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CASE REPORT

Coronavirus disease 2019 (COVID-19) in two pediatric patients with kidney disease on chronic immunosuppression: A case series

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a highly infectious disease caused by the severe acute respiratory syndrome coronavirus 2 virus (SARS-CoV-2). While children appear to experience less severe disease than adults, those with underlying conditions such as kidney disease may be more susceptible to infection. Limited data are present for children with kidney disease, and there are limited prior reports of pediatric hemodialysis patients with COVID-19. This report describes the mild clinical disease course of COVID-19 in two pediatric patients with chronic kidney disease, one on hemodialysis and both on chronic immunosuppression. We review treatment in these patients, as well as our measures to reduce transmission among our hemodialysis patients and staff.

Keywords: Coronavirus, SARS-CoV-2, pediatrics, end-stage kidney disease, hemodialysis

INTRODUCTION

Coronavirus disease 2019 (COVID-19), the disease caused by severe acute respiratory syndrome coronavirus 2 virus (SARS-CoV-2), has resulted in a global pandemic.[1] The outbreak began in Wuhan, China, and spread rapidly across the world, resulting in a global health emergency.[1] Although the majority of cases of COVID-19 are mild, a subset of patients develops critical illness.[2] Children appear to be less susceptible to severe disease than adults with death reported in <1%.[3] However, disease course in children with comorbidities has not been well described. Chronic kidney disease (CKD), including end-stage renal disease (ESRD) impairs immune function. Reports from China and Italy indicate that adults with kidney disease may be at higher risk of severe disease, with case fatality rates of between 10% and 30% reported.[4] Paradoxically, the limited experience with patients with ESRD on hemodialysis suggests that these patients may have a more mild course. Small studies report COVID-19 death rates in adult patients with ESRD on chronic dialysis ranging from <5% to 16%.[1,4,5] This contradictory epidemiologic data, along with the typically mild course of COVID-19 in pediatric patients, has led to uncertainty regarding the expected course and severity of SARS-CoV-2 in pediatric patients with kidney disease on dialysis and/or chronic immunosuppression.

This report describes the clinical characteristics of SARS-CoV-2 infection in two pediatric patients with

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kidney disease on chronic immunosuppression, one of whom has ESRD, managed with chronic in-center hemodialysis. We review the clinical presentation and treatment of these patients, as well as measures undertaken to reduce transmission to other hemodialysis patients and staff. This report does not require ethical approval per the Institutional Review Board at our institution, and informed consent was obtained from each patient reported in this article for publication of the information that appears within this case report.

CASE REPORTS

Patient 1

A 13-year-old, African American male presented to the Emergency Department (ED) with complaints of fever, fatigue, headache, and poor appetite. His past medical history included ESRD secondary to Henoch-Schonlein Purpura, managed with thrice-weekly hemodialysis. Chronic medications to control ongoing symptoms of his Henoch-Schonlein Purpura included colchicine (almost 2 years of treatment) and mycophenolate mofetil (approximately 6 months of treatment). He had no travel history over the preceding 28 days and no sick contacts. He had no rhinorrhea, conjunctivitis, shortness of breath, cough, nausea, vomiting, nor diarrhea. He was afebrile at presentation, with an oxygen saturation of 98% and a respiratory rate of 16 breaths per minute. He was mildly tachycardic with a heart rate of 114 bpm and hypertensive with a blood pressure of 143/86 mmHg. Physical examination was normal with clear breath sounds. Laboratory testing was unremarkable, and influenza swab was negative (Table 1). He was discharged home to follow-up for hemodialysis per routine.

The next day, the patient arrived for in-center hemodialysis and was placed in an isolation room. He reported ongoing fatigue, poor appetite, and headache. Given his symptoms, he wore a surgical mask throughout hemodialysis, and hemodialysis providers wore surgical masks, gowns, gloves, and goggles. He became febrile to 38.4°C during his hemodialysis session and was given vancomycin and cefepime (until blood culture returned negative). Additional labs were obtained including a nasopharyngeal swab for SARS-CoV-2 by polymerase chain reaction (PCR) using the Roche Cobas SARS-COV-2 system for nucleic acid amplification, with RNA extraction by the Roche automatic 6800 system. Following an uneventful hemodialysis session, the patient was discharged home to self-quarantine. The SARS-CoV-2 test returned positive the next day, and the patient was diagnosed with COVID-19. Subsequently, he had seroconversion on a SARS-CoV-2 enzyme-linked immunosorbent assays (ELISAs) (#KA5826, Abnova) with confirmatory ELISAs performed at Mount Sinai Medical Center using standard methodology previously reported.[6] The threshold for a positive ELISA result was 0.14, a value greater than the mean plus three times the standard deviation of negative control, consistent with standard methodology and with serum values of PCR-confirmed positive control patients. Patients were considered to have seroconverted if positive for IgM or IgG. The ELISA sensitivity and specificity were not provided by the manufacturer.[6]

On the day following his hemodialysis session, he continued to feel tired, but no worse. His mother also reported dry cough and subjective shortness of breath. His mycophenolate mofetil was held for 1 week, and he was prescribed hydroxychloroquine (300 mg orally twice a day for 1 day, then 150 mg orally twice daily for 8 days) per the institutional COVID-19 treatment protocol in place at that time, which restricted hydroxychloroquine use based on a risk- and illness severity-stratified classification scheme.

The patient returned for scheduled hemodialysis 2 days later. He was afebrile with improved appetite and energy level. He did not develop any additional symptoms. Repeat labs were performed (Table 1). He had a chest X-ray obtained, which was normal (Figure 1).

Table 1 Laboratory results for patient 1

Laboratory test	2 Weeks prior to presentation	At presentation	1 day following	3 days after
WBC	7.5 k/cumm	6.4 k/cumm	5.4 k/cumm	3.9 k/cumm
Hgb	10.6 gm/dL (L)	11.7 gm/dL (L)	10.9 gm/dL (L)	11.1 gm/dL (L)
Plts	309 k/cumm	124 k/cumm (L)	216 k/cumm	185 k/cumm
Abs Neut	4.5 k/cumm	4.5 k/cumm	3.1 k/cumm	1.3 k/cumm (L)
Abs Lymph	1.0 k/cumm	1.0 k/cumm	1.5 k/cumm	2.1 k/cumm
ESR	—	—	19 mm/h (H)	25 mm/h (H)
CRP	—	—	<0.5 mg/dL	<0.5 mg/dL

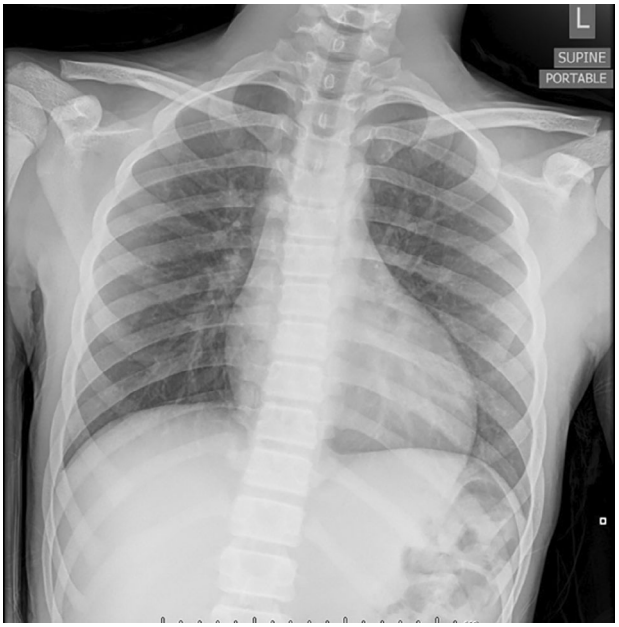

Figure 1 Normal chest X-ray obtained 4 days after patient 1's presentation.

Family reported compliance with hydroxychloroquine and no side effects. The patient's hemodialysis schedule was altered so patient would dialyze in unit on days without other patients present. Consistent staff members were identified to provide care in order to limit potential exposures. He remained asymptomatic thereafter. Despite rapid clinical recovery, follow-up nasopharyngeal swab remained positive for 21 days after first fever indicating prolonged viral shedding, with first of two negative swabs obtained 28 days after the initial fever.

Patient 2

An 18-year-old Hispanic male with membranoproliferative glomerulonephritis (MPGN) type 1 presented for a scheduled outpatient eculizumab infusion, and incidentally reported sudden onset anosmia. His past medical history included CKD stage I due to MPGN. Chronic medications for MPGN and CKD included prednisone, losartan, and weekly eculizumab infusions (900 mg weekly due to heavy proteinuria to target appropriate CH50 and eculizumab trough levels). On further inquiry, he reported complete anosmia and ageusia which had developed abruptly 1 week prior to presentation. A nasopharyngeal swab for SARS-CoV-2 was obtained and returned positive the next day, and the patient was diagnosed with COVID-19. Additionally, he had seroconversion on SARS-CoV-2 enzyme-linked immunosorbent assays (ELISAs) and confirmatory ELISA.[6] He reported no other symptoms including no fever, sore throat, coughing, shortness of breath, vomiting, nor diarrhea. His mother and father, however, had experienced abrupt onset of fever, cough, decreased appetite, fatigue, and night sweats beginning 2 to 3 weeks prior to onset of the patient's anosmia. He received no additional treatment, and required no alterations in his chronic immunosuppression with all eculizumab doses administered per usual schedule given mild symptoms. All symptoms resolved on day 10 of illness.

DISCUSSION

In this report, we describe the clinical course of two pediatric patients with kidney disease and chronic immunosuppression who developed COVID-19. To our knowledge, this includes one of the first reported cases of COVID-19 in a pediatric hemodialysis patient. The clinical presentation of these patients was more mild than that which has been described in adult patients with kidney disease that have been reported to date. Although neither patient had cough, sore throat, nasal congestion, or dyspnea, each had at least one typical symptom of COVID-19 (fever and anosmia).

Children with COVID-19 appear to have milder disease than that seen in adults.[7] While children are often asymptomatic, fever—as was seen in our first patient—is a common presenting sign.[7,8] Patients with ESRD have abnormal B- and T-cell function, blunted immune response, and increased infection risk.[5,9] This impaired immune response, however, may also be responsible for mild disease severity.[10] We note that patient 1 had an initial relative decrease in his white blood cell count at the time of acute SARS-CoV-2 infection, followed by a slow and more sustained increase in absolute lymphocyte count following infection. Lymphopenia is common in COVID-19 and may be a factor associated with severity of disease and mortality.[11] Both patients' immune responses may have been further impaired due to immunosuppressive medications (colchicine and mycophenolate mofetil in the first, eculuzimab and chronic prednisone in the second). This mild course is similar to other reports of children on chronic immunosuppressive therapy including immunomodulators and biologic therapies.[12,13] We speculate that immunosuppression may be at least in part responsible for the mild disease course observed in these patients; however, we acknowledge that this may also simply reflect the overall more mild course generally seen in children. We also note the prolonged viral shedding in patient 1 (21 days), which has been reported in other case

series and others have speculated may be due to immunosuppression.[14]

Hemodialysis patients represent a high-risk group for COVID-19 for several reasons. First, they are unable to strictly quarantine at home due to need for hemodialysis treatment several times weekly. Additionally, in the United States, pediatric hemodialysis patients often reside far from their dialysis centers in communities with relatively lower population density than that of their "home" dialysis unit. This imposes a medical need for significantly more than average mobility as they travel to and from areas with differing COVID-19 disease prevalence, even during stay-at-home orders. Due to financial and social constraints related to the costs of their medical care, it is also common for these patients to require either subsidized (i.e., "Medicaid transportation") or shared transportation to their dialysis treatments. Thus, as they travel to and from dialysis, they may inadvertently become a source of respiratory virus spread to their family or local community. Additionally, the design of hemodialysis units (with several patients, family members, and care providers in a confined space) increases the risk of ongoing transmission within the health care environs.[15] Finally, dialysis units have limited isolation rooms available, and nursing is often tasked with taking care of multiple patients at a time. Due to these factors, the infection rate of hemodialysis patients in Wuhan was higher than that of the general population.[5] It is essential to take precautions to limit exposure to other hemodialysis patients and healthcare staff. To decrease the risk of transmission, all hemodialysis patients and staff wore surgical masks at all times when in the dialysis unit once community-based transmission of SARS-CoV-2 was identified, and nonessential personnel entry into the hemodialysis unit was sharply limited. Our first patient was also placed in an isolation room as soon as symptoms were reported, according to unit protocols established based on contemporaneous CDC recommendations. Finally, his hemodialysis schedule was changed to avoid contact with other patients and staff as much as possible. During the ongoing COVID-19 pandemic additional measures to reduce risk of transmission of COVID-19 within dialysis units have been implemented. These CDC recommended measures include intensive cleaning procedures, universal PPE, and quarantining/isolating suspected cases.[16] Other centers have reported implementation of similar precautions with low incidence of COVID-19 cases thereafter.[17] The pandemic has resulted in deaths in COVID-19 infected hemodialysis patients; however, a percentage of these deaths have been attributed to reductions in hemodialysis therapy.[6] Therefore, it is imperative that hemodialysis patients with COVID-19 continue to receive appropriate hemodialysis therapy to prevent these complications.[18]

In conclusion, we report the first two case of COVID-19 in pediatric patients with kidney disease. Their mild disease, which may be influenced by young age, chronic immunosuppression, or immune dysregulation due to kidney disease also provides additional credence to studying new treatments targeting the immune system in COVID-19 patients. We also describe an effective method of limiting ongoing SARS-CoV-2 transmission in a busy, pediatric dialysis center.

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