

# Positive SARS-CoV-2 RNA with Significant Inflammatory State and Thrombophilia after 12 Weeks of Initial Diagnosis of COVID-19 Infection

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## Abstract

The ongoing COVID-19 pandemic has affected most countries in the world, with significant economic and public health implications. There is rising concern that patients who recover from COVID-19 may be at risk of reinfection. Another potential concern is the uncommon clinical scenario of a patient having persistent SARS-CoV-2 RNA test over 3 months after the initial COVID-19 infection, as the patient presented. Whether presenting as a long-term infection (12 weeks) or reinfection, patients with COVID-19 will continue to have a severe inflammatory and prothrombotic state that could carry potential life-threatening thrombosis.

**Keywords:** COVID-19, pandemic, reinfection, SARS-CoV-2, thrombophilia

## INTRODUCTION

As a novel coronavirus, information regarding persistent or reinfection of the SARS-CoV-2 virus during the pandemic is limited. Further, data on the effects of prolonged or recurrent viremia in patients with thrombophilia are scarce. This case report presents this unusual but clinically relevant scenario and highlights the critical need for further investigation in this setting.

## CASE REPORT

A 33-year-old truck driver, male patient who developed symptoms of fever, chills, and dry cough in the month of March 2020. He was evaluated in an urgent care in the state of Florida. A few days prior to developing symptoms, the patient had been in New York City delivering a truck load. His nasopharyngeal swab SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR) test was positive on March 28, 2020. He was advised by the Florida Department of Health to self-isolate for 14 days and did so at their recommendation. The patient subsequently improved in 5 days. He did not undergo repeat testing at 14 days. The patient did not receive medications after obtaining results 5 days later as his symptoms had already resolved. On June 06, 2020, he presented to a hospital in Georgia due to right lower extremity

pain. He was diagnosed with extensive right iliofemoral deep venous thrombosis. The patient underwent US access of right popliteal vein, venogram of the right lower extremity, chemical thrombolysis, and percutaneous mechanical thrombectomy. The patient was discharged on apixaban.

The patient was evaluated in the ED at our institution on June 26, 2020, due to complains of bilateral lower extremity swelling. Lower extremity US disclosed bilateral extensive deep venous thrombosis. The patient reported being compliant in taking apixaban as prescribed. He denied fever, chills, viral prodrome, cough, dyspnea, or exposure sick persons. On physical examination, vital signs were normal with oxyhemoglobin saturation of 98% on room air. The only positive finding on physical examination was bilateral lower extremity swelling with evidence of edema. A repeat

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**How to cite this article:** Betancourt MF, Grant KM, Johnson JS, Kelkar DS, Sharma K. Positive SARS-CoV-2 RNA with significant inflammatory state and thrombophilia after 12 weeks of initial diagnosis of COVID-19 infection. *J Global Infect Dis* 2021;13:42-3.

**Received:** 25 August 2020 **Revised:** 03 October 2020

**Accepted:** 22 December 2020 **Published:** 26 February 2021

### Access this article online

#### Quick Response Code:



**Website:**  
www.jgid.org

**DOI:**  
10.4103/jgid.jgid\_286\_20

nasopharyngeal swab SARS-CoV-2 RT-PCR test done on June 28, 2020 was again positive. The admission inflammatory markers were elevated including C-reactive protein 6.59 mg/dL, ferritin 1283 ng/ml, and lactate dehydrogenase of 473 IU/L. Quantitative D-dimer was 35200 ng/dL. Computed tomography (CT) angiogram chest was negative for pulmonary embolism. The CT scan of the chest disclosed clear lungs.

The SARS-CoV-2 IgG antibody collected on 07/08/2020 was positive  $\geq 1.4$ . In order to try to understand if the patient was reinfected after 12 weeks of his initial COVID-19 infection diagnosis, SARS-CoV-2 IgM Antibody was ordered on July 7, 2020 and was negative. During this 3-month period, the patient was unaware of infecting any close contacts. Since the patient had no pulmonary complaints and did not require oxygen therapy at this visit, he did not receive steroids or antivirals.

The patient was started on anticoagulation with unfractionated heparin drip. He was evaluated by interventional radiology and underwent bilateral lower extremity venogram and placement of bilateral thrombolysis infusion catheters from the superficial femoral veins into the inferior vena cava. Hypercoagulable work up showed that the patient has a heterozygous factor V Leiden. Subsequently, the patient developed heparin-induced thrombocytopenia with both positive PF4-heparin antibody and serotonin release assay. The patient was discharged on Fondaparinux. He continued to follow as outpatient in the hematology clinic. Since the RT-PCR has a high specificity, the test was not repeated a third time.

## DISCUSSION

The WHO characterized COVID-19 infection as a pandemic on March 11, 2020. SARS-CoV-2 was initially recognized in Wuhan, China, in December 2019. One of the most important diagnostic tools to detect the infection is the SARS-CoV-2 RNA test. It has been noticed that in some cases viral RNA has been detected by RT-PCR even beyond week 6 following the first positive test.<sup>[1]</sup> There are also reported cases of recurrence of positive SARS-CoV-2 RNA in the convalescent period.<sup>[2]</sup> The patient described has a positive SARS-CoV-2 RNA test after 12 weeks of initial diagnosis of COVID-19 infection.

Clinical recurrences of COVID-19 symptoms have been reported after recovery, most described as pneumonia.<sup>[3,4]</sup> The patient described was found to have extensive deep venous thrombosis 3 months after his initial COVID-19 infection, with significant elevation in inflammatory markers and thrombophilia. This type of presentation along with a repeated positive nasopharyngeal SARS-CoV-2 RT-PCR test raises one more time the question of reinfection versus viral relapse.

COVID-19 infection can be detected indirectly by measuring IgM and IgG. ELISA-based IgM and IgG antibody tests have greater than 95% specificity for diagnosis of COVID-19. In the confirmed patients with COVID-19, sensitivity of IgM is 77.3% and negative predictive value is 80%.<sup>[5]</sup> Our patient had a positive nasopharyngeal SARS-CoV-2 RT-PCR test and positive IgG. The IgM was negative despite of the

significantly elevated inflammatory markers and clinical thrombosis (thrombophilia). It is not completely clear whether the negative IgM represented a false negative result. Further research including the potential measurement of quantitative viral load could be beneficial to answer this question.

This is the first report of positive nasopharyngeal SARS-CoV-2 RT-PCR test 3 months after an initial diagnosis of COVID-19 infection. COVID-19 results in a unique, profoundly prothrombotic milieu leading to both arterial and venous thrombosis.<sup>[6]</sup> Thrombotic events have been observed in outpatients with COVID-19 infection, but data on the incidence are not available. Whether presenting as a potential long-term infection (up to 3 months as this case) or reinfection, patients with COVID-19 will continue to have a severe inflammatory and prothrombotic state that could carry potential life-threatening thrombosis.

Informed consent was obtained from this patient to present this case report. The patient did not wish to present a patient perspective for this report.

## Research quality and ethics statement

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting, and reproducibility guidelines set forth by the EQUATOR Network. The authors all attest that this clinical investigation was determined to not require Institutional Review Board/Ethics Committee review, and the corresponding protocol/approval number is not applicable. We also certify we have not plagiarized the contents in this submission and have done a Plagiarism Check.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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