Can SARS-CoV-2 Viral RNA Continually Persist in an Asymptomatic COVID-19 Patient?

Sen Variaveettil Thomas^a Anjala Nizam^b Tarab Iqbal^b

^aPediatric Department, Dubai Hospital, Dubai, United Arab Emirates; ^bDubai Medical College, Dubai, United Arab Emirates

Keywords

Antibodies · COVID-19 · SARS-CoV-2 · RT-PCR ·
Cycle-threshold value · Re-positive cases

Abstract

An asymptomatic 39-year-old male patient with well-controlled hypertension on a combination of antihypertensives including angiotensin receptor blocker was screened positive for SARS-CoV-2 by RT-PCR nasopharyngeal (NP) swab and was admitted to an isolation facility in Dubai on March 23, 2020. He had a history of exposure to a COVID-19 patient a few days prior to the screening test. His chest X-ray showed signs of pneumonitis. He was discharged from the isolation facility on day 28 with 2 consecutive negative SARS-CoV-2 RT-PCR NP swab results, 24 h apart. After 14 days of home quarantine, he tested positive again for SARS-CoV-2 on day 44 and was again isolated in our facility. He continued testing positive until day 51, after which he was discharged again following 2 consecutive negative tests 24 h apart.

© 2020 The Author(s).
Published by S. Karger AG, Basel

Introduction

The emergence of SARS-CoV-2 in December 2019 in Wuhan, China, with the successive spread of the virus has resulted in a pandemic of COVID-19. As researchers and healthcare workers try to decode the virus and its characteristics, continuous developments are being made on the understanding of the exact infective period, incubation period, and duration of RT-PCR positivity in a patient with the virus. According to a recent study, 26–49% of cases were tested positive again after discharge. From the date of onset of symptoms to testing positive after discharge by RT-PCR, it took an average of 45 days (range: 8–82 days), based on 226 cases [1]. “Re-positive cases” referred to those cases which tested positive for SARS-CoV-2 after discharge but are currently referred to as “PCR re-detected after discharge from isolation” as per expert recommendations. Here, however, we report an asymptomatic patient who had persistence of SARS-CoV-2 viral RNA by nasopharyngeal (NP) swabs till day 51 after being tested negative twice on day 26 and day 28.

Fig. 1. Chest X-ray done on March 26, 2020, showing signs of pneumonitis.

Case Report/Case Presentation

A 39-year-old male patient with no significant past medical history except for well-controlled hypertension on a combination of antihypertensives including angiotensin receptor blocker was screened positive for SARS-CoV-2. The test of diagnosis was the nucleic acid amplification test using the real-time RT-PCR assay for detecting SARS-CoV-2 RNA using a NP swab. He had a history of exposure to a COVID-19 patient a few days prior to the screening test. He was admitted to an isolation facility in Dubai on March 23, 2020 (day 1). He denied any history of fever, cough, myalgia, dyspnea, smell, and taste disorders upon admission, along with normal vitals, and was classified as an asymptomatic COVID-19 patient. A chest X-ray was done on day 3 (shown in Fig. 1) and showed features of pneumonitis as commonly seen in COVID-19 patients with no signs of pneumothorax or pleural effusion. However, the patient continued to be clinically asymptomatic. A repeat chest X-ray done on day 9 showed signs of improvement (shown in Fig. 2). The complete blood picture (shown in Table 1), which includes differential counts on day 2 and day 51, suggests a mild increase in neutrophil percentage along with a decrease in lymphocyte percentage on day 2 that normalized by day 51.

RT-PCR NP swabs for SARS-CoV-2 were done repeatedly for surveillance, the results of which are shown in Table 2. The patient tested positive on day 8, day 14, and day 21. He tested negative consecutively on day 26 and day 28, after which he was discharged and advised to follow home quarantine guidelines for 14 days as per state protocol. However, 16 days (day 44) after the last NP swab was taken, the patient retested positive for COVID-19 and was still asymptomatic. He reported no possibility of a breach during the period of home quarantine. He was readmitted to our isolation

Fig. 2. Chest X-ray done on May 12, 2020, showing signs of improvement of pneumonitis.

facility. The patient retested positive again after 7 days (day 51) and was finally discharged as per the COVID-19 discharge protocol on day 56, after 2 consecutive negative swabs on day 53 and day 55. He continued to be asymptomatic during the second hospitalization.

Discussion/Conclusion

According to current discharge criteria by the UAE National Emergency Crisis and Disasters Management Authority and COVID-19 Crisis and Control Center, asymptomatic and mild COVID-19 patients are usually kept in home isolation or admitted to an institutional isolation facility. They are isolated for 14 days and discharged after they display no symptoms and no fever without taking antipyretics for 3 days prior to the scheduled discharge date, and 2 consecutive negative NP RT-PCR tests are obtained 24 h apart in case of health care workers [2]. There have been reports of several patients that have retested positive after discharge [1, 3]. Among some plausible causes of recurrence of positivity is firstly the possibility of RT-PCR false negativity, which can be attributed to the sampling procedures of NP swabs, quality of sampling tube, sample storage temperature and time, transportation process of samples, and quality of detec-

Table 1. FBC results

Parameter	Reference range	Day 2 (March 24, 2020)	Day 51 (May 12, 2020)
WBC count, $\times 10^3/\mu\text{L}$	3.6–11.0	6.0	5.9
RBC count, $\times 10^6/\mu\text{L}$	4.50–5.50	5.13	5.10
Hemoglobin blood, g/dL	13.0–17.0	14.1	14.1
Hematocrit, %	40.0–50.0	42.0	41.9
MCV, fL	77.0–95.0	81.8	82.1
MCH, pg	27.0–32.0	27.4	27.6
MCHC, g/dL	31.5–34.5	33.5	33.6
RDW, %	11.5–14.0	14.0	14.5
Platelets count, $\times 10^3/\mu\text{L}$	140–410	215	304
MPV, fL	7.4–10.4	7.9	7.5
Neutrophil absolute, $\times 10^3/\mu\text{L}$	2.0–7.0	4.1	2.8
Lymphocytes absolute, $\times 10^3/\mu\text{L}$	1.0–3.0	1.3	2.3
Monocytes absolute, $\times 10^3/\mu\text{L}$	0.2–1.0	0.6	0.5
Eosinophils absolute, $\times 10^3/\mu\text{L}$	0.0–0.5	0.0	0.2
Basophils absolute, $\times 10^3/\mu\text{L}$	0.0–0.1	0.0	0.1
Neutrophil, %	–	67.7	48.0
Lymphocyte, %	–	21.7	38.6
Monocyte, %	–	9.9	8.7
Eosinophil, %	–	0.5	3.8
Basophil, %	–	0.2	0.9
Nucleated RBCs	0 per 100 WBC	0	0

Table 2. SARS-CoV-2 RT-PCR NP swab results (Ct value not evaluated)

Sample 1: March 23, 2020 (day 1)	Detected (positive) (A)
Sample 2: March 30, 2020 (day 8)	Detected (positive) (A)
Sample 3: April 5, 2020 (day 14)	Detected (positive) (A)
Sample 4: April 12, 2020 (day 21)	Detected (positive) (A)
Sample 5: April 17, 2020 (day 26)	Not detected (negative)
Sample 6: April 19, 2020 (day 28)	Not detected (negative)
Sample 7: May 5, 2020 (day 44)	Detected (positive) (A)
Sample 8: May 12, 2020 (day 51)	Detected (positive) (A)
Sample 9: May 14, 2020 (day 53)	Not detected (negative)
Sample 10: May 16, 2020 (day 55)	Not detected (negative)

tion reagents (kits) [4]. Second, prolonged viral shedding can be seen especially in immunocompromised patients [3]. Reports suggest that the cycle threshold (Ct) value of RT-PCR can be used as a surrogate marker of viral load. On detecting the Ct value of RT-PCR above 33–34 in COVID-19 patients, they can be deemed “not contagious” and hence discharged from isolation [5, 6]. In a study, viral cell culture testing of 108 PCR re-detected cases, all cases had tested negative; hence, viral RNA detection by PCR does not equate to infectiousness or a viable virus [1, 3]. In another study, antibody responses to SARS-CoV-2

start about 7 days from the onset of symptoms, and most patients develop detectable antibodies by day 14–28 [7, 8]. The use of spike protein of the SARS-CoV-2 in an ELISA by the Centers for Disease Control and Prevention could offer 99% specificity and 96% sensitivity [9].

Our report shows isolating patients just based on SARS-CoV-2 RT-PCR of NP swabs would lead to erroneously deciding that all patients are infective, leading to isolation either at home or hospital facility. This will increase the physical and emotional well-being and financial burden of the family. This also adds significantly to the patient burden and economic burden of the health-care system of the country.

Hence, we suggest that rather than detecting SARS-CoV-2 by RT-PCR of NP swabs, this should be coupled with the Ct value of RT-PCR and antibody blood test particularly in patients who had prior COVID-19 infection. Large-scale serological screening with validated tests will identify individuals who may have protective immunity to infection and a better measure of disease activity. It is very highly unlikely that COVID-19 infection strikes the person twice in a short window. For better management of the patient, more studies should be done with a good sample size as this is a reflection based on a single patient.

Acknowledgement

I thank Dr. Karunakar Vadlamudi for his support in preparing this manuscript.

Statement of Ethics

All necessary patient consent has been obtained to publish his case.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding sources were required for the above case report.

Author Contributions

S.V.T., A.N., and T.I. contributed to the design and implementation of the research, analysis of the results, and writing of the manuscript.

References

- 1 Korea Centers for Disease Control and Prevention [Internet]. Findings from investigation and analysis of re-positive cases. 2020 May 19.
- 2 UAE National Emergency Crisis and Disaster Management Authority and COVID19 Command and Control Center [Internet]. Home Isolation and Quarantine Guidelines during Coronavirus (COVID-19) Pandemic Version 2. [2020 June 9].
- 3 Position Statement from the National Centre for Infectious Diseases and the Chapter of Infectious Disease Physicians, Academy of Medicine, Singapore [Internet]. Period of Infectivity to Inform Strategies for De-isolation for COVID-19 Patients. [2020 May 23].
- 4 Kucirka L, Lauer S, Laeyendecker O. Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. *Ann Intern Med*. 2020 Aug 18;173(4):262–67.
- 5 La Scola B, Le Bideau M, Andreani J, Hoang VT, Grimaldier C, Colson P, et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. *Eur J Clin Microbiol Infect Dis*. 2020;39:1059–61.
- 6 Yu F, Yan L, Wang N, Yang S, Wang L, Tang Y, et al. Quantitative detection and viral load analysis of SARS-CoV-2 in infected patients. *Clin Infect Dis*. 2020 Mar;71(15):793–8.
- 7 Long QX, Liu BZ, Deng HJ, Wu GC, Deng K, Chen YK, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat Med*. 2020;(6):845–48.
- 8 Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature*. 2020;581:465–9.
- 9 National Center for Immunization and Respiratory Diseases (NCIRD), Division of Viral Diseases [Internet]. Serology Testing for COVID-19 at CDC. [2020 May 23].