

Recurrence of Positive SARS-CoV-2 RNA in a COVID-19 Patient: Two Case Reports from Saudi Arabia

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Case Report

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Abstract

Background The rapid spread of the COVID-19 pandemic which took a place in Wuhan, China and diffused globally required the international public health to take a coordinated international response. As other coronaviruses were described, SARS-CoV-2 was thought to be an immunizing, monophasic disease. Herein, we reported first two COVID-19 cases registered in Saudi Arabia whose nasopharyngeal swabs turned positive for SARS-CoV-2 ribonucleic acid (RNA) after recovery.

Case presentation First patient who is symptomatic with recurrence of positive SARS-CoV-2 RNA occurred 115 days after the first symptomatic infection and did not develop protective immune response. Second patient who is asymptomatic during the recurrence of positive SARS-CoV-2 RNA occurred 60 days after the first symptomatic infection in an apparently immunocompetent patient.

Conclusion These findings highlight the recurrence of positive SARS-CoV-2 after recovery even if SARS-CoV-2 antibodies were developed.

Background

Since the fast expansion of the ongoing global pandemic Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in December 2019, the number of Coronavirus disease (COVID-19) cases have exceeded 27 million worldwide [1]. Saudi Arabia was among the impacted countries that reported the first case of COVID-19 on March 2, 2020. By September 8, 2020, the Ministry of Health (MOH) reported over 322,000 positive cases, with 4137 deaths and 298,246 recoveries [2].

COVID-19 is a respiratory illness, person to person contact, and respiratory droplets are the primary route of infection. When the pandemic first started, it was thought to be an immunizing, non-relapsing disease [3]. However, in some countries, there have been reports of rare suspected cases of COVID-19 reinfection [4]. Herein, we reported two COVID-19 cases registered in Saudi Arabia with recurrence of positive SARS-CoV-2 ribonucleic acid (RNA).

Case Presentation

First case

Patient 1 is a 23-year old healthy male, with no underlying medical conditions, who had a nasopharyngeal (NP) swab collected on April 13 using a viral transport media (VTM). As recommended by the Saudi Ministry of Health, the diagnostic testing for SARS-CoV-2 was performed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) using at least one confirmatory target, in addition to the screening targets [5]. The RT-PCR test was done as a standard infection control procedure after the patient arrived from a trip abroad. The test result was positive and confirmed by the National Health Laboratory (NHL; Table 1). Two days later, the patient started complaining from joints pain, mild headache, and diarrhea. According to the Saudi Ministry of Health guidelines for COVID-19 positive patients, the local

health authorities urged him to self-isolate until his symptoms resolve, and the subsequent test is negative [6]. He received no prescription medications during his quarantine period. To follow up, on April 20 and 25 two NP swabs were collected for RT-PCR assay test at two different laboratories, and both results were negative. As a result, the patient resumed his normal life. Just over three months later (August 6), he developed the following symptoms: moderate headache, fatigue, sore throat, and diarrhea. He suspected reinfection due to close contact with COVID19 patient and performed two SARS-CoV-2 RT-PCR tests at two different laboratories; both were positive. The symptoms were subjectively more intense this time and lasted for three days. A follow-up and confirmatory tests were carried out on August 13 and 16, respectively, and both yielded negative results. For further investigations, a SARS-CoV-2 IgG assay was conducted (August 16) for the detection of SARS-CoV-2 antibodies development, and it came out negative with a titer of 0.16 AU/mL (Reference value < 0.7 AU/mL) indicating a possible non-protective immune response [7].

Table 1
Timelines and testing results of the SARS-CoV-2 recurrence cases

	Age (years)	Sex	Timelines	Symptoms	NP ^a Swab	Confirmation	Serology (SARS- CoV-2 IgG)
Patient 1	23	Male	April 13	Arthralgia Mild headache Diarrhea	Positive ^b	Positive (NHL ^d)	
			April 20	No	Negative ^c	Negative (DL ^e)	
			April 25	No	Negative	Negative (DL)	
			August 6	Moderate headache Fatigue Sore throat Diarrhea	Positive	Positive (DL)	
			August 13	No	Negative		
			August 16	No	Negative		Negative
Patient 2	59	Male	June 16	Fever Arthralgia, Myalgia Fatigue	Positive	Positive (NHL)	
			July 1	No	Negative		
			July 4	No	Negative		

^a NP: Nasopharyngeal

^b Positive; SARS-CoV-2 detected

^c Negative; SARS-CoV-2 not detected

^d NHL: National Health Laboratory

^e DL: Different Laboratory with new NP swab collection

Age (years)	Sex	Timelines	Symptoms	NP ^a Swab	Confirmation	Serology (SARS- CoV-2 IgG)
		August 15	No	Positive		
		August 16	No	Positive		Positive
^a NP: Nasopharyngeal						
^b Positive; SARS-CoV-2 detected						
^c Negative; SARS-CoV-2 not detected						
^d NHL: National Health Laboratory						
^e DL: Different Laboratory with new NP swab collection						

Second Case

Patient 2 is a 59-year male with no underlying medical conditions who presented on June 16 for COVID-19 testing after developing flu-like illness symptoms. The test result came out positive and was confirmed by the NHL (Table 1). A week later, the patient's health started to improve, and symptoms began to disappear gradually. On July 1 and 4, two consecutive follow-up tests were done, and both results were negative for SARS-CoV-2, which suggested that the patient was cured. At the beginning of August, some of the patient's family members were infected with SARS-CoV-2 experienced flu-like symptoms such as fever, fatigue, and headache. Although the patient himself did not experience any symptoms, he decided to do a cautionary SARS-CoV-2 test on mid-August, and it revealed a positive result which was also confirmed on a subsequent NP swab collection. Furthermore, we performed IgG assay at that time, which came back positive (titer of 5.7 AU/mL), confirming the presence of SARS-CoV-2 antibodies.

Discussion And Conclusion

We report here two cases of healthy adults who had two episodes of possible COVID-19 infection. Interestingly, in one case, the symptomatic patient with recurrence of positive SARS-CoV-2 occurred after three months of the initial infection that did not trigger a protective immune response. In the other case, asymptomatic patient with recurrence of positive SARS-CoV-2 occurred within three months of the initial infection.

Recently, Yao et al. demonstrated that SARS-CoV-2 viral particles remain in previously positive patients' lungs whose NP swabs results were negative three times consecutively; this suggests that SARS-CoV-2 virus may not be eliminated when the symptoms disappear [8]. Therefore, there is still a reason to be

cautious, and we need to be aware of recovered patients and their potential infectivity. Interestingly, there have not been any studies demonstrating that recovered patients are infectious.

To our knowledge, our cases are the first to describe positive SARS-CoV-2 viral RNA in recovered COVID-19 patients in the Middle East. According to the Centers for Disease Control and Prevention (CDC), reinfection of SARS-CoV-2 is highly considered in a patient who becomes symptomatic around 90 days after onset of infection and has been in close contact with an infected person, supporting our first case [9]. A similar case presenting recurrence of SARS-CoV-2 has been reported in Hong Kong, bringing more attention lately. To and his colleagues demonstrated that second episode of asymptomatic infection occurred after the first symptomatic episode in an apparently immunocompetent patient [4]. In addition, they confirmed SARS-CoV-2 reinfection by performing whole genome sequencing for the first and second episodes indicating different clades [4]. We assume that the recurrence of COVID-19 is possible due to the presence of nonprotective IgG and recovered patients might be carriers and actively transmitting the virus even after their two negative tests [10, 11]. Thus, gatherings of positive cases are not safe, and there should be an emphasis upon such social practices, and for those in convalescence, we suggest that they undergo regular tests for infectivity assessments.

The presence of SARS-CoV-2 virus appears to be unstable because of the possibility of false-negative results of the molecular test which might be due to fluctuations in the viral load or pre-analytical errors during the sample collection [12]. In our case reports, reducing the chance of false-negative and false-positive results was done by confirming each test result in different laboratory with new NP swab collection. For both cases, first positive test results were confirmed by the NHL, and two consecutive negative tests were done before the patients were considered to be cured. Although these are only two case reports and the evidence is not determinant, it gives insight and encourages future cohort studies.

In conclusion, the global public health is at risk of the possibility of recurrence of SARS-CoV-2 as we exhibited in our case reports, which could contribute to the spread of the virus. Therefore, additional virologic, immunological, and epidemiological studies should be done to have better understanding of SARS-CoV-2 recurrence mechanism.

Abbreviations

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

COVID-19: Coronavirus disease 2019

RT-PCR: Real-time reverse transcriptase-polymerase chain reaction

IgG: Immunoglobulin G

MOH: Ministry of Health

RNA: Ribonucleic acid

NP: Nasopharyngeal

VTM: viral transport media

NHL: National Health Laboratory

CDC: Centers for Disease Control and Prevention

Declarations

Ethics approval and consent to participate

Not Applicable.

Consent of publication

Written consent was obtained from the patient for publication.

Availability of data and material

Derived data are available on reasonable request.

Competing interests

The authors have declared that no competing interests exist.

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Contributions

Sara Alturaif, Remaaz Alharbi, Abdulaziz Alsadoon, and Meshari Alabdullatif conceptualized and refined research idea, and collected and processed the patients' samples. Sara Alturaif, Remaaz Alharbi, and Waleed Alqurashi created case report design and wrote the manuscript. Waleed Alqurashi and Meshari Alabdullatif edited the manuscript

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