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Clinical Notes

Risk of acute kidney injury in a pediatric patient with severe acute respiratory syndrome coronavirus 2 infection

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A 12-year-old girl with fever, oliguria, and gross hematuria was admitted to our hospital on the sixth day of her illness. She had a history of cystitis when she was 1 year old. She tested positive for severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) by nucleic acid amplification on the fourth day of her illness. Before the onset of her illness, several people in her school presented with fever.

On admission, she had a temperature of 36.5 °C, blood pressure of 116/69 mmHg, and a heart rate of 100 beats per minute (bpm). She had bilateral lower leg edema (2 kg more than the dry weight) and bilateral costovertebral angle tenderness. No skin rashes or common cold symptoms were noted. The blood tests showed leukopenia (3,930/μL; neutrophils, 52.8%; lymphocytes, 37.2%; monocytes, 9.2%; eosinophils, 0.5%; basophils, 0.3%) and elevated creatinine levels (0.67 mg/dL; baseline, 0.52 mg/dL). The acute phase reactive protein levels were mildly elevated (C-reactive protein, 0.39 mg/dL; serum amyloid A, 100.9 μg/mL). Neither hypocomplementemia nor elevated anti-streptolysin O antibodies were detected. The antinuclear and anticardiolipin antibodies were negative. Urinalysis revealed proteinuria and hematuria without bacteriuria. The estimated glomerular filtration rate was 93.29 mL/min/1.73 m^2. The urinary β2-microglobulin and *N*-acetylglucosamine were normal, and the fractional excretion of Na was 0.32%. The blood and urine culture results were negative. Kidney ultrasound showed no renal enlargement, hydroureter, or thrombus formation in the renal arteries or veins.

The patient's clinical course is shown in Figure 1. After admission, she was placed on bed rest and administered cefazolin. However, cefazolin was discontinued after confirmation of the negative urine culture results. The patient remained anuric for 8 h after admission. Based on the acute kidney injury (AKI) classification of the pediatric-modified Risk, Injury, Failure, Loss, End-Stage Renal Disease criteria,[1] the patient met the Risk criteria. Nonetheless, her weight decreased, while her urine output improved. She was discharged on the 15th day of illness after she had recovered to her baseline weight (57 kg) on the 14th day of illness. The anti-SARS-CoV-2 S antibodies (Elecsys Anti-SARS-CoV-2 S RUO, Roche Diagnostics GmbH, Basel, Switzerland), which were negative on admission, increased to 42.3 U/mL.

Acute kidney injury caused by SARS-CoV2 infection is a common complication among adults and has been reported in children worldwide. Its incidence, which varies depending on the region and ethnicity, ranges from 1.2% in China[2] to 21% in Saudi Arabia.[3] There have been no reports of SARS-CoV-2-related renal damage among previously healthy Japanese children. Microscopic hematuria has been reported as an AKI symptom in patients with coronavirus disease-2019 (COVID-19). However, gross hematuria has rarely been reported. Almeida *et al.*[4] reported the first case of gross hematuria, associated with SARS-CoV-2 infection, in a previously healthy 10-year-old female. Her renal function and erythrocyte morphology were normal, and she had a favorable clinical outcome. This report documents the second case of COVID-19 with gross hematuria. This case differed from the former because of the absence of respiratory symptoms and decreased renal function. This patient also had a favorable clinical course.[4] The host cell receptor for SARS-CoV-2, angiotensin-converting enzyme 2 (ACE2), is highly expressed in human tissues, including the lung, heart, testes, gastrointestinal tract, and kidney tissues. In a steady-state, the expression of ACE2 is higher in the kidneys than in the lungs. Multiple etiologic agents have been identified. A systematic review and meta-analysis showed that AKI developed in patients, infected with SARS-CoV-2, through direct infection or systemic effects, including host immune clearance and immune tolerance disorders, endothelium-mediated vasculitis, thrombus formation, glucose and lipid

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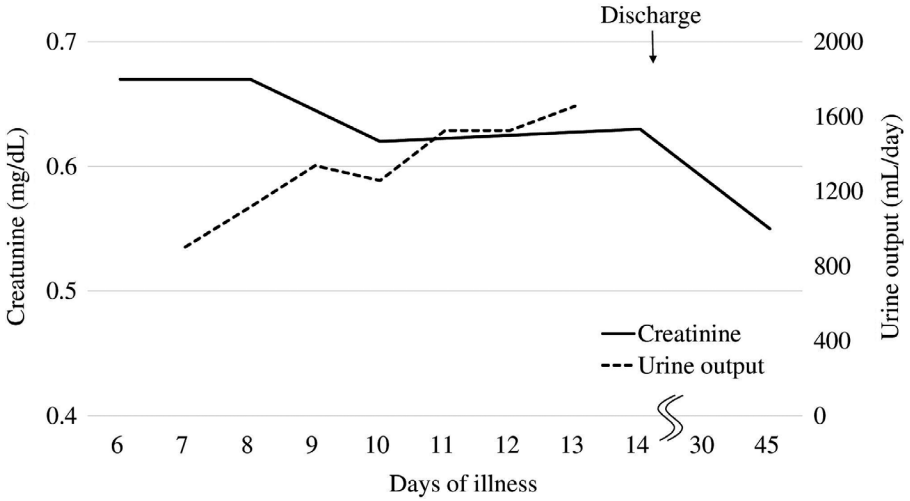

Fig. 1 The clinical course of a pediatric patient presenting with acute kidney injury and COVID-19.

metabolism disorders, and hypoxia.[5] AKI is classified into pre-renal, parenchymal, or post-renal based on its various mechanisms. Various autoimmune diseases were also reportedly induced by SARS-CoV-2 infection.[6] According to a systematic review on the native kidney histopathological manifestations among COVID-19 patients,[7] focal segmental glomerulosclerosis, thrombotic microangiopathy, and acute tubular injury accounted for 75% of cases. The remaining 25% consisted of connective tissue disorders, such as systemic lupus erythematosus, antiphospholipid syndrome, ANCA-associated vasculitis, and immunoglobulin A vasculitis. These differentials should be considered in patients with hematuria or proteinuria. Pediatric AKI patients reportedly do not require renal replacement therapy, and improved with fluid resuscitation and inotropic support.[3] However, patients, requiring vasopressors and extracorporeal membrane oxygenation, have also been reported.[8] In our patient, gross hematuria preceded the initial symptoms. There were no noted upper respiratory tract symptoms, and the patient later developed decreased fluid and food consumption. Urinalysis revealed dysmorphic red blood cells, indicative of damage or glomerular inflammation, and mild elevation of urinary neutrophil gelatinase-associated lipocalin. No tubulointerstitial damage was noted. Her urine volume and body weight improved with conservative treatment. These findings suggested that she possibly developed mild parenchymal renal failure due to direct kidney damage or pre-renal failure, caused by dehydration and infection. She had a favorable clinical outcome, consistent with the outcomes of previously reported pediatric patients with hematuria, associated with SARS-CoV-2 infection.[4]

We reported a pediatric case of SARS-CoV-2-related renal injury, which improved without complications, after conservative treatment. The case highlighted the importance of evaluating the patient's general condition and selecting the appropriate treatment for SARS-CoV-2 infection.

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Disclosure

The authors declare no conflict of interest.

Author contributions

Y. U. wrote the first draft of this manuscript. Y.T. performed the experiments. E.S., I.K., and H.N. revised and supervised the manuscript. All authors have reviewed and approved the final manuscript.

Informed consent

Informed consent for publication of this report was obtained from the patient's parents. A copy of the consent form is available for review by the editors of this journal.

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