Crit Care Shock (2023) 26:63-70

Persistent positive COVID-19 PCR results for over 360 days: A case report

Shreyaa Rajpal[1], Prithvi Raghavan[1], Andrea Terrazas[1,2], Victor A. Gomez[1], Najia Hussaini[1,3], Joseph Varon[1-3]

Abstract

Coronavirus disease 2019 (COVID-19) is an acute infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The first case of COVID-19 was identified in Wuhan, China, and quickly spread to the world, resulting in the COVID-19 pandemic more than three years ago. The incubation period varies from 2-14 days. People who are either immunocompromised due to a medical condition or by medications or treatments are more likely to be sick with COVID-19 for longer periods when compared to immunocompetent people. We report a case of an 83-year-old gentleman who has reported a positive reverse transcription polymerase chain reaction (RT-PCR) test for COVID-19 for 360 days. He had been hospitalized six times since the onset of symptoms in February 2022. He had a history of melanoma and non-Hodgkin's lymphoma.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has been a worldwide medical emergency and has impacted all fields of medical care. The spectrum of symptoms associated with COVID-19 can widely range from asymptomatic or mild infection to acute respiratory failure. Patients identified to be at increased risk of morbidity and mortality are those with malignancies, immunodeficiency, chronic lung disease, diabetes, hypertension, male sex, and older age. Patients with cancer are believed to follow a severe and rapid disease course, often requiring intensive care. (1) In addition, there is a concern about decreased immunogenicity and effectiveness of all COVID-19 vaccines in immunocompromised patients. For example, non-response rates among patients with lymphoma have been reported from 30 to 58%. (2)

Groundwork research on the epidemiology, clinical features, and risk factors for mortality of COVID-19 has shown that the duration of viral shedding (DVS) is not identical among patients. The precise contributors directly affecting the time of persistent positive nucleic acid have yet to be reported. (3) We recently had a patient with prolonged positivity to COVID-19.

Case presentation

An 83-year-old Caucasian man presented to the clinic with extreme fatigue and a severe cough. A respiratory pathogen panel reverse transcription polymerase chain reaction (RT-PCR) was ordered, which yielded positive for COVID-19. This man has been vaccinated five times against COVID-19. The patient had been hospitalized six times in the past year for cough, fever, and shortness of breath and had received eight rounds of intravenous remdesivir. He first tested positive for COVID-19

[1.] Dorrington Medical Associates, Houston, Texas, USA
[2.] Universidad Autonoma de Baja California, Tijuana, Mexico
[3.] Caribbean Medical University, Willemstad, Curaçao

Address for correspondence:
Joseph Varon, MD, FACP, FCCP, FCCM, FRSM
2219 Dorrington Street, Houston, Texas, USA
Tel: +1-713-669-1670
Fax: +1-713-669-1671 FAX
Email: jvaron@uh.edu

RT-PCR in February 2022. His hospitalizations and treatment are depicted in **Table 1**.

In each hospitalization, he tested positive for COVID-19 via RT-PCR. His medical history was significant for melanoma treated with radiation and surgery in 2015. He has active non-Hodgkin's lymphoma, for which he underwent chimeric antigen receptor (CAR)-T cell therapy in 2021. The patient had a history of mitral valve replacement due to mitral valve regurgitation in 2005. Night-time oxygen support was started in June 2022, which progressed to full-time oxygen support (2 l/min) by November 2022.

On examination, he was febrile (100 °F), tachypneic (28/min), blood pressure 100/60 mmHg, and had an oxygen saturation of 92% while breathing 28% fraction of inspired oxygen (FiO2), and he was well-oriented to time, place, and person. He was pale with dry mucous membranes. Lung auscultation revealed crackles on both fields.

Laboratory investigations during his visit to our clinic are depicted in **Table 2**.

Moreover, a COVID-neutralizing antibodies test was performed with the result that the sample did not contain detectable Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) antibodies.

A high-resolution computed tomography of his chest (**Figure 1**) revealed extensive parenchymal lung disease, including dilated bronchi in the right upper lobe of the lung and mild pleural thickening.

The patient's condition deteriorated over the next few days, and the family elected hospice care because of his advanced age and underlying malignancy.

Discussion

Our patient contracted a COVID-19 infection and has been experiencing sustained positive RT-PCR results for over 360 days. Unfortunately, the patient was immunocompromised, which placed him at an increased risk of developing severe symptoms of COVID-19. Despite receiving various treatments and adhering to quarantine protocols, the patient's positive RT-PCR results have persisted, posing a unique challenge to healthcare providers.

This case highlights the complexities of managing COVID-19 in immunocompromised patients, particularly those with underlying conditions and a history of cancer treatments. COVID-19 in oncologic patients presents a dilemma given the competing priorities of providing timely anticancer therapy, avoiding immunosuppression during infection, and minimizing exposure to others. Our patient had received CAR-T cell therapy a few months before his infection.

Recent studies showed that patients undergoing CAR-T cell therapy shed viable SARS-CoV-2 for a long time, reportedly up to 2 months. (4) CAR-T-cell therapy recipients are believed to be at risk of poor outcomes from COVID-19 due to their immunocompromised state caused by prior immunochemotherapy and adverse effects from CAR-T-cell therapy, such as cytopenias and low immunoglobulins. (5) Patients receiving cluster of differentiation 19 (CD19) CAR T-cell therapy for relapsed/refractory non-Hodgkin lymphoma experience prolonged and profound B-cell aplasia and hypogammaglobulinemia, placing them at higher risk for severe COVID-19 regardless of their receiving supplemental intravenous immunoglobulins. (6)

In a meta-analytical study by Bonanand and coinvestigators, patients showed an increase in mortality due to COVID-19 related to age, which was evident in patients aged >60 years old. This might be influenced by the physiological aging process in general or the greater ubiquity of comorbidities which decreases their intrinsic power to fight infections. (7)

Our patient had been hospitalized six times over 360 days and presented with complaints of fever, cough, and shortness of breath. His diagnosis was established through repeated nucleic acid testing. The neutralizing antibody test yielded a negative result, but his clinical symptoms suggested evidence of infection. It often takes months for the immune system to generate antibodies to be detected by a test. Thus, immunocompromised individuals like our patient might take longer to produce antibodies to detect a positive result. (8) It can be hypothesized that the immunocompromised state of this individual impaired the ability to ward off the virus and remain contagious for a longer period. Even though the patient tested positive for COVID-19 for several days, which might imply he was actively shedding the virus, his wife and children did not test positive. This might reveal no association between contagiousness and a positive RT-PCR test.

Gao and coworkers found that patients who presented with prolonged viral shedding were usually elderly and with a history of hypertension. (9) Symptoms seen in this patient, such as shortness of breath, expectoration, and fatigue, were more frequent in patients with prolonged viral shedding. In addition, such patients had significantly higher neutrophil counts and lower lymphocyte counts. Together with higher levels of inflammatory markers such as C-reactive protein, erythrocyte sedimentation rate, and ferritin, this evidence suggests that patients with impaired immune function might have a prolonged period of viral shedding. As patients may

have particles of the SARS-Cov-2 after such agent is dead, amplification techniques such as RT-PCR may give false positive results. However, our patient had clear evidence of active viral infection.
Finally, the use of remdesivir in our patient did not yield positive results. Clearly, this agent is suboptimal, and many believe it should not be part of the armamentarium for the treatment of COVID-19 including multiple control trials performed on adult patients revealed with moderate certainty that usage of this drug had minimal effect on clinical improvement and mortality up to day 28 of hospitalization. Several updates and additional studies are yet to show reliable evidence of the effectiveness and harms of this drug. (10)

Conclusions

COVID-19 can remain active in patients, particularly those immunosuppressed, for prolonged periods. Therefore, clinicians of all specialties must be vigilant of this potential clinical course.

Conflicts of interest

The authors have no conflict of interest in the preparation of this manuscript. This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Table 1. Hospitalizations course

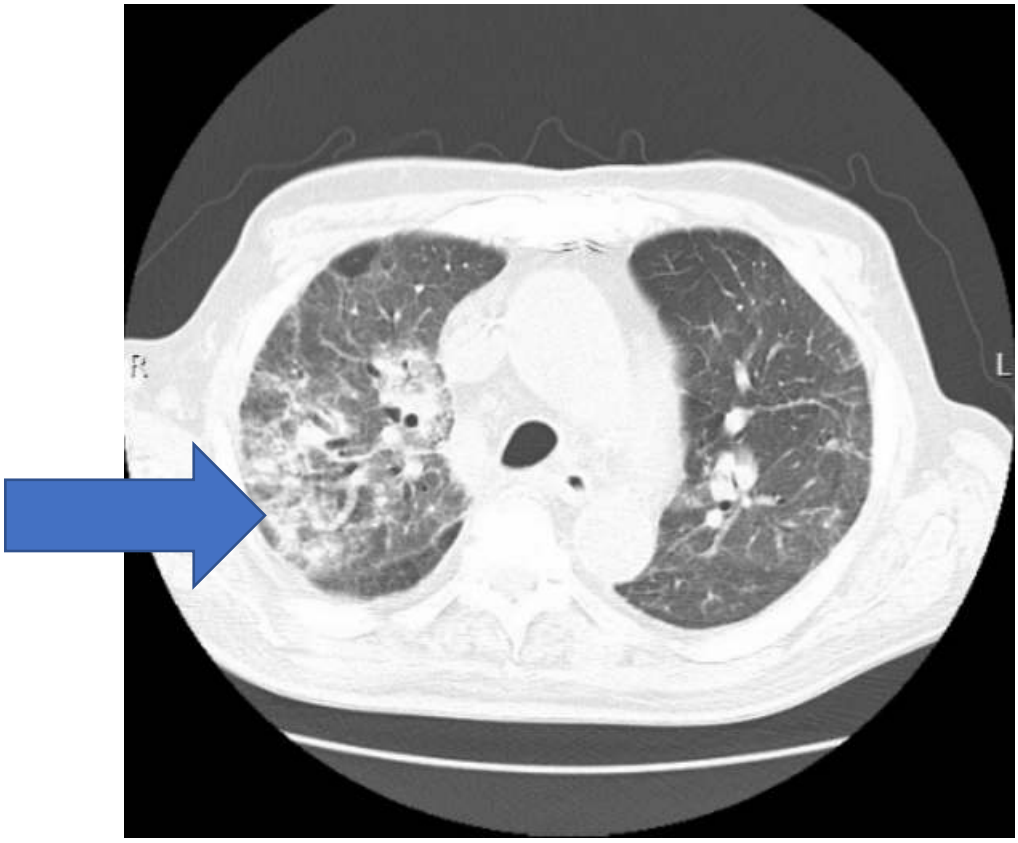
Hospitalization	Date	Treatment
First hospitalization	March 1-7, 2022	Received 1 dose of remdesivir
Second hospitalization	April 1-13, 2022	Received 1 dose of remdesivir
Third hospitalization	May 18-27, 2022	Received 1 dose of remdesivir
Fourth hospitalization	June 21-28, 2022	Received 1 dose of remdesivir
Fifth hospitalization	July 7-20, 2022	Received 2 doses of remdesivir
Sixth hospitalization	January 1-14, 2023	Received 2 doses of remdesivir

Table 2. Results of laboratory investigations at our clinic

Laboratory investigation	Result	Reference values
RBC ($x10^6$/ul)	$3.69x10^6$/ul	$4.14\text{-}5.80x10^6$/ul
Hemoglobin (g/dl)	8.5 g/dl	13.0-17.7 g/dl
Hematocrit (%)	27.9%	37.5-51.0%
MCV (fl)	76 fl	79-97 fl
MCH (pg)	23.0 pg	26.6-33.0 pg
MCHC (g/dl)	30.5 g/dl	31.5-35.7 g/dl
RDW (%)	20.4%	11.6-15.4%
Platelets ($x10^3$/ul)	$136x10^3$/ul	$150\text{-}450x10^3$/ul
WBC ($x10^3$/ul)	$10.6x10^3$/ul	$3.4\text{-}10.8x10^3$/ul
Neutrophils ($x10^3$/ul)	$5.1x10^3$/ul	$1.4\text{-}7.0x10^3$/ul
Lymphocytes ($x10^3$/ul)	$1.5x10^3$/ul	$0.7\text{-}3.1x10^3$/ul
Monocytes ($x10^3$/ul)	$3.8x10^3$/ul	$0.1\text{-}0.9x10^3$/ul
Glucose (mg/l)	92 mg/l	70-99 mg/l
BUN (mg/l)	11 mg/l	8-27 mg/l
Creatinine (mg/l)	0.48 mg/l	0.76-1.27 mg/l
eGFR (ml/min/1.73 m^2)	102 ml/min/1.73 m^2	>59 ml/min/1.73 m^2
BUN/creatinine ratio	23	10-24
Sodium (mmol/l)	139 mmol/l	134-144 mmol/l
Potassium (mmol/l)	4.3 mmol/l	3.5-5.2 mmol/l
Chloride (mmol/l)	98 mmol/l	96-106 mmol/l
Calcium (mg/l)	8.7 mg/l	8.6-10.2 mg/l
Carbon dioxide (mmol/l)	26 mmol/l	20-29 mmol/l
Phosphorous (mg/l)	3.4 mg/l	2.8-4.1 mg/l
Magnesium (mg/l)	2.1 mg/l	1.6-2.3 mg/l
Ferritin (ng/l)	416 ng/l	30-400 ng/l
Sedimentation rate (Westergren) (mm/hr)	98 mm/hr	0-30 mm/hr
C-reactive protein (mg/l)	152 mg/l	0-10 mg/l
Total protein (g/l)	5.8 g/l	6.0-8.5 g/l
Albumin (g/l)	3.7 g/l	3.6-4.6 g/l
Direct bilirubin (mg/l)	0.5 mg/l	0-1.2 mg/l
Indirect bilirubin (mg/l)	0.25 mg/l	0-0.40 mg/l
Alkaline phosphatase (IU/l)	106 IU/l	44-121 IU/l
AST (IU/l)	33 IU/l	0-40 IU/l
ALT (IU/l)	19 IU/l	0-44 IU/l

Legend: RBC=red blood cells; MCV=mean corpuscular volume; MCH=mean corpuscular hemoglobin; MCHC=mean corpuscular hemoglobin concentration; RDW=red cell distribution width; WBC=white blood cells; BUN=blood urea nitrogen; eGFR=estimated glomerular filtration rate; AST=aspartate aminotransferase; ALT=alanine transaminase.

Figure 1. High-resolution chest computerized tomography scan revealed bilateral opacities (see arrow) and the presence of bullous lung disease



References

1. Bonuomo V, Ferrarini I, Dell'Eva M, Sbisà E, Krampera M, Visco C. COVID-19 (SARS-CoV-2 infection) in lymphoma patients: A review. World J Virol 2021;10:312-25.
2. Galmiche S, Luong Nguyen LB, Tartour E, Wittkop L, Loubet P, et al. Immunological and clinical efficacy of COVID-19 vaccines in immunocompromised populations: a systematic review. Clin Microbiol Infect 2022;28:163-77.
3. Li T-Z, Cao Z-H, Chen Y, Cai M-T, Zhang L-Y, Xu H, et al. Duration of SARS-CoV-2 RNA shedding and factors associated with prolonged viral shedding in patients with COVID-19. J Med Virol 2021;93:506-12.
4. Xu W, Piper-Vallillo AJ, Bindal P, Wischhusen J, Patel JM, Costa DB, et al. Time to SARS-CoV-2 clearance among patients with cancer and COVID-19. Cancer Med 2021;10:1545-9.
5. Spanjaart AM, Ljungman P, de La Camara R, Tridello G, Ortiz-Maldonado V, Urbano-Ispizua A, et al. Poor outcome of patients with COVID-19 after CAR T-cell therapy for B-cell malignancies: results of a multicenter study on behalf of the European Society for Blood and Marrow Transplantation (EBMT) Infectious Diseases Working Party and the European Hematology Association (EHA) Lymphoma Group. Leukemia 2021;35:3585-8.
6. Auletta JJ. Buckling up against COVID-19 after CAR T-cell therapy. Blood 2022;140:85-7.
7. Bonanad C, García-Blas S, Tarazona-Santabalbina F, Sanchis J, Bertomeu-González V, Fácila L, et al. The effect of age on mortality in patients with COVID-19: A meta-analysis with 611,583 subjects. J Am Med Dir Assoc 2020; 21:915-8.
8. Chaudhry B, Didenko L, Chaudhry M, Malek A, Alekseyev K. Longest reported case of symptomatic COVID-19 reporting positive for over 230 days in an immunocompromised patient in the United States. SAGE Open Med Case Rep 2021;9:2050313X211040028.
9. Gao C, Zhu L, Jin CC, Tong YX, Xiao AT, Zhang S. Proinflammatory cytokines are associated with prolonged viral RNA shedding in COVID-19 patients. Clin Immunol 2020;221: 108611.
10. Ansems K, Grundeis F, Dahms K, Mikolajewska A, Thieme V, Piechotta V, et al. Remdesivir for the treatment of COVID-19. Cochrane Database Syst Rev 2021;8:CD014962.

This page is intentionally left blank