. Here, we describe a case of SARS-CoV-2 infection in a young immunocompetent patient with a virological course lasting for 71 days. Following antiviral treatment, but no additional glucocorticoid or interferon therapy, the patient recovered from COVID-19 pneumonia (moderate). Detection of viral RNA via throat swabs showed negative results. However, the viral RNA reappeared and persisted in stool samples for an additional 27 days, while the patient remained asymptomatic and exhibited no abnormal signs. This case indicates that SARS-CoV-2 can result in a prolonged fecal RNA shedding, even in an immunocompetent patient with zero exposure to immunosuppressive therapies.

KEYWORDS

COVID-19, immunocompetent, prolonged viral RNA shedding, SARS-CoV-2

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic is a global public health crisis that has caused social and economic disasters in many countries. Managing the source of infection is crucial for controlling this epidemic; however, the emergence of asymptomatic carriers, patients experiencing relapse, and prolonged viral shedding in patients, frequently overlooked by infection prevention and control protocols, hinder the control of the source of infection.[1–3] Therefore, understanding the clinical course and virological course of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is important.

In China, two consecutive negative results of nucleic acid tests for SARS-CoV-2 from respiratory samples are required to end the quarantine of COVID-19 patients.[4] However, clinicians face a predicament in the case of patients with long-term viral shedding through the respiratory tract or feces. Evidence indicates that SARS-CoV-2 RNA positivity may persist for several weeks following symptom resolution[5–7]; fecal samples have shown positive results for a mean of 27.9 days after the onset of symptoms. The fecal positive timeline is longer than that for respiratory samples,[8] with fecal viral shedding persisting for 1–33 days following a negative nasopharyngeal swab test result.[7] In cases of exceptionally prolonged fecal shedding (shedding for >70 days), patient age, glucocorticoid use, and immunocompromised status were identified as the major factors for delayed SARS-CoV-2 RNA clearance.[9–11]

Here, we report the case of a young immunocompetent COVID-19 patient who achieved clinical recovery but exhibited persistently positive results upon a fecal SARS-CoV-2 nucleic acid test for up to 71 days after disease onset. We studied the combined long-term treatment and management practices used for this patient to analyze the clinical characteristics, pathogenesis, response to antiviral treatment, and infectivity.

2 | CASE PRESENTATION

The patient provided written informed consent for publication of the case. On February 9, 2020, a 34-year-old man was admitted to a hospital in Guangxi with reported fever and fatigue for 16 days.

He had a medical history of hyperthyroidism but no immunodeficiency-related diseases. He developed low-grade fever without any obvious cause on January 24, 2020, with a peak temperature of 39.0°C, accompanied by fatigue. However, he was not tested for SARS-CoV-2 nucleic acids and was quarantined at home. During this period, he was treated with antipyretic medicine (details unknown), and his elevated body temperature returned to normal. From January 29 to 31, the patient visited the clinic for infusion treatment due to urticaria (details unknown). On February 3, 2020, his grandfather and wife developed COVID-19 and tested positive for SARS-CoV-2 nucleic acids. On February 8, 2020, a throat swab test yielded positive results for SARS-CoV-2 RNA by reverse-transcription quantitative PCR (RT-qPCR, two pairs of primers targeting the regions of ORF1 and N), and the patient was admitted to the hospital for treatment. After disease onset, his mental state, sleep, and diet remained fair, and bowel movements and micturition were normal. On admission, his temperature was 37.0°C, oxygen saturation (SpO_2) was 96% on room air, respiratory rate was 20 breaths per minute, and lung auscultation showed rough breathing sounds but did not exhibit signs of dry or wet rale. Laboratory examinations showed mildly elevated levels of alanine amino-transferase (55 U/L) but no abnormalities in routine blood tests, renal function, C-reactive protein level, D-dimer level, and thyroid function. As shown in Figure 1, chest computed tomography (CT) scans on February 9, 2020 showed patchy and cloud-like high-density shadows with blurred edges in the upper and lower lobes of both lungs near the pleura. The patient was diagnosed with COVID-19 (nucleic acid-positive, moderate disease). After hospitalization, he received antiviral therapy with arbidol (CSPC Pharmaceutical Co., Ltd.) 200 mg, three times a day and Lopimune (lopinavir/ritonavir; AbbVie Deutschland GmbH & Co. KG) 400/100 mg, twice a day. Thymosin (Disai Pharmaceutical Co., Ltd.) 80 mg, once a day was used to enhance immunity, and traditional Chinese medicine (Xuebijing injection, Hongri Pharmaceutical Co., Ltd.) 50 ml, twice a day was used for detoxification treatment. Hepatocytes were protected by administering diammonium glycyrrhizinate enteric-coated capsules (Zhengda Tianqing Pharmaceutical Co., Ltd.) at 150 mg, three times a day. Glucocorticoids, interferons, and plasma were not administered at any point during his hospital stay. CT scans on February 14, 2020 showed significant improvement to the bilateral lung lesions, with no new lesions detected. Vital signs and SpO_2 in the absence of oxygen inhalation (99%) were normal; no abnormalities were found on physical and laboratory examinations. The patient was transferred to another hospital for centralized management and treatment on February 16. His nasopharyngeal swab test for SARS-CoV-2 nucleic acids yielded negative results (Ct value > 40) on February 24, 2020. However, on February 29, 2020, his nasopharyngeal swab test for SARS-CoV-2 nucleic acids returned positive results (Ct value was 39.60 for the ORF1 gene and 40.28 for the N gene). The patient remained asymptomatic (no gastrointestinal symptoms) and showed no abnormal signs. He was treated for 5 days with chloroquine phosphate (Xinyi Tianping Pharmaceutical Co., Ltd.) at 500 mg twice a day. CT scans on March 03, 2020, showed that the upper lobes of the lungs were scattered with thin and fuzzy shadows; bilateral lung lesions improved, and no new lesions were observed. Subsequently, his nasopharyngeal swab test for SARS-CoV-2 nucleic acids yielded negative results for 2 consecutive days, and he was discharged on Day 44 after disease onset on March 7, 2020. We recommended that the

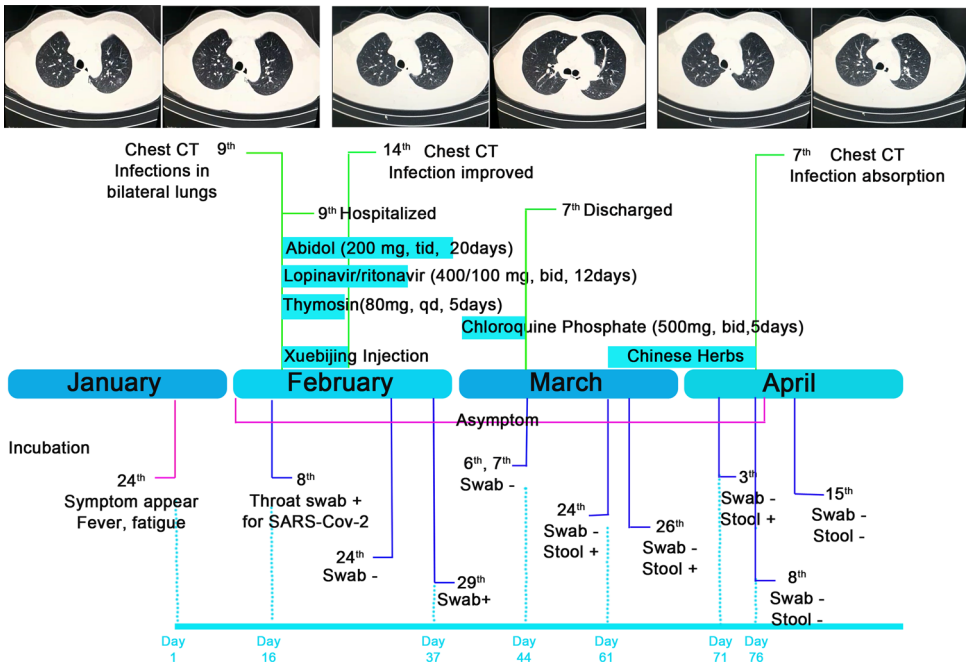

FIGURE 1 Timeline of clinical presentation, diagnostic tests, and treatments of the patient. CT, computed tomography; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

patient continue with quarantine and observation, in addition to wearing masks and maintaining ventilation. He was advised to maintain social distancing, eat alone, and practice good hand hygiene. However, viral nucleic acid tests on Day 17 after discharge (Day 61 after disease onset), Day 19 (Day 63 after disease onset), and Day 27 (Day 71 after disease onset) showed positive results in stool samples, with a relatively low viral load (CT values between 38 and 40); during this time, his nasopharyngeal swab test for SARS-CoV-2 nucleic acids yielded negative results, the serum IgM and IgG antibodies were also negative. He remained asymptomatic and showed no abnormal signs. Traditional Chinese medicine (Honeysuckle 15 g, Perilla leaf 15 g, Shandougen 5 g, Cangzhu 15 g, *Morinda officinalis* 30 g, Epimedium 20 g, Peilan 15 g, French Pinellia 9 g, tangerine peel 15 g, ginger 20 g, forsythia 15 g, and reed root 30 g; five doses of decoction in water, one dose per day) was used for treatment. After the test results on Days 76, 82, and 83 after disease onset were negative, quarantine was terminated.

3 | DISCUSSION

Recently, COVID-19 patients who have exhibited persistently positive SARS-CoV-2 nucleic acid test results despite resolved clinical symptoms have attracted attention. The duration of SARS-CoV-2 RNA shedding is approximately 3 weeks after symptom onset.[7,12] Here, we describe an immunocompetent individual who exhibited long-term fecal SARS-CoV-2 shedding of up to 71 days after symptom onset. The precise date when this individual acquired SARS-CoV-2 is unknown; however, the exposure might have occurred in late December 2019. As shown in Table 1, persistent SARS-CoV-2 RNA shedding has been documented[6,13–16]; however, the prolonged persistence of detectible SARS-CoV-2 is generally identified in upper respiratory tract specimens, not fecal samples. The longest reported case of fecal viral shedding was 100 days and was found in an 11-month-old baby. Multi-sample studies have revealed several independent parameters associated with extended SARS-CoV-2 RNA shedding, including corticosteroid treatment, male sex, older age, delayed hospital admission, immunoglobulin use, lymphocyte count, invasive mechanical ventilation, lack of lopinavir/ritonavir treatment, and maximum body temperature over 38.5°C.[17–24] Furthermore, a decrease in the humoral immune response, to some extent, was considered to be the root cause of prolonged viral shedding.[25] Interestingly, the patient in our study was particularly young, had no fever at admission, showed no abnormalities upon routine blood tests, and received no immunosuppressive medicines during the hospital stay. He was healthy and had no underlying conditions. Currently, the cause of this individual's situation in response to SARS-CoV-2 remains unclear. High-quality studies are imperative to enhance our understanding of and to better characterize the virus. It is worth mentioning that we have indeed tried a lot of medicines including traditional Chinese medicine in the treatment, however, according to the World Health Organization (WHO), there are no specific medicines for SARS-CoV-2. Available drugs including lopinavirritonavir, arbidol,

TABLE 1 Overview of patient demographics from studies included in the review

References	Number of patients	Type of patients	Type of sample	SARS-CoV-2 existing time	Severity	Past medical history	Therapy/key findings of the study
Wang et al.[6]	1	Male 50 yrs	Sputum	92 days	Moderate	None	TCM, umifenovir, interferon, chloroquine phosphate, convalescent plasma, danoprevir and ritonavir
Avanzato et al.[13]	1	Female 71 yrs	Throat swab	105 days	Mild	Chronic lymphocytic leukemia	Intravenous immunoglobulin (IVIG) convalescent plasma
Chen et al.[14]	1	Female 68 yrs	Sputum	137 days	Moderate	None	Interferon-α, lopinavir/ritonavir, intravenous immunoglobulin, methylprednisolone
Chen et al.[15]	1	Female 11 ms	Feces	100 days	Mild	None	Not mentioned
D'Ardes et al.[16]	1	Female 65 yrs	Throat swab	51 days	Serious	Hypertension, hypothyroidism	Darunavir/cobicistat, hydroxychloroquine
Li et al.[17]	38	52.6% >65 yrs	Sputum	58–118 days	92.1%—mild	Not mentioned	Infectious SARS-CoV-2 was isolated from the sputum
Gupta et al.[18]	26 studies	3 ms–87yrs	Feces	1–47 days			High incidence and persistence of SARS-CoV-2 positive fecal tests in COVID-19 patients
Han et al.[19]	206	56.8% >60 yrs	Feces	15–62 days	Not mentioned	Not mentioned	Patients with digestive symptoms had a longer duration and were more likely to be fecal virus positive

Abbreviations: ms, months; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TCM, traditional Chinese medicine; yrs, years.

chloroquine and analogs hydroxychloroquine tested in clinical trials, results were not very promising for any of them to be a definite therapy yet.[26–28]

The presence of viral ribonucleic acid (RT-PCR positivity) may not represent a transmissible live virus and its specific load, and infectious viruses can be readily isolated from throat- and lung-derived samples; however, since no isolates were obtained from samples taken after Days 8–18 from this individual despite ongoing high viral loads,[29,30] the duration of infectivity remains uncertain. Given that fecal viral shedding mainly occurs in patients subsequent to the loss of virus from respiratory specimens, as in our case, identifying whether the patient is contagious becomes critical. A few studies have reported the infectivity of SARS-CoV-2 in the stool. Wang et al. cultured four SARS-CoV-2-positive fecal specimens with high copy numbers and successfully demonstrated live viruses using electron microscopy in two specimens. Zhang et al. also demonstrated the presence of culturable SARS-CoV-2 in fecal samples from COVID-19 patients.[29,31] However, a more recent study failed to isolate the live virus from stool samples despite high viral RNA concentrations, which aligns with the findings of other viral culture attempts.[1,32] These observations raise questions about the duration of infectious fecal SARS-CoV-2 shedding and transmission potential in COVID-19 patients. The implications of these prolonged viral shedding patients as potential sources of infection require to be elucidated.

Although the possibility of reinfection could not be excluded because of the discontinuous PCR positivity and sequencing data of SARS-CoV-2 RNA in respiratory and fecal specimens not available, our data strongly suggested it was unlikely. First, there were no new clinical symptoms during the whole course; second, no elevation of antibodies (IgM or IgG) was found after hospitalization; third, he had no opportunity for re-exposure to SARS-CoV-2 after the first hospitalization.

In China, it is recommended that patients continue the 14-day isolation management and health monitoring after discharge, and follow-up hospital visits are recommended in the second and fourth weeks after discharge.[4] The risk of infectious viruses being shed from the persistently positive recovered patients is uncertain, and the patients may suffer personal risk from prolonged hospitalization or sheltering place, particularly when considering the social distress and economic burden associated with these measures. It would be prudent to further examine the subsequent management and treatment of such patients.

AUTHOR CONTRIBUTIONS

Concept and design: Yanhong Yu, Peiqi Wan, and Fang Xiao. *Acquisition, analysis, or interpretation of data*: Fang Xiao, Qiuling Wei, and Guiyang Wei. *Drafting manuscript*: All authors.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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