Recurrent COVID-19 in Hemodialysis: A Case Report of 2 Possible Reinfecions

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Patients receiving in-center hemodialysis are at high risk for infections due to relative immunosuppression, limited ability to physically distance, and frequent encounters with the health care setting. This has been particularly evident during the coronavirus disease 2019 (COVID-19) pandemic. We describe 2 patients with suspected recurrent COVID-19 infection, each with documented clearance of virus between episodes. The duration between a negative reverse-transcription polymerase chain reaction test result for severe acute respiratory syndrome coronavirus 2 and symptomatic reinfection was 31 and 55 days, respectively, in the 2 patients. A higher risk for infection with COVID-19 and poor outcomes if infected, including ≥20% short-term mortality risk, is worrisome in this patient population. Continued measures such as infection prevention, community outreach, and early testing may play a role in establishing protocols to protect the vulnerable dialysis population.

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INTRODUCTION

As the coronavirus disease 2019 (COVID-19) pandemic evolves, the possibility of reinfection among patients who have recovered from COVID-19 infection is being recognized.1 Recent data confirm that patients with mild COVID-19 infection often fail to mount a humoral response to the virus.2 Even patients with a robust antibody response may experience a rapid decline in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–specific antibodies up to undetectable levels by 3 months postinfection.3 There are now several reports of reinfection in the literature.1,4,5 Certain patient groups are likely at higher risk for reinfection due to poor immune response against SARS-CoV-2, including persons with immunosuppression from medications or underlying medical conditions.

Dialysis centers are a high-risk environment for transmission of certain infectious diseases, including those caused by respiratory viruses, and dialysis patients may have more severe disease due to multiple comorbid conditions. The dialysis population, particularly those receiving in-center hemodialysis, assumes particular significance due to unique exposure risks, namely: (1) recurrent exposure to medical personnel and other patients thrice weekly in the dialysis units, (2) lower ability to mount a stronger immune response,6 and (3) frequent additional confounding exposures, such as residing in nursing homes, long-term acute care, and rehabilitation facilities. For example, the reported incidence of COVID-19 infection in dialysis patients was 3.3% compared with 0.2% in the general population in the French National Cohort of dialysis patients.7 There is also concern for much higher mortality in the dialysis population affected by COVID-19, with rates of 20% as compared with 4% in the general population.7–9

Currently, our understanding of the ability to prevent reinfection after the first episode of COVID-19 infection is limited, but certain factors have been linked to greater vulnerability, including the strength and duration of immunity, as well as differences in the underlying immune system of certain patient populations. Although studies among primates suggest that acquired immunity prevents COVID-19 recurrence, responses in humans are currently being investigated.10 Some studies suggest declining titers of SARS-CoV-2 immunoglobulin G (IgG) antibodies in humans in the ensuing months postinfection.11 Reports of persistently positive reverse-transcription polymerase chain reaction (RT-PCR) test results in patients after symptom resolution have been well described, and most patients, including those with severe infection, are not infectious after a period of 20 days.12–15 The Centers for Disease Control and Prevention (CDC) has set guidance for the general population to quarantine for 10 days after the onset of symptoms based on data that ambulatory patients with COVID-19 infection no longer shed viable virus after day 9 of symptoms.16 However, immunocompromised patients and those with severe illness have been demonstrated to shed for longer and should remain in quarantine for 20 days.17,18 Many centers are using serum IgG antibodies to assess COVID-19 status and use this test as a measure of immunity, but it remains unclear whether an elevated IgG antibody titer affords subsequent protection given reports of short-lived immunity and COVID-19 recurrence in the medical literature.2 This debate assumes special importance in the clinical management of dialysis patients given the inherent risks for re-exposure and well-described inability to mount and sustain immune responses in this population, similar to other populations with extensive comorbid conditions.7,15,16

At the University of Alabama in Birmingham, in partnership with our dialysis provider, we established a COVID cohort unit for hemodialysis in March 2020. All in-center dialysis patients followed up at our medical center who
were designated either as patients under investigation or confirmed cases of COVID-19 infection received hemodialysis in the cohort unit, with protocol-driven testing to confirm a negative RT-PCR test result at 2 weeks after onset of symptoms and after asymptomatic. For patients still positive at 2 weeks, PCR testing was repeated on a weekly basis. Patients were transferred back to the “home” dialysis facility when they tested negative.

It is important to note that CDC guidance using a test-based strategy recommended 2 negative test results before a patient could be deemed not infectious. However, our organization’s ability to conduct multiple tests, like many others, was limited. Accordingly, to use resources judiciously, we relied on a single negative test result. This protocol was modified in October 2020 to incorporate a time-based protocol as recommended by CDC; we now dialyze patients with COVID-19 infection in the cohort unit for a period of 10 days, and certain high-risk patients for 20 days, before transferring them back into the general population. In addition, all patients admitted to the hospital from the emergency department are tested for SARS-CoV-2 with nasal swab RT-PCR.

We describe 2 adult hemodialysis patients with COVID-19 reinfection after recovery from prior infection with RT-PCR results documented during both infection episodes (Fig 1).

**CASE REPORTS**

**Case 1**

A man in his 70s who resides in a nursing home with a medical history of hypertension, diabetes mellitus, and coronary artery disease receiving maintenance in-center hemodialysis initially had COVID-19 infection diagnosed after nasal swab RT-PCR testing in May 2020 (cycle threshold [CT] of 36). At this time, the patient was asymptomatic and had undergone testing secondary to prolonged close contact with a COVID-19–infected patient at the nursing home. He was placed in the COVID-19 cohort unit at the dialysis clinic and quarantined at the nursing home as well. The patient remained asymptomatic and tested negative by nasal swab RT-PCR test on day 15 after the initial positive results, and isolation was discontinued.

At 31 days after negative RT-PCR test results, the patient presented to the emergency department with symptoms of shortness of breath, cough, chest pain, and myalgias for the preceding 24 hours. He was afebrile, with normal vital signs and benign physical examination findings. Radiograph of the chest was unremarkable. His nasal swab COVID-19 RT-PCR test was positive (CT, 42.7), and he was hospitalized and managed conservatively with albuterol and ipratropium meter dose inhalers. He did not...
receive oral steroids or remdesivir. He had positive COVID-19 IgG results with a reported signal to cutoff ratio of 8.53 (signal to cutoff ratio > 1.4 is considered positive). With improvement in symptoms and 59 days after his first positive RT-PCR test result, he was discharged.

**Case 2**

A woman in her late 50s who resides in a nursing home with an additional medical history of hypertension, hepatitis C, and heart failure receiving maintenance in-center hemodialysis tested positive by nasal swab RT-PCR (CT, 33) after prolonged close contact with a roommate with symptomatic COVID-19 infection. The patient was asymptomatic and as per protocol, underwent dialysis at the COVID-19 cohort shift at the dialysis unit and was quarantined at the nursing home. Two weeks later, as per protocol for discontinuing isolation, she underwent nasal swab RT-PCR testing on days 14 and 20 after her first positive test result and both tests were negative. Isolation and cohort dialysis precautions were discontinued at this time.

Fifty-five days later, the patient described myalgias, low-grade fevers, and a sore throat to the medical team at the nursing home. Her nasal swab RT-PCR for SARS-CoV-2 was positive (CT unavailable) and workup did not reveal any alternative explanation of her symptoms. She was again placed in the COVID dialysis cohort unit and quarantined at the nursing home. She did not require hospitalization and was managed conservatively. As per the testing protocol, she underwent COVID-19 testing weekly after the first 2 weeks. At day 22 of the second episode, her RT-PCR remained positive (CT, 28). She subsequently tested negative by nasal swab RT-PCR at 36 days from the onset of symptoms and was discharged back into the general dialysis population.

**DISCUSSION**

We describe 2 patients with chronic kidney failure dependent on in-center hemodialysis who developed symptomatic SARS-CoV-2 infection after a prior episode of COVID-19 infection, with resolution based on negative RT-PCR test results. Both patients were asymptomatic during their first episode. Although reinfection with other human coronavirus can occur, the possibility and frequency of SARS-CoV-2 reinfection is unknown. Although some patients have persistent shedding of SARS-CoV-2 RNA, the current consensus suggests that most patients are not infectious 20 days after the onset of symptoms. As of September 30, 2020, a total of 36 patients had dialyzed in our COVID cohort dialysis unit. Of these, 22 patients had persistently positive RT-PCR SARS-CoV-2 RNA at 2 weeks; 10 of these 22 patients continued to be persistently positive at 3 weeks, and 5, at 4 weeks. Although, 13.3% of our patients were persistently positive with the RT-PCR test at 4 weeks after the initial test, we cannot determine whether these tests reflect replication-competent virus.

The duration between a negative test result and then symptomatic reinfection was 31 and 55 days, respectively, in the 2 patients we describe. The first patient developed a symptomatic second infection despite having positive COVID-19 IgG antibodies. Seroconversion of IgM and IgG antibodies usually occurs in the first week after onset of symptoms, increasing until the fourth week, and by the seventh week, IgM is not detected in most patients, though IgG antibodies persist longer. A study that performed serial IgG testing of 34 patients with mild symptoms showed that the half-life of IgG was 36 days and the decline in antibody titers was faster than that reported for SARS-CoV-1. The antibody data need to be interpreted with caution because commercially available serologic tests may reflect a false-positive result. In general, the growing body of medical literature indicates that patients with mild symptoms have limited initial humoral responses to the virus and a rapid loss of IgG antibodies with a half-life of approximately 36 days, and that these lower titers may not be adequate to provide immunity. One other case of a dialysis patient with suspected reinfection and antibody-dependent enhanced response driving severe symptoms requiring the intensive care unit has been described.

There is uncertainty regarding the best use of the RT-PCR test, especially with well-described reports of prolonged positivity and false-negative test results. It is important to differentiate between true reinfections and persistent viral shedding. In our patients, the confirmation of a negative test result between the 2 episodes, the long duration between the 2 episodes of COVID-19 infection, the CT values, and the presence of symptoms on the onset of the second viral infection suggest that these cases are true reinfection episodes. Both patients were residents of nursing homes with a high prevalence of infection at that time, exposing them to risk for COVID-19 infection.

Unavailability of whole-genome sequencing and serial antibody titer data are limitations of this report. Current CDC recommendations have since evolved to suggest that testing may be warranted only in patients who develop new symptoms consistent with COVID-19 infection during the 3 months after the date of initial symptom onset if an alternative cause cannot be identified.

In-center hemodialysis patients are a unique population with multiple risk factors for severe illness with COVID-19, including repeat exposures to a health care setting. The higher incidence of infection and mortality are concerning and call for evidence-based interventions for infection control that help mitigate the spread of COVID-19. This includes strict in-center protocols, measures during transportation of patients, and education in the community. We hope to continue to learn more about COVID-19 infection in dialysis patients as the pandemic evolves and incorporate the knowledge to develop best practices and protocols to prevent serious illness in this group of patients.
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