COVID-19 in Children With Kidney Disease: A Report of 2 Cases

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The presentation of novel coronavirus disease 2019 (COVID-19) in children with kidney disease is largely unknown. We report on 2 children with kidney disease not receiving long-term immunosuppression who were hospitalized due to COVID-19. The first case is an infant with end-stage kidney disease secondary to bilateral cystic dysplastic kidneys and posterior urethral valves receiving peritoneal dialysis, with a history of prematurity previously requiring mechanical ventilation in the neonatal intensive care unit, who presented with fever, hypertension, and emesis. He had no respiratory symptoms and recovered with supportive care. His hypertension was managed well with amlodipine. The second case is a child with steroid-sensitive nephrotic syndrome who presented with a relapse of nephrotic syndrome with concurrent peritonitis and sepsis caused by *Streptococcus agalactiae*. He was treated with antibiotics and prophylactic anticoagulation therspy. Steroid therapy was initiated after 48 hours of antibiotic therapy. Neither child required mechanical ventilation or developed COVID-19–related multisystem inflammatory syndrome.

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INTRODUCTION

As of April 24, 2020, the Montefiore-Einstein Hospital system admitted more than 170 adults with end-stage kidney disease (ESKD) receiving dialysis and 70 kidney transplant recipients with coronavirus disease 2019 (COVID-19).[1,2] In contrast, during the same period, only 3 pediatric patients with pre-existing kidney disease were admitted with COVID-19. Previous reports describe worse outcomes and more severe COVID-19 in adult patients with chronic kidney disease, ESKD, and a transplant,[3-7] whereas early reports suggest mild illness in European children with chronic kidney disease.[8,9] In addition, atypical presentation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection with predominant gastrointestinal symptoms has been reported in these populations.[10] Because COVID-19 presentation in children with kidney disease from the United States is not well described, we report on 2 children with kidney disease not receiving long-term immunosuppression admitted to our Children's Hospital due to COVID-19.

CASE REPORTS

Case 1

A Hispanic male infant with ESKD secondary to bilateral cystic dysplastic kidneys and posterior urethral valves receiving peritoneal dialysis (PD) presented to the emergency department with 1 day of lethargy and abdominal distension. He had no feeding difficulties, rhinorrhea, cough, shortness of breath, diarrhea, vomiting, or sick contacts; however, in the week before admission, New York State "stay at home" orders were not yet in place.

Medical history was notable for preterm birth at 34 weeks' gestation and prenatal diagnosis of lower urinary tract obstruction. The patient required high-flow oscillator ventilation for the first 4 days of life and his postnatal course was complicated by hyperkalemia, hyponatremia, congenital hypothyroidism, and bilateral inguinal hernias. A PD catheter and gastrostomy tube were placed. He was initiated on PD by 3 weeks of age.

Vital signs on presentation were notable for temperature of 38.1 °C, blood pressure of 126/63 mm Hg, heart rate of 163 beats/min, respiratory rate of 48 respirations/min, and oxygen saturation as measured using pulse oximetry of 100% while breathing room air. On physical examination, the patient appeared lethargic with mild abdominal distension. *SARS-CoV-2* reverse transcriptase-polymerase chain reaction test result was positive. Initial laboratory results (Table 1) were consistent with ESKD. PD effluent cell count was 10 cells/high-power field and PD fluid culture, urine culture, blood culture, respiratory pathology panel, and infectious gastroenteritis panel results were all negative.

During the patient's hospitalization, he developed persistent brown emesis. An x-ray and ultrasound of the abdomen showed no evidence of small bowel obstruction. He received bowel rest, intravenous (IV) fluids, and lansoprazole. Emesis improved after 2 days. Hypertension was controlled with amlodipine. He did not require supplemental oxygen. The patient was discharged to home after 3 days and on follow up was thriving and tolerating feeds with normal blood pressures.

Case 2

An elementary school–aged Hispanic male with steroid-sensitive nephrotic syndrome presented with 2 days of

Table 1. Initial Laboratory Results on Presentation

Laboratory Test[a]	Case 1	Case 2
White blood cells, k/μL	17.5 (normal range for age, 6-17.5)	17.3 (normal range for age, 4.5-13.5)
% neutrophils	19	80
% lymphocytes	72	14
Hemoglobin, g/dL	8.6 (normal range for age, 11.3-12.5)	11.6 (normal range for age, 12-14.4)
Hematocrit, %	28.9	35.2
Platelet count, k/μL (normal range, 150-400)	506	210
Serum sodium, mEq/L	140	142
Serum potassium, mEq/L	5.3	4.1
Serum chloride, mEq/L	99	108
Serum bicarbonate, mEq/L	24	22
Serum urea nitrogen, mg/dL	15	11
Serum creatinine, mg/dL	3.2	0.5
Serum calcium, mg/dL	8.7	7.6, corrected for albumin 9.2
Phosphorus, mg/dL	2.4	5.8
Magnesium, mg/dL	3.2	1.7
Serum glucose, mg/dL	76	80
Total protein, mg/dL	4.6	3.4
Serum albumin, mg/dL	2.9	<2.0
AST/ALT, U/L	23/<10	<20/<10
Total/direct bilirubin, mg/dL	0.1/<0.2	0.4/<0.2
Lipid panel, mg/dL	Not done	Cholesterol, 182; LDL-C, 131
D-dimer, μg/mL (normal range, 0.0-0.5)	Not done	1.96
Fibrinogen, mg/dL (normal range, 187-502)	Not done	902
Prothrombin time, s	Not done	14.3 (11.8-14.8)
Partial thromboplastin time, s	Not done	33.4 (31.8-43.7)
Pro-BNP, pg/mL (normal range, <450)	Not done	5,864
Troponin, ng/mL (normal range, <0.10)	Not done	0.02
Urinalysis	Specific gravity, 1.010; pH > 9; rest negative	Specific gravity, >1.030; pH 6.5; protein > 1,000 mg/dL; moderate blood; rest negative
Urine microscopy (WBC, RBC/high-power field	Not done	6-10 WBC, 4-10 RBC, +hyaline casts
Urinary protein-creatinine ratio, mg/mg	Not done	18.7

Note: Conversion factors for units: creatinine in mg/dL to μmol/L, ×88.4; calcium in mg/dL to mmol/L, ×0.2495; phosphorus in mg/dL to mmol/L, ×0.3229; glucose in mg/dL to mmol/L, ×0.05551.
Abbreviations: AST/ALT, aspartate/alanine aminotransferase; LDL-C, low-density lipoprotein cholesterol; BNP, brain natriuretic peptide; RBC, red blood cell; WBC, white blood cell.
[a]When applicable, normal range shown in parentheses.

subjective fever, nonbilious nonbloody emesis, anasarca, and right lower quadrant abdominal pain. The morning of presentation, the mother gave 1 dose of prednisolone at home for presumed relapse. Review of systems was notable for 2 weeks of cough and sick contacts (2 household members with cough and anosmia).

The patient's medical history was notable for presentation with steroid-sensitive nephrotic syndrome at 3 years of age. He had infrequent relapses, most recently 3 months before presentation. Vital signs on presentation were notable for temperature of 38.5 °C, blood pressure of 91/69 mm Hg, heart rate of 165 beats/min, respiratory rate of 22 respirations/min, and oxygen saturation as measured using pulse oximetry of 100% while breathing room air. The patient's weight was ∼6 kg higher than his estimated dry weight. On physical examination, he was ill appearing with pallor, poor peripheral perfusion, moderate ascites, and right lower quadrant abdominal tenderness with rebound.

SARS-CoV-2 reverse transcriptase-polymerase chain reaction test result was positive. The patient's initial laboratory evaluation demonstrated relapse of nephrotic syndrome (Table 1). An x-ray of the chest showed small patchy opacities in the right upper lung field and the left lung base was concerning for an early pneumonia. An ultrasound of the abdomen showed mild to moderate complex ascites with septations. Computed tomography demonstrated ascites, small bilateral pleural effusions, and mild pulmonary interstitial edema. Blood cultures were positive for *Streptococcus agalactiae*.

The patient received IV fluid boluses and IV ceftriaxone and piperacillin-tazobactam due to concern for spontaneous bacterial peritonitis. He also received stress-dose hydrocortisone and 25% albumin (1 g/kg) with IV furosemide (1 mg/kg per dose). Within 12 hours after admission, he developed oxygen desaturations to 80% and was placed on low-flow oxygen with nasal cannula at 3 L/min. He was started on prophylactic enoxaparin due to concern for increased risk for thrombosis due to nephrotic syndrome and COVID-19. Remdesivir, which may accelerate recovery from advanced COVID-19,[11] was offered but declined. After 48 hours, the patient became afebrile and no longer required oxygen. He was started on treatment with prednisolone (2 mg/kg per day) for nephrotic syndrome and responded after 7 days. He received a total of 10 days of antibiotic treatment and was continued on 2 weeks of prophylactic enoxaparin therapy following discharge.

The patient's nephrotic syndrome remained sensitive to steroids. He was initially diagnosed $3^1/_2$ years before the current presentation and presented with urinary protein-creatinine ratio (UPCR) of 46 mg/mg. Following steroid treatment, he entered complete remission by the following month with UPCR of 0.1 mg/mg, within normal range. Subsequently, he had 3 relapses of nephrotic syndrome, occurring approximately 3 years, $2^1/_4$ years, and 2 years before the current presentation. After each of these relapses, he went into remission following steroids with urinalyses negative for proteinu. Prior to this current admission, his urine dipstick test was negative for protein. UPCR upon this admission was 18.7 mg/mg. Following steroid treatment, his urinalysis became negative for protein before discharge. On follow-up, his urine dipstick results remain negative for protein.

DISCUSSION

We report 2 Hispanic children with different preexisting kidney diseases admitted with COVID-19. The presentation, disease severity, and treatment were variable; however, none required mechanical ventilation or experienced SARs-CoV-2–related multisystem inflammatory syndrome.

The first patient was an infant with ESKD secondary to posterior urethral valves receiving PD presenting with fever, hypertension, and gastrointestinal symptoms. Remarkably, despite his history of prematurity requiring substantial respiratory support at birth, he experienced no respiratory symptoms.

The second patient with nephrotic syndrome presented with relapse of nephrotic syndrome, sepsis caused by *S agalactiae*, and peritonitis. Although rare, *S agalactiae* has been reported as an infectious bacterium in nephrotic syndrome.[12] SARs-CoV-2 infection may have triggered relapse in this patient, as was recently reported in a Spanish study.[9] It is unclear whether it contributed to his severity of illness. Secondary focal segmental glomerulosclerosis has been noted in adults with high-risk *APOL1* genotype and COVID-19 infection.[13] However this patient's *APOL1* genotype was unknown because genetic studies were not performed. High-dose steroid therapy was postponed until the patient was afebrile and had negative blood cultures for 48 hours, but the patient responded well to steroid therapy. The patient also had an elevated D-dimer level and was treated with prophylactic enoxaparin. Hypercoagulability is associated with both nephrotic syndrome and COVID-19, and it is unclear if they synergistically increase the risk for thrombosis.[14-16]

Early reports have indicated mild COVID-19 illness in European children with kidney disease.[17,18] However, increased morbidity and mortality have been reported in Black and Hispanic adults.[19] One of the 2 children reported here with COVID-19 required intensive care with oxygen support. Additional studies of COVID-19 in children with kidney disease are needed.

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REFERENCES

1. Akalin E, Azzi Y, Bartash R, et al. Covid-19 and kidney transplantation. *N Engl J Med*. 2020;382(25):2475-2477.
2. Columbia University Kidney Transplant Program. Early description of coronavirus 2019 disease in kidney transplant recipients in New York. *J Am Soc Nephrol*. 2020;31(6):1150-1156.
3. Mokrzycki MH, Coco M. Management of hemodialysis patients with suspected or confirmed COVID-19 infection: perspective of two nephrologists in the United States. *Kidney360*. 2020;1(4):273-278.
4. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Int Urol Nephrol*. 2020;52(6):1193-1194.

5. Zhu L, Gong N, Liu B, et al. Coronavirus disease 2019 pneumonia in immunosuppressed renal transplant recipients: a summary of 10 confirmed cases in Wuhan, China. *Eur Urol*. 2020;77(6):748-754.
6. Goicoechea M, Sánchez Cámara LA, Macías N, et al. COVID-19: clinical course and outcomes of 36 maintenance hemodialysis patients from a single center in Spain. *Kidney Int*. 2020;98(1):27-34.
7. Alberici F, Delbarba E, Manenti C, et al. A report from the Brescia Renal COVID Task Force on the clinical characteristics and short-term outcome of hemodialysis patients with SARS-CoV-2 infection. *Kidney Int*. 2020;98(1):20-26.
8. Marlais M, Wlodkowski T, Vivarelli M, et al. The severity of COVID-19 in children on immunosuppressive medication. *Lancet Child Adolesc Health*. 2020;4(7):e17-e18.
9. Melgosa M, Madrid A, Alvárez O, et al. SARS-CoV-2 infection in Spanish children with chronic kidney pathologies. *Pediatr Nephrol*. 2020;35(8):1521-1524.
10. Wang R, Liao C, He H, et al. COVID-19 in hemodialysis patients: a report of 5 cases. *Am J Kidney Dis*. 2020;76(1):141-143.
11. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19 — preliminary report. *N Engl J Med*. 2020;383(10):994.
12. Sickler SJ, Edwards MS. Group B streptococcal cellulitis in a child with steroid-responsive nephrotic syndrome. *Pediatr Infect Dis J*. 2001;20(10):1007-1009.
13. Wu H, Larsen CP, Hernandez-Arroyo CF, et al. AKI and collapsing glomerulopathy associated with COVID-19 and APOL-1 high-risk genotype. *J Am Soc Nephrol*. 2020;31(8):1688-1695.
14. Sexton DJ, Clarkson MR, Mazur MJ, Plant WD, Eustace JA. Serum D-dimer concentrations in nephrotic syndrome track with albuminuria, not estimated glomerular filtration rate. *Am J Nephrol*. 2012;36(6):554-560.
15. Yang Y, Lv J, Zhou F, et al. Risk factors of pulmonary thrombosis/embolism in nephrotic syndrome. *Am J Med Sci*. 2014;348(5):394-398.
16. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, et al. Hematological findings and complications of COVID-19. *Am J Hematol*. 2020;95(7):834-847.
17. Ma H, Hu J, Tian J, et al. A single-center, retrospective study of COVID-19 features in children: a descriptive investigation. *BMC Med*. 2020;18(1):123.
18. Shekerdemian LS, Mahmood NR, Wolfe KK, et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. *JAMA Pediatr*. 2020;174(9):868-873.
19. Webb Hooper M, Nápoles AM, Pérez-Stable EJ. COVID-19 and racial/ethnic disparities. *JAMA*. 2020;323(24):2466-2467.