Successful Treatment of COVID-19-Related Immune-Complex Glomerulonephritis, Case Report

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Acute kidney injury (AKI) , proteinuria in the nephrotic or subnephrotic range and hematuria might be seen in patients with coronavirus disease 2019 (COVID-19) infection. In this case study we present a 59 years old manwho was diagnosed with immune-complex glomerulonephritis after development of rapidly progressive kidney failure accompanied by pulmonary hemorrhage, 2 months after COVID-19 infection. The patient was hospitalised with the diagnosis of acute kidney injury and nephrotic syndrome. Hemodialysis was performed due to uremic symptoms. Cyclophosphamide, methylprednisolone and plasmapheresis were started. Pathologic examination of kidney biopsy revealed features compatible with immune complex-related acute glomerulonephritis. Cyclophosphamide and plasmapheresis were discontinued , and treatment with 1 mg/kg/day methylprednisolone was continued. Immune-complex glomerulonephritis can be seen following COVID-19 infection. İt is important to diagnose this disease entity as soon as possible . Steroidtherapy and other supportive modalities might be sufficient in the treatment.

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Case Report

INTRODUCTION

Acute kidney injury (AKI), proteinuria in the nephrotic or subnephrotic range, and hematuria might be seen in patients with coronavirus disease 2019 (COVID-19) infection.[1] Although the most commonly reported glomerular disease is collapsing glomerulopathy, glomerulopathies such as antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, anti-glomerular basement membrane (GBM) disease and immunoglobulin A vasculitis have also been reported.[2] In this article we present a 59-years-old male patient who was diagnosed with immune-complex glomerulonephritis and rapidly progressive kidney failure accompanied by pulmonary hemorrhage following COVID-19 infection. This patient is one of the few cases reported in the literature who ended up in immune-complex glomerulonephritis following COVID-19 infection, with no previous history of kidney disease.

Informed written consent was obtained from the patient for this presentation.

CASE REPORT

The patient was a 59-years-old male patient with a recent COVID-19 infection confirmed by nasopharyngeal swab polymerase chain reaction (PCR). He had a persistent cough, when his second PCR test became negative, after 15 days. The patient presented to our hospital with dyspnea and edema in the lower extremities, approximately 2 months after COVID-19 infection.

He had no history of cough and headache before the COVID-19 infection, was not a smoker, or

alcohol consumer, and was not on any medications.

Pleural effusion was diagnosed in the posteroanterior chest X-ray, accompanied by low serum albumin level at 1.1 gr/dL. He was hospitalized with a diagnosis of nephrotic syndrome. Serum urea and creatinine levels were 191 mg/dL and 5.2 mg/dL, respectively on the second day despite the normal levels at the time of admission. The patient also developed hemoptysis on the second day. COVID PCR test was negative. There was hematuria in urinalysis and 4.2 g/d of proteinuria. Possible alveolar hemorrhage and necrotizing pneumonia were reported on a non-contrast thoracic computed tomographic (CT) scan. In echocardiography the ejection fraction was normal.

Goodpasture syndrome (GPS) or antineutrophil cytoplasmic antibody-related vasculitis (ANCA) were considered as a possible diagnoses considering the rapidly progressive glomerulonephritis, hemoptysis, and suspicious thoracic CT scan findings. singledose of cyclophosphamide (500 mg and three daily 500 mg doses of methylprednisolone were administered and plasmapheresis was performed). Hemodialysis was performed due to uremic symptoms. Diagnostic thoracentesis showed hemorrhagic fluid. Serologic studies for anti glomerular basement membrane antibody (Anti-GBM), antinuclear antibody (ANA), ANCA, C3 C4, cryoglobulins, hepatitis B and C infection, human immunodeficiency virus, and monoclonal gammopathy were negative Pathological study of kidney biopsy was compatible with immune complex-related acute glomerulonephritis (Figure 1 to 2). Due to the negative mentioned serologic test

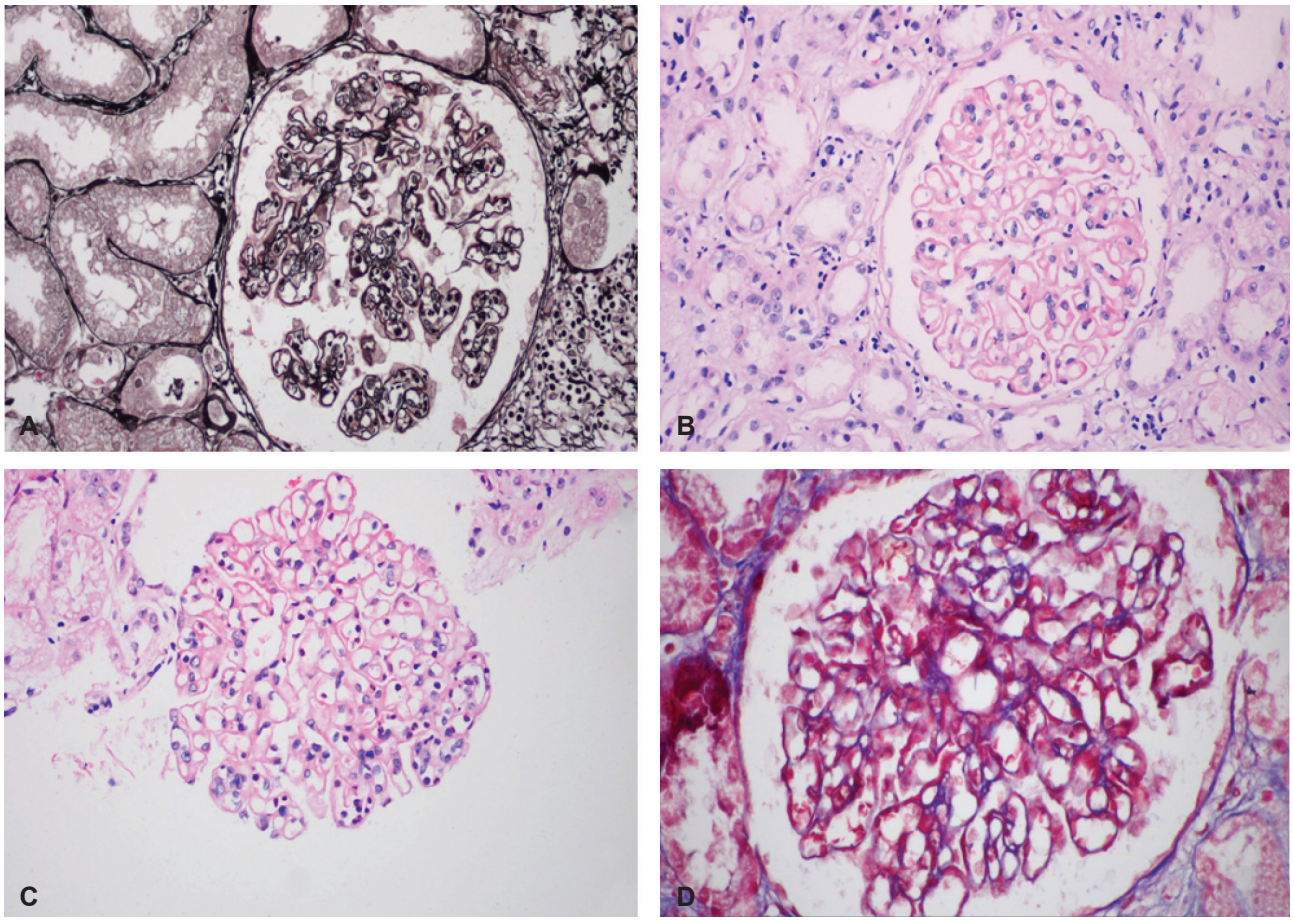

Figure 1. Global thickening of the capillary basement membrane in the glomeruli in the kidney biopsy specimen, increased polymorphic leukocytes in capillary spaces and fuxinophilic deposits in capillary walls and mesengial areas in mason trichrome staining (A: ×400, silver staining), (B:×200, hematoxylin&eosin staining), (C: ×200, Periodic acid-schiff staining), (D: ×600, mason trichrome staining). There were 22 glomeruli, 2 of which were globally sclerotic. In the glomeruli, there was diffuse, globally thickening of the capillary walls and an increase in polymorph leukocytes within the capillary spaces, and a mild to moderate increase in mesangial matrix/cells.There was no extra capillary cell proliferation, fibrin necrosis, duplication in capillary walls, and no spikes. There was no significant tubular atrophy or interstitial fibrosis in the tubulointerstitium. There was widespread edema and minimal inflammation in the interstitium.

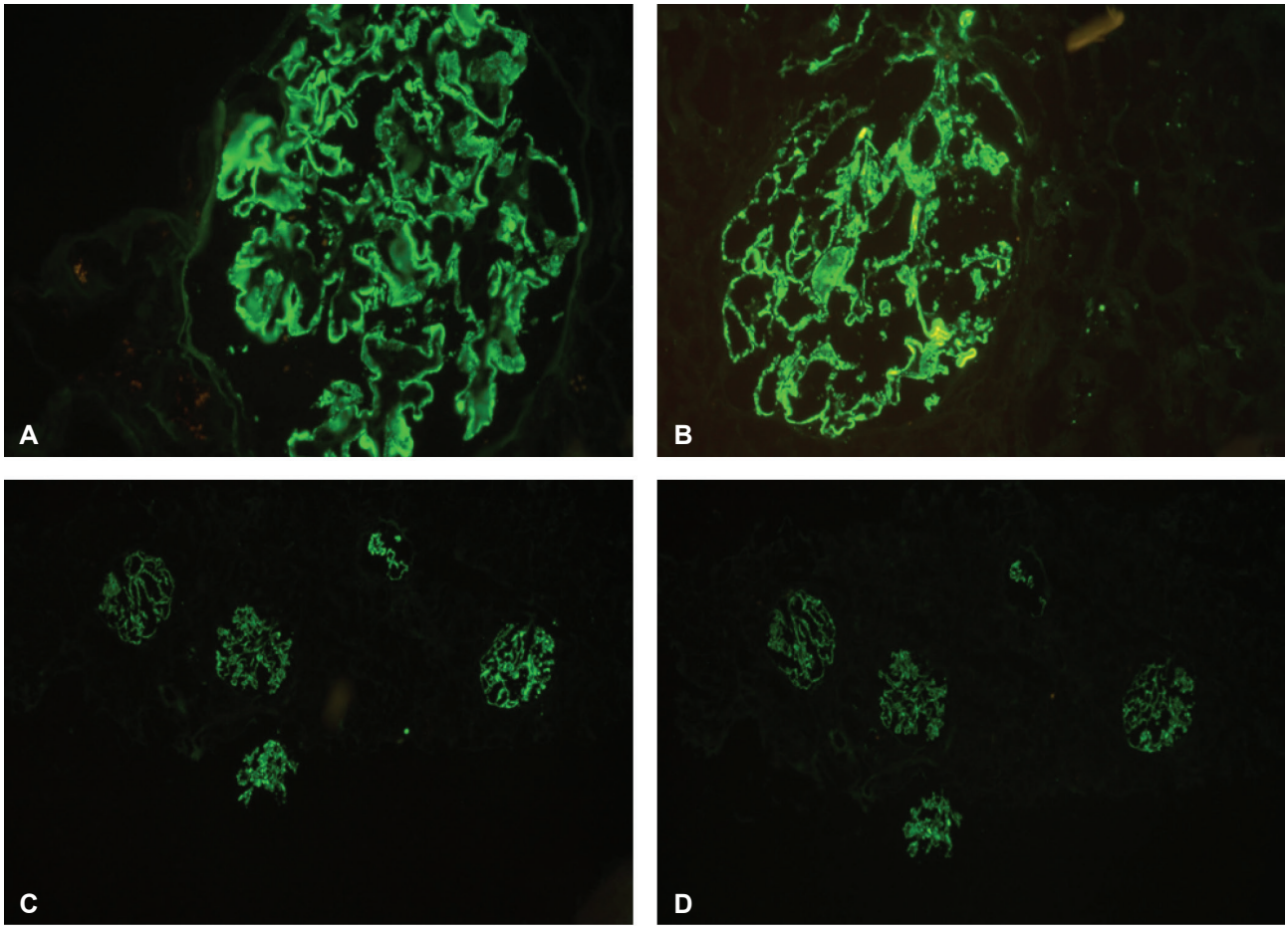

Figure 2. In immunofluorescence microscopic examination, in kidney biopsy, with IgG (A: ×600), C3 (B: ×400) antibody globally, granular staining in the capillary wall and mesangial areas at 3+ intensity. Diffuse globally on the capillary wall and mesangial areas in a granular 2+ intensity staining with Kappa (C: ×20) and Lambda (D: ×20) antibodies. Diffuse global staining was observed in the glomeruli, in the capillary walls, and the mesangial areas with IgG (3+), C3 (3+), Kappa (2+), Lambda (2+) antibodies. There was no staining with IgA, IgM, C1q antibodies.

results and the pathologic pattern, the diagnosis of COVID-19 infection-related postinfectious glomerulonephritis was made.

Cyclophosphamide and plasmapheresis were discontinued following the negative test results of anti-GBM, ANA, ANCA, and methylprednisolone was continued with a dose of 1 mg/kg/day. Hemoptysis recoveredkidney function reversed back to normal (Table 1) and the patient was discharged after 17 days.

DISCUSSION

In this 59 year old man, who presented with rapidly progressive glomerulonephritis and nephrotic syndrome 2 months after a CVOD-19 infection, therapeutic strategy was implemented with the initial diagnosis of GPS or ANCA-related vasculitis considering the presence of hematuria, proteinuria, hemoptysis and rapidly progressive kidney failure. However, the biopsy result, together with negativeanti-GBM and ANCAs tests was compatible with immune-complex glomerulonephritis, which was attributed to the recent COVID-19 infection. Therefore, the patient was considered as COVID-19 related immune-complex glomerulonephritis. The coexistence of post-infectious glomerulonephritis and pulmonary hemorrhage is rare. [3-5] In addition, most of the glomerular diseases reported to be associated with COVID-19 infection, have beenin the form of collapsing glomerulopathy. Another case of COVID-19 related immune-complex glomerulonephritis has been reported by Sanjeev *et al.* Howevere in that case, the patient had a previous history of focal segmental glomerulosclerosis.[6] It is suggested that the

Table 1. Results of Laboratory Tests

Laboratory Test	Admision Day	Day 2	Day 6	Day 10	Day 14	Day 17 (Discharge)
Urea, mg/dL	18	191	160	99	74	48
Creatinine, mg/dL	0.95	5.2	4.33	2.52	1.92	1.2
Albumin, g/L	1.12	1.14	2.6	2.5	2.5	2.9
ALT, U/L	17	14	11	17		
AST, U/L	286	16	6	16		
LDH, U/L	394	417	396	359		
WBC, 10^3 /uL	9	14	9.8	9.5		
Hemoglobin, g/dL	11.8	11	12.5	11.8		
Platelet. 10^3 /uL	241	340	262	194		
CRP, mg/L	145	349	170	6		
c-ANCA			Negative			
p-ANCA			Negative			
Anti-GBM Antibody			Negative			
C3, g/L			1.31 (Normal)			
C4, g/L			0.36 (Normal)			
ANA			Negative			
Anti-dsDNA			Negative			
Urine Analysis						
pH	5		5		5	
Specific gravity	1030		1011		1017	
Protein	++++		+++		+++	
Leukocyte	-		-		-	
nitrite	-		-		-	
Erythrocyte	+		++		++	
Ketone	-		-		-	
Glucose	-		-		-	

Abbreviations: ALT, alanin aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; WBC, white blood cell; CRP, c-reactive protein; c-ANCA, cytoplasmic-anti-neutrophil cytoplasmic antibodies; p-ANCA, perinuclear- anti-neutrophil cytoplasmic antibodies; ANA, antinuclear antibodies; Anti-ds DNA, anti-double stranded *DNA*; Anti-GBM, anti-glomerular basement membrane.

virus causes glomerulonephritis through direct and indirect mechanisms and This has also been supported by autopsy results reports that revealed tropism of virus to podocytes in patients with COVID-19 associated glomerulonephritis and suggested a central role for podocytopathy. It also has been observed that angiotensin converting enzyme-2 receptors are highly expressed in podocytes, which may facilitate the entry of the virus into podocytes.

Although COVID-19 viral RNA has been shown in kidney tissue in a number of studies, this has not been reported in other studies. Additionally, microvascular damage caused by the complement system, coagulopathy, and endothelial damage, and endothelial dysfunction in COVID-19 infection, have an important role in kidney damage.[7,8]

CONCLUSION

In conclusion, immune-complex glomerulonephritis can occur following COVID-19 infection, and may present asrapidly progressive kidney failure, nephrotic syndromeand pulmonary hemorrhage.. Early diagnosis and implementation of appropriate therapy are essential in resolving kidney function.

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