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Case Report

Spontaneous remission of nephrotic syndrome associated with COVID-19 infection in an 8-year-old boy

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ABSTRACT

Background. It is already known that viral infections, exclusively upper respiratory tract infections may trigger relapses of nephrotic syndrome. Recently, COVID-19 disease has also been reported to be related with relapse of nephrotic syndrome in a few pediatric cases.

Case. Here we present an 8-year-old boy who had relapse of nephrotic syndrome due to COVID-19 infection. He was asymptomatic except for mild edema. He was managed supportively, no medication was started and went into spontaneous remission in 7 days.

Conclusions. Viral infections particularly upper respiratory tract infections may trigger relapse of nephrotic syndrome. COVID-19 has also been reported to be related with relapses of nephrotic syndrome in a few pediatric cases. Spontaneous remission in our patient indicates the importance of close monitoring of patients before starting long term treatment with steroids.

Key words: COVID-19, SARS-CoV-2, nephrotic syndrome, child.

Although kidneys are among the most affected organs in COVID-19 disease and there is an increasing number of publication on this area, the number of studies regarding the clinical profile of COVID-19 in children with known kidney disease is still scarce.[1] A global survey on children receiving immunosuppressive medications for kidney diseases showed that most of the patients had a mild clinical course of COVID-19.[2] In an Italian national study including 159 children with nephrotic syndrome on chronic immunosuppression with B cell depleting agents, none of the patients reported clinical symptoms of COVID-19.[3] In a recent study from Turkey, Canpolat et al.[4] demonstrated that although the clinical course was mild the frequency of COVID-19 was increased in children undergoing chronic dialysis with a kidney transplant.

There are limited number of case reports describing simultaneous occurrence of new onset nephrotic syndrome and COVID-19.[5,6] There are also few case reports presenting relapse of nephrotic syndrome with COVID-19.[7,8] In these reports both the cases with new onset nephrotic syndrome and the relapsing cases had favorable response to oral steroids.[5-8]

Here we present an 8-year-old boy who had a relapse of nephrotic syndrome with asymptomatic COVID-19 infection and went into spontaneous remission in seven days without any treatment. To our knowledge this is the first case of asymptomatic COVID-19 infection triggering relapse in nephrotic syndrome.

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Case Report

An 8-year-old boy was admitted to our emergency department because of swelling in the eyelids and legs. He was diagnosed with nephrotic syndrome four years prior, he had two relapses following the first two years after diagnosis and was in remission for two years without any medication. Recently his father was diagnosed with the COVID-19 infection. At admission, physical examination revealed: height 136 cm, weight 27 kg, blood pressure 106/60 mmHg, heart rate 84/min, respiratory rate 20 /min, O_2 saturation 98%; and he was afebrile. Except periorbital and pretibial edema physical examination was normal. On laboratory examination dipstick urine analysis revealed 4+ proteinuria. Spot urine protein-to-creatinine ratio was 2.2 (mg/mg). Biochemistry parameters were as follows: hemoglobin 14.1 g/dl, leukocytes 5,190/mm^3, absolute neutrophil count 2,060/mm^3, lymphocyte count 2,640/mm^3, CRP negative, serum albumin 1.8 g/dl, creatinine 0.4 mg/dl, cholesterol 298 mg/dl and triglycerides 200 mg/dl. Serum electrolytes and liver function tests were in normal limits. Chest X-ray was normal. With these clinical and laboratory features the patient was diagnosed as relapsing nephrotic syndrome. To identify the triggering factor, he was tested with nasopharyngeal multiplex PCR assay for upper respiratory tract infections with influenza, parainfluenza, adenovirus and rhinovirus and all were negative. Because he had a close household contact, he was also tested for SARS-CoV-2 and real-time PCR (RT-PCR) assay was positive, so he was also diagnosed to have asymptomatic COVID-19 infection. He was hospitalized in order to observe the possible undesired course; but because he was asymptomatic no medication was started for COVID disease; he was also managed conservatively for nephrotic syndrome. On the third day of his admission urine output increased and spot urine protein-to-creatinine ratio decreased to 1.8 mg/mg. Because his vital signs were in normal limits and he did not have weight gain and had improving edema, we decided to manage him without steroids. His edema improved day by day and proteinuria decreased. On the seventh day of his admission spot urine protein-to-creatinine ratio was 0.2 mg/mg and serum albumin was to 2.9 g/dl. SARS-CoV-2 RT-PCR also turned to negative. No fever or any new complaints developed during hospitalization; so he was discharged with complete spontaneous remission. After two weeks of discharge he was still in remission.

Written informed consent was obtained from the parents of the patient for publication.

Discussion

Renal involvement is reported to be relatively common particularly among hospitalized adult patients with COVID-19. The spectrum ranges from isolated hematuria and/or proteinuria to acute kidney injury requiring renal replacement therapy.[9-11]

Although there is mounting evidence about kidney involvement of COVID-19 in adults, the data regarding renal complications in children and how the disease effects this age group with underlying nephropathies are scarce.[2,3] Angeletti et al.[3] evaluated 159 children with nephrotic syndrome who had received B cell depleting therapy and were on chronic immunosuppression. Among these only 6 children who had close household contacts were tested positive for SARS-CoV-2 by nasopharyngeal swab, but none of these patients developed symptoms.[3] A multicentric study hosted by European Rare Kidney Diseases Reference Network revealed that most children with kidney diseases on immunosuppressive medication had a mild disease of COVID-19.[2] The authors also demonstrated that the number of the immunosuppressive drugs did not affect the severity of COVID-19 in children.[2]

A handful of cases with renal manifestations of COVID-19 has been reported in the pediatric age group (Table I). Macroscopic hematuria was described in a 10 year old boy during mild upper respiratory tract infection due to

Table I. Published reports of pediatric patients with renal manifestations due to COVID-19 infction.

Reference	Age	Gender	Symptom	Renal manifestations/ disease	Renal dysfunction	Renal biopsy	Treatment	Outcome
Almeida FJ et al.[12]	10	F	Fever, cough, sore throat	Gross hematuria	No	No	Supportive	Hematuria resolved in five days
Alvarado A et al.[5]	15	M	Dyspnea	Edema anasarca, new onset nephrotic syndrome	No	No	PMP (5 days), chloroquine, azithromycin	Respiratory symptoms and edema improved (no data for duration)
Enya T et al.[7]	3	M	Fever	Eyelid edema Relapse of nephrotic syndrome	No	No	Oral prednisolone (2mg/kg/day)	Remission of nephrotic syndrome in one week
Basiratnia et al.[9]	17	M	Feeling unwell for last two weeks, nausea, vomiting	Decreased urine output, hypertension, glomerulonephritis	Yes (serum creatinine: 17 mg/dl)	Acute necrotizing glomerulonephritis	PMP (3 days) followed by oral prednisolone, hemodialysis, enoxoparine	Follow-up on hemodialysis
Basiratnia et al.[9]	16	M	Fever	Oliguria, tea colored urine, glomerulonephritis	Yes (serum creatinine:15 mg/dl)	Acute necrotizing glomerulonephritis; negative for COVID-19	PMP (3 days) followed by oral prednisolone, hemodialysis, enoxoparine	Remission achieved in 2 weeks (last serum creatinine 0.8 mg/dl)
Shah AS, Carter H[6]	8	M	Vomiting, diarrhea	Facial swelling, new onset nephrotic syndrome	No	No	Oral prednisolone 30 mg	Remission in seven days

PMP: pulse methylprednisolone

COVID-19.[12] New onset nephrotic syndrome associated with COVID-19 in two boys and acute necrotizing glomerulonephritis in two adolescents were described.[5-6,9] Also relapses of nephrotic syndrome due to COVID-19 have been observed.[7] Except for the two adolescents with necrotizing glomerulonephritis, the other patients reported with relapses and new onset nephrotic syndrome did not undergo renal biopsy because their clinical picture was highly suggestive of minimal change nephrotic syndrome and they responded well to steroid treatment.[5-7,9] In adult studies it is demonstrated with renal biopsies that COVID-19 may cause a spectrum of podocytopathy ranging from minimal change disease to collapsing glomerulopathy. The underlying mechanism of podocyte injury in COVID 19 yet remains unknown.[10]

It is already known that viral infections, particularly upper respiratory tract infections are associated with the onset or exacerbations and relapses of nephrotic syndrome. Among these influenza, parainfluenza and adenoviruses are reported to be the most common pathogens triggering relapses.[13] Additionally, new onset nephrotic syndrome or relapses has been previously reported during other viral outbreaks such as H1N1.[14] The underlying mechanism by which infections cause relapses is not exactly identified but might be related to upregulation of T cells, altered balance of T helper 1/T helper 2 and as a result of these cytokine mediated podocyte injury.[14] Various studies demonstrated T lymphocyte abnormalities in COVID-19 infection and as in other viral infections these alterations may be responsible for the relapses of nephrotic syndrome.[15]

Except for multisystem inflammatory syndrome, the most remarkable feature of COVID-19 is the lower risk of severe forms of disease in children when compared with adult counterparts. But even asymptomatic disease course may be responsible for relapses in nephrotic syndrome patients as demonstrated here. Although we did not study the antibody profile of the patient; because all possible causal factors were excluded, and because he had close household contact with COVID-19 along with a positive RT-PCR test result, we attributed the relapse of nephrotic syndrome to COVID-19. We think this report shows that as in other viral infections even an asymptomatic COVID-19 infection may trigger relapse of nephrotic syndrome. As far as we know this is the first asymptomatic case of COVID 19 resulting in relapse in nephrotic syndrome. It is well known that relapses of nephrotic syndrome, which was triggered by an upper respiratory tract infection can go into remission spontaneously in up to 20% of the patients.[16] Considering the relatively mild course in children we think that before administrating steroids that will last for months, patients should be clinically observed for a couple of days for spontaneous remission.

Ethical approval

Written informed consent was obtained from the parents of the patient for publication.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: ÖM, AY; data collection: GAD, ÖM; draft manuscript preparation: AKA, GAD. All authors critically reviewed the manuscript and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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