

## Anti-Glomerular Basement Membrane Disease in a Pediatric Patient with SARS-CoV-2 Infection: A Case Report

Bağdagül Aksu<sup>1</sup> , Nuran Küçük<sup>2</sup> , Zeynep Yuruk Yıldırım<sup>1</sup> , Mesude Yasemin Özlük<sup>3</sup> ,  
Özge Hürdoğan<sup>3</sup> , Alev Yılmaz<sup>1</sup> 

<sup>1</sup>Istanbul University İstanbul Faculty of Medicine, Institute of Child Health, Department of Pediatric Basic Sciences, Division of Pediatric Nephrology, İstanbul, Türkiye

<sup>2</sup>Istanbul Kartal Dr. Lütfi Kırdar City Hospital, Division of Pediatric Nephrology, İstanbul, Türkiye

<sup>3</sup>Istanbul University, İstanbul Faculty of Medicine, Department of Pathology, İstanbul, Türkiye

**ORCID ID:** B.A. 0000-0003-3274-8024; N.K. 0000-0002-2397-5826; Z.Y.Y. 0000-0003-2891-2231; M.Y.O. 0000-0002-7191-0488; O.H. 0000-0001-8352-8158; A.Y. 0000-0003-1743-1491

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### ABSTRACT

Anti-glomerular basement membrane (anti-GBM) disease is a rare autoimmune condition that leads to rapidly progressive glomerulonephritis, particularly uncommon in children. An 8-year-old boy was admitted to the emergency department presenting with macroscopic hematuria and oliguria. Notably, he had been hospitalized 5 weeks earlier due to a COVID-19 infection, with subsequent negative COVID-PCR results upon discharge. The systemic physical examination revealed pretibial and periorbital edema, but it was otherwise unremarkable. Importantly, there was no hypocomplementemia, and all autoantibodies tested were negative, except for anti-GBM antibodies. Over the 2-day follow-up, serum creatinine levels exhibited a steady increase from 0.63 to 6.4 mg/dL. Renal biopsy result indicated crescentic glomerulonephritis associated with anti-GBM disease. The patient responded positively to treatment with methylprednisolone, cyclophosphamide, and plasmapheresis, followed by intravenous immunoglobulin. The patient showed remarkable improvement, with the last recorded serum creatinine level at 0.57 mg/dL. Our case report suggests a potential pathogenic association between COVID-19 infection and the development of anti-GBM disease, resulting in a rapidly progressive form of crescentic glomerulonephritis in children.

**Keywords:** Anti-GBM disease, children, SARS-CoV-2 infection

### INTRODUCTION

Anti-glomerular basement membrane (anti-GBM) disease is an autoimmune condition associated with rapidly progressive glomerulonephritis (1, 2). It is characterized by circulating autoantibodies and the linear deposition of immunoglobulin G (IgG) along the GBM and alveolar basal membrane (1, 2). Extremely rare in children, there are only a few case reports and retrospective case series in the literature on anti-GBM disease in pediatric patients. An increase in the incidence of anti-GBM disease has been observed due to the pandemic of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection (3). In this case report, we present the case of an 8-year-old boy who developed anti-GBM disease following an infection with SARS-CoV-2.

### CASE REPORT

An 8-year-old boy was admitted to the emergency department presenting with macroscopic hematuria and oliguria. Five

weeks prior, he had been hospitalized due to a COVID-19 infection and was discharged with negative COVID-PCR results. He was the only child of nonconsanguineous parents. A systemic physical examination showed no remarkable findings, except for pretibial and periorbital edema. Vital signs were within normal ranges: blood pressure of 117/77 mmHg (95<sup>th</sup> centile), heart rate of 85 bpm, respiratory rate of 20 bpm, and body temperature of 36.7°C.

His laboratory results are presented in Table 1. No blasts or schistocytes were observed on the peripheral smear. Viral markers, including hepatitis B, hepatitis C, Epstein-Barr virus, human immunodeficiency virus, cytomegalovirus, chickenpox, rubella, toxoplasma, parvovirus, and brucella, were all negative. However, the COVID-PCR test showed positive. There was no hypocomplementemia, and all autoantibodies were negative except for anti-GBM. Urinalysis revealed 2+ proteinuria and 3+ hematuria, with urine microscopy showing dysmorphic erythrocytes, erythrocyte casts, and epithelial casts. The spot

**Corresponding Author:** Bağdagül Aksu E-mail: [bagdagul@yahoo.com](mailto:bagdagul@yahoo.com)

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**Table 1: Main laboratory results on admission**

Parameter	Result	Reference Range
White blood cell ( $10^3/\mu\text{L}$ )	6.3	5.0-13.5
Hemoglobin (g/dL)	11.4	11.8-15.0
Platelet ( $10^3/\mu\text{L}$ )	236	200-500
Urea (mg/dL)	37.0	17-49
Creatinine (mg/dL)	0.63	0.4-0.6
Sodium (mmol/L)	140	136-145
Potassium (mmol/L)	4.4	3.5-5.1
Albumin (g/dL)	4.7	3.8-5.4

urine protein/creatinine ratio was 1.2 mg/mg creatinine. Renal ultrasonography showed increased echogenicity and kidney sizes of 10.7 cm on the right and 11.6 cm on the left.

The bladder was catheterized, and urine output was 0.8 mL/kg/h. During the 2-day follow-up, serum creatinine steadily increased from 0.63 to 6.4 mg/dL, with an estimated glomerular filtration rate (eGFR) of 9.9 mL/min/1.73 m<sup>2</sup> according to the Schwartz formula.

Renal biopsy was performed, yielding eight glomeruli. Fibrocellular crescents were present in five glomeruli (Figure 1a). Intense erythrocytes, desquamated cells, and interstitial focal inflammatory cell infiltration were observed in the tubules. Immunofluorescence staining revealed diffuse, linear IgG deposition in the basement membrane (Figure 1b). In summary, the renal biopsy was consistent with crescentic glomerulonephritis associated with anti-GBM disease.

He received methylprednisolone pulse therapy (10 mg/kg/day for 5 alternate days), followed by oral methylprednisolone at 1 mg/kg/day and cyclophosphamide pulse therapy (500 mg/m<sup>2</sup>/month for 6 continuous months). Meanwhile, three sessions of hemodialysis were performed. Plasmapheresis was conducted three times, with each session followed by intravenous immunoglobulin (0.2 g/kg/dose). He responded clinically well

to the treatment, with anti-GBM antibodies turning negative after plasmapheresis, pulse steroid administration, and the initial dose of cyclophosphamide therapy.

The patient remained COVID-PCR positive for 16 days. During the last outpatient visit, he was taking oral corticosteroids (1 mg/kg prednisolone equivalent) administered on alternate days. His serum creatinine level was 0.57 mg/dL (eGFR 100 mL/min/1.73 m<sup>2</sup>), and the spot urine protein/creatinine ratio was 0.16 mg/mg. Written informed consent was obtained from the parents.

## DISCUSSION

Anti-GBM disease is an exceedingly rare autoimmune disorder, with a reported incidence of 0.5–1.0 cases per million populations per year in adults. However, the incidence in children remains uncertain (4). While the pathogenesis of anti-GBM disease is well-established, the factors initiating the autoimmune process remain unclear (5). There is evidence to suggest that environmental factors, including infections, may act as triggers for the disease (6).

Notably, COVID-19 infection is characterized by severe endothelial damage and impaired endothelial cell membranes (7). Localized inflammation resulting from endothelial injury may increase capillary permeability and disrupt the basement membrane structure. This disruption exposes sequestered antigens, providing access to pathogenic autoantibodies (8).

Glomerular injuries such as proteinuria and hematuria have been reported in many COVID-19 patients during infection. During the COVID-19 pandemic, Predecki et al. (3) reported a fivefold increase in the number of anti-GBM cases in the UK, detecting eight new cases between December 2019 and April 2020. Among these cases, circulating IgM and/or IgG antibodies to the SARS-CoV-2 spike protein were identified in 4 of 8 patients. Although these cases represent the first instances revealing a potential link between anti-GBM disease and SARS-CoV-2 infection, the exact causal relationship remains

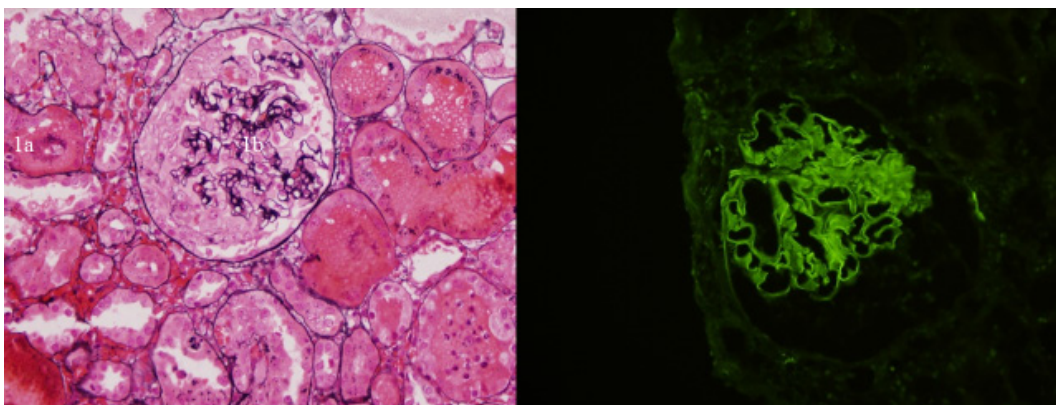


Figure Legends: 1a. Fibrocellular crescent in a glomerulus (Methenamine silver-Periodic acid-Schiff stain, x400)  
1b. Diffuse and linear IgG deposition in the glomerular basement membranes (Anti-IgG antibody, direct immunofluorescence, x400)

unexplained. Another case series published by Sebastian et al. (9) described four adult patients who were initially infected with COVID-19 and later presented with anti-GBM disease.

Our patient presented with macroscopic hematuria and oliguria, exhibiting neither pulmonary nor other extrarenal symptoms. Similarly, neither of the two case series on anti-GBM disease (3, 9) reported pulmonary symptoms. Interestingly, our patient, previously discharged as negative for COVID-PCR 5 weeks ago, manifested crescentic glomerulonephritis and tested positive again for COVID-PCR, despite the absence of COVID-19 infection symptoms.

The average period between prodromal illness and renal symptoms was approximately 5 weeks in our case, which was slightly shorter than the 5.5–6 weeks observed in these cases. Most patients experienced mild-to-moderate prodromal illness, similar to our case. In the series by Sebastian et al., 2 of 4 patients and in the series by Predecki et al., 1 of 4 patients developed end-stage kidney disease and required hemodialysis (3, 9). Fortunately, the others showed clinical improvement, and our patient's kidney function ultimately recovered.

Winkler et al. (10) observed a recurrence of anti-GBM disease after COVID-19 in a 30-year-old woman with hemoptysis and rapidly progressive renal failure, further supporting the potential association between COVID-19 and anti-GBM disease in adults. Notably, our case represents the first reported case of COVID-19-associated anti-GBM disease in children.

## CONCLUSION

Our case report suggests a potential pathogenic association between COVID-19 infection and anti-GBM disease, leading to a rapidly progressive form of crescentic glomerulonephritis in children. The patient responded positively to treatment, which included plasmapheresis and intensive immunosuppressive therapy, ultimately recovering independent renal function. Nevertheless, additional clinical and experimental investigations are necessary to further validate the causal link between anti-GBM disease and SARS-CoV-2 infection.

**Informed Consent:** Written consent was obtained from the participants.

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