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Longest reported case of symptomatic COVID-19 reporting positive for over 230 days in an immunocompromised patient in the United States

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Abstract

Coronavirus 2019 (COVID-19) pneumonia was first noted in Wuhan, China. Since the start of the pandemic, there have been millions of cases diagnosed. The average time from onset of symptoms to testing negative SARS-CoV-2 via reverse transcription polymerase chain reaction is roughly 25 days. In patients who continually test positive for COVID-19, it is essential to determine precisely which risk factors contribute to the increase in viral shedding duration. We present a case about a 62-year-old man who has persistently tested positive for COVID-19 for more than 230 days. We followed his treatment course, in which he had been hospitalized multiple times since the onset of symptoms back in April 2020. We have determined that patients with immunosuppression, especially those taking corticosteroids, are at increased risk of prolonged viral shedding. It is essential to continually monitor these immunocompromised patients as they required a greater time period in order to have an appropriate immune response in which antibodies are created.

Keywords

COVID-19, reverse transcription polymerase chain reaction, viral shedding, immunocompromised, corticosteroids

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Introduction

To date, there have been more than 185 million cases of COVID-19 diagnosed worldwide, and nearly 4 million deaths.[2] COVID-19 is commonly associated with cough, shortness of breath (SOB), fever, loss of sense of smell, and fatigue. Pre-existing conditions such as coronary artery disease, hypertension, and diabetes mellitus, and those who are immunocompromised are susceptible to complications from COVID-19.[1] The average time from onset of symptoms until patients have a negative SARS-CoV-2 reverse transcription-polymerase chain reaction (RT-PCR) is 25 days.[2] There are several documented cases exist in which a prolonged duration of viral shedding has occurred in individuals with SARS-CoV-2 after being classified as asymptomatic. To date, there have been two reported cases with prolonged SARS-CoV-2 viral shedding duration greater than 100 days.[3] We now present a case where a patient tested positive for 32 weeks/230 days.

Case report

We present a case about a 62-year-old man who had persistently tested positive via RT-PCR for more than 230 days. He first tested positive on 23 April 2020. He has multiple comorbidities, including systolic heart failure with a left ventricular ejection fraction of 15%, mild intermittent asthma, and hyperlipidemia. He had a history of non-Hodgkin's lymphoma diagnosed in 2001 that was treated with Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone. He has since been in remission. He also had a history of anti-neutrophil cytoplasmic antibody

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(ANCA)-colitis, Sweet's syndrome, and vasculitis that was diagnosed in 2018. He receives Rituximab every 6 months, and his last dose was given in September 2019. The patient was scheduled to receive his next dose the previous week but did not because he fell ill.

On 23 April 2020, he presented to the emergency department (ED) with a 48-h history of fever that peaked at 39.4°C/103°F. He stated that he had an increasing cough and breathlessness without orthopnea and paroxysmal nocturnal dyspnea. Upon arrival in the ED, he was given an albuterol treatment with some improvement to his hypoxia. The patient had denied any phlegm production or expectoration. A SARS-CoV-2 RT-PCR test was ordered and returned positive. He was started on ceftriaxone and azithromycin, hydroxychloroquine, and steroids. After a short hospital stay, the patient's oxygen level normalized on room air, and he was discharged and told to social distance.

On 21 May 2020, he visited with his primary care physician. A chest X-ray was obtained and showed improving pneumonia. He did not have any chest pain, SOB, or cough. On 22 May, he was started on cefuroxime, but the treatment failed to clear his infection. Further analysis of his complete blood count (CBC) showed that his white count showed a leukocytosis of 11.8. His white count on CBC was rechecked on 28 May and showed an increase to 14.4.

On 2 June 2020, he returned to the ED, presenting with hypotension and tachypnea. His procalcitonin was 0.09, and he was noted to be in acute renal failure with a creatinine of 1.46, while the basic metabolic panel (BMP) showed a sodium of 131. His baseline creatinine was indicated in his chart as 1.1. The results of his CBC with differential are noted in Table 1.

A chest X-ray revealed the progression of left lung opacity. A SARS-CoV-2 RT-PCR was requested and returned positive. He was given intravenous (IV) fluids and broad-spectrum antibiotics consisting of cefepime, azithromycin, and vancomycin. Rheumatology, hematology, and oncology were consulted; he received intravenous immune globulin (IVIG) as well as Rituximab. Upon discharge home, he was placed on prednisone 60 mg daily with a plan to taper slowly. He had been receiving dapsone; however, this was changed to Atovaquone.

A repeat chest computed tomography (CT) at the end of August revealed bilateral ground-glass opacities. On 1 September 2020, he presented to the ED with SOB and reported that he had increased dyspnea on exertion over the last 3 days. Also, he reported a low-grade fever over the past couple of days. His maximum temperature was 38.3°C/101°F. He denied any associated cough, chest pain, palpitations, or any other infectious symptoms. A chest X-ray was obtained in the ED, and a CT of the chest without contrast showed chronic and improved pneumonia compared to previous CT imaging. A SARS-CoV-2 RT-PCR was requested and returned positive. Together, the positive SARS-CoV-2 RT-PCR and radiographic imaging remained consistent with COVID-19, and no further testing was ordered.

His labs showed elevated lactate at 3.2 and mild chronic hyponatremia at 130 with a baseline at 134. His renal function mildly worsened with a creatinine of 1.31 and a baseline between 1.1 and 1.2. He was treated with steroids, IVIG, and immunoglobulin G (IgG) on 3 September. A second SARS-CoV-2 RT-PCR was requested and returned positive. He had an adverse reaction that consisted of shaking, chills, and increased work of breathing. He was admitted to the intensive care unit (ICU) for monitoring and pre-treatment, where the Infectious Disease team administered convalescent plasma. A SARS-CoV-2 RT-PCR was requested on 1 October and 10 October and returned positive. He was discharged and told to social distance.

On 18 October, he presented with respiratory distress. He was noted to be febrile at 39.3°C, tachycardia in the 150s, tachypneic in the 50s, and with an oxygen saturation of 88% on nonrebreather. He was given 125 mg of methylprednisolone and covered with broad-spectrum antibiotics while blood cultures were pending. A chest X-ray showed multifocal pneumonia with bilateral opacities. Labs were notable for white blood cell (WBC): 20.2 with no bandemia, potassium: 5.3, bicarbonate: 18, creatinine: 0.99, and lactate: ~10. Initial blood gas of 7.17/60 (pH/$PaCO_2$) improved to 7.4/33 (pH/$PaCO_2$) after he was placed on bilevel positive airway pressure (BiPAP) and given the above interventions. He was placed on Atovaquone prophylactically to prevent *Pneumocystis jirovecii*. He received steroids that were slowly tapered, and at discharge, he was on 50 mg of oral prednisone with a plan to taper slowly.

On 16 November, he presented with abdominal pain, SOB, and dysphagia. In the previous 24 h, he complained of SOB and fevers for the past 2–3 days. The patient at baseline had been on 2 L of oxygen via nasal cannula. However, starting the morning of 15 November, he had some SOB and increased his oxygen to 3 L, which did not help. He also reported subjective fevers over the past couple of days, along with decreased appetite. There was epigastric abdominal pain that was constant and had been going on for the past couple of days. He denied cough, chest pain, nausea, vomiting, and diarrhea. A CT of the abdomen and pelvis was performed and revealed acute cholecystitis. CTA (computed tomography angiography) of the lung revealed multifactorial pneumonia. The surgery team was consulted, and they recommended antibiotics. He was treated with IV antibiotics and IV steroids for possible COVID-related fibrosis. Gradual improvement was noted.

On 23 November, a COVID-19 RT-PCR was requested and returned positive. On reviewing labs and physical, he was noted to have persistent idiopathic thrombocytopenic purpura (ITP), for which he was given IVIG. On 3 December, an acute change in respiratory status prompted the rapid response team to initiate respiratory distress protocols. He required an increase in high-flow nasal cannula (HFNC) from 60% to 80% FiO_2 due to the saturation to mid-80s. Another SARS-CoV-2 RT-PCR was requested and returned positive.

Table 1. CBC with differential from 14 March 2020 until 20 July 2020.

	Normal values	14 March 2020	1 June 2020	2 June 2020	0 June 2020	8 June 2020	9 June 2020	17 July 2020	20 July 2020
WBC	3.5–10.5 × 10^9 L	8.3 × 10^9 L	5.6 × 10^9 L	5.0 × 10^9 L	11.3 × 10^9 L (H)	13.5 × 10^9 L (H)	13.3 × 10^9 L (H)	9.5 × 10^9 L	13.7 × 10^9 L (H)
HGB	13.8–17.2 g/dL	12.4 (L)	11.7 (L)	11.4 (L)	10.0 (L)	11.5 (L)	11.8 (L)	12.7 (L)	12.9 (L)
HCT	40.7%–50.3%	36.1 (L)	35.1 (L)	36.0 (L)	30.5 (L)	34.6 (L)	35.2 (L)	39.7 (L)	38.2 (L)
RBC	4.3–5.9 × 10^{12}/L	4.49	4.23 (L)	4.35 (L)	3.73 (L)	4.25 (L)	4.33 (L)	4.63	4.58
MCV	80–100 μm^3	80.4	83.0	82.8	81.8	81.4	81.3	85.7	83.4
MCH	26.4–35.6 pg/cell	27.6	27.7	26.2 (L)	26.8	27.1	27.3	27.4	28.2
MCHC	31–36 g/dL	34.3	33.3	31.7	32.8	33.2	33.5	32.0	33.8
RDW	11.8%–15.6%	13.2	17.0 (H)	16.7 (H)	16.3 (H)	16.5 (H)	17.3 (H)	17.8 (H)	16.7 (H)
MPV	7.5–12.0 fl	9.8	8.7	9.1	9.5	9.7	9.3	10.0	9.8
Platelet	150–400 × 10^9/L	197	321	397	358	357	326	267	248
Ab. IG	<0.1/nL	0.0	0.9 (H)	0.1 (H)				0.1 (H)	
Ab. Lymph	0.9–4.4/nL	1.1	1.1	0.7 (L)				0.9	
Ab. Mono	0.1–1.1/nL	0.7	0.7	0.1				0.2	
Ab. Eos	0.0–0.3/nL	0.4 (H)	0.2	<0.1				<0.1	
Ab. Baso	0.0–0.1/nL	0.0	<0.1	0.0				0.0	
Automated neutrophil	50%–60%	72.6 (H)	61.9 (H)	82.9 (H)				86.4 (H)	
Fibrinogen	15–300 μg/L			654 (H)				298	
D-Dimer	<250 ng/mL			401 (H)		160		<150	

WBC: white blood cell; HGB: hemoglobin; RBC: red blood cell; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; RDW: red cell distribution width; MPV: mean platelet value; Ab. IG: absolute immature granulocyte; Ab. Lymph: absolute lymphocyte; Ab. Mono: absolute monocyte; Ab. Eos: absolute eosinophil; Ab. Baso: absolute basophil.

Table 2. Patient's CRP level, COVID test, and COVID test result for each admission.

Date	Test	COVID +/−	CRP (mg/L)
23 April 2020	RT-PCR	+	182.5
3 June 2020	IgG	−, <1.01	151
1 September 2020	RT-PCR	+	37.6
3 September 2020	RT-PCR	+	135.9
1 October 2020	RT-PCR	+	227.8
10 October 2020	RT-PCR	+	107.1
23 November 2020	RT-PCR	+	78.6
3 December 2020	RT-PCR	+	40.3

RT-PCR: reverse transcription polymerase chain reaction; IgG: immunoglobulin G.

Discussion

Our patient first tested positive for COVID-19 on 23 April 2020 and has since tested positive for 32 weeks/230 days. There have been only two other reported cases with prolonged SARS-CoV-2 viral shedding duration greater than 100 days.[3,4] There have been several documented cases in which a prolonged duration of viral shedding has occurred in individuals with SARS-CoV-2 after being classified as asymptomatic. The extended period of viral shedding in these individuals has been concomitant with fever, time from symptomology onset to hospitalization, age, and corticosteroid use.[1] All of these factors were observed in our patient, as he continually tested positive. Prolonged viral shedding duration has also been linked to lower lymphocyte levels and elevated ferritin, C-reactive protein, and neutrophil count.[5]

Patients who are immunocompromised are likely to have long-term shedding due to atypical symptom presentation. There are two explanations for why immunocompromised individuals continuously test positive via PCR: either they are shedding residual RNA or shedding the infectious replication-competent virus.[6] It is thought that immunosuppression with persistent viral shedding may be a protective factor because of the reduced immune response. The use of Rituximab, a monoclonal antibody, dampens the seroconversion immune response.[1]

A recent study conducted by Prescott et al.[8] found that immunocompromised animal subjects exhibited even more prolonged viral shedding than their immunocompetent counterparts. There was earlier detection of viral RNA and elevated viral RNA levels in the respiratory tract tissues in these animal subjects. Furthermore, the immunocompromised animal subjects exhibited significantly milder pathology because of the dampened immunological response. It can be presumed that viral replications will be much higher in the absence of a proficient immune reaction, while an exaggerated inflammatory response will likely lead to pathology.[7]

Persistent viral shedding is more common in older patients, especially those with a higher viral load.[1] While many COVID-19 patients attain a clinical recovery, a small percentage of patients may have persistent viral shedding that should be monitored.[8] It is imperative to monitor patients who are immunocompromised, those taking corticosteroids, and those with signs of elevated inflammatory markers.

Furthermore, although our patient had one COVID-19 antibody test that was negative, he displayed symptoms and clinical evidence of having contracted the virus. His diagnosis was confirmed through multiple positive RT-PCRs, as depicted in Table 2. The Food and Drug Administration (FDA) urges healthcare providers not to use antibody tests to diagnose active COVID-19 infections. A positive antibody test only indicates that a patient has been infected with coronavirus in the past. It often takes days and even several weeks for the immune system to create enough antibodies to be detected in a test.[9,10] Therefore, immunocompromised individuals, such as our patient, may take months to produce an appropriate number of antibodies to yield a positive antibody test.

In addition, several studies confirm that molecular diagnostic tests, such as RT-PCR, should be used as the gold standard for diagnosing patients with coronavirus. They have found that antibody tests yield a sensitivity of 77.3% with a false-negative rate of 22.7%.[11] Thus, it is fair to consider that the negative antibody test on 3 June represented a false negative.

Conclusion

Our patient tested positive for SARS-CoV-2 for more than 230 days. During this time, he was hospitalized multiple times and was treated appropriately. With the continuous rise in COVID-19 cases worldwide, healthcare providers need to note the various presentations and length of disease seen in patients who have contracted the virus. The average immunocompetent patient tests negative 25 days after the manifestation of coronavirus symptoms and immunocompromised patients may continue to have positive RT-PCR for weeks, and in rare cases, months after the symptom onset. As seen in our patient, it is crucial to monitor these immunocompromised patients continually.

Authors' Note

Andrew Malek is now affiliated to Institute For Family Health, Kingston, NY.

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Ethical approval

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