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CASE REPORT

IgA Nephropathy Secondary to COVID-19 Infection - A Case Report

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Abstract

We present a case of a 73-year-old African American lady with COVID-19 infection who developed acute Kidney Injury (AKI) and significant proteinuria. Renal biopsy showed IgA nephropathy. Patient was eventually diagnosed with IgA nephropathy secondary to COVID Infection. This unique case highlights the complexity of renal involvement in COVID-19. Notably, the onset of IgA nephropathy in the patient occurred several weeks after her COVID-19 diagnosis, deviating from the typical synpharyngitic presentation. This article contributes to the growing body of evidence regarding renal complications associated with COVID-19 and highlights the need for vigilance in assessing and managing renal conditions in COVID-19 patients, especially when atypical presentations occur.

Keywords: IgA nephropathy, COVID-19, Renal, Focal segmental glomerulosclerosis, FSGS, COVID nephropathy

1. Introduction

Since the onset of the Severe acute Respiratory Syndrome Coronavirus 19 (SARS COVID-19) pandemic, concurrent renal disease has been commonly observed in infected patients. Multiple studies have revealed several renal pathologies, including AKI (acute kidney injury), nephrotic syndrome and RPGN (Rapidly progressive glomerulonephritis).[1-3] While the majority of renal biopsies in COVID-19 patients with concurrent renal disease revealed a combination of acute tubular injury and collapsing glomerulopathy, a distinct form of glomerular injury called IgA nephropathy has been associated with COVID-19 virus infection. There is limited data regarding IgA nephropathy in the setting of COVID-19. Here, we present a case of AKI with severe proteinuria with biopsy results showing both FSGS (focal segmental glomerulosclerosis) and IgA nephropathy in the setting of recent COVID-19 infection (see Figs. 1–4).

2. Case presentation

A 73-year-old obese African American female with past medical history of COPD, hypertension, COVID-19 infection in August 2020 presented to the hospital in October 2020 for shortness of breath, lower extremity swelling and unintentional weight gain.

Two months prior to presentation, she presented to an outside hospital with cough, wheezing and chest congestion. She tested positive for COVID-19 infection. She was kept in the observation unit for 24 h and was discharged home. No specific treatment was given. Initial labs at that time showed a creatinine of 1.37 mg/dL (Baseline creatinine 1.07 mg/dL with estimated glomerular filtration rate (EGFR) of over 60 cc/min). Urinalysis negative for hematuria but found to have 3+ proteinuria. (Previous urinalysis from February 2017 was negative for proteinuria and hematuria). Urine protein/creatinine ratio (UPCR) was not done during her

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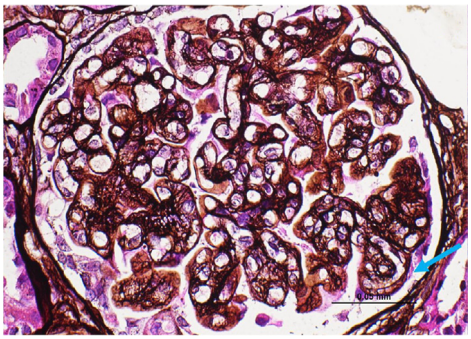

Fig. 1. Glomerulus with capillary wall thickening and segmental duplication. Endocapillary hypercellularity was absent (periodic acid silver methanamine, 400x).

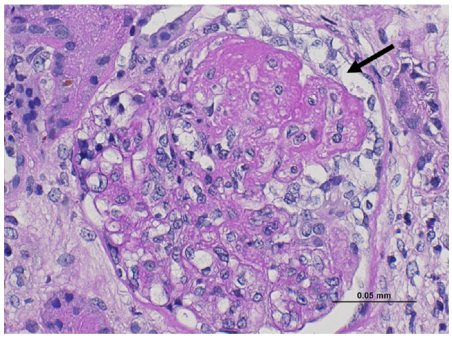

Fig. 2. Glomerulus with segmental consolidation and prominent podocytes (periodic acid Schiff, 400x).

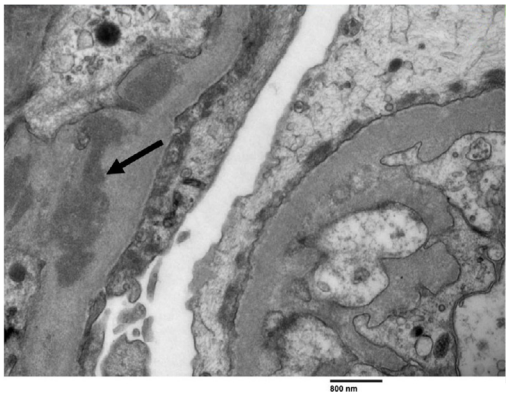

Fig. 3. Podocyte injury with severe foot process effacement, and mesangial electron dense deposits (arrow) (transmission electron microscopy, 23000x).

brief hospital stay. Since that time patient had reported progressive weight gain and lower extremity edema. One week prior to this current hospitalization she was seen by her primary care physician via video telehealth visit due to progressive unintentional weight gain of 30 pounds despite being on furosemide 20 mg daily. Metolazone 5 mg daily was added. Despite this, symptoms worsened.

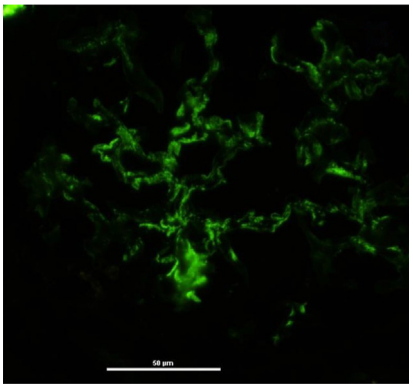

Fig. 4. Coarse granular mesangial staining for IgA, 3+ (anti-IgA immunofluorescence, 400x).

On initial presentation her blood pressure was 211/76 mm Hg, O2 sat 98% on room air. She was found to have anasarca on physical examination. Chest x-ray showed cardiomegaly and bilateral minimal pleural effusions. Transthoracic echocardiogram showed grade 2 left ventricular diastolic dysfunction, with normal ejection fraction of 55–60%. Cardiac work-up including nuclear cardiac perfusion scan and stress test revealed no reversible defect to suggest ischemia.

Patient was admitted to the congestive heart failure (CHF) unit and was diuresed with IV furosemide 40 mg twice daily. Initial diuretic therapy was ineffective, requiring higher doses of furosemide with IV albumin. Her initial weight was 123 kg. Her documented weight back in February 2020 was 111 kg. Nephrology service was consulted due to renal insufficiency and significant proteinuria of over 300 mg/dL and microscopic hematuria. Initial UPCR was 3.1 g/g creatinine (Normal <0.05 g/g). Serum albumin level was low at 2.2 g/L. Her serum creatinine level was 1.76 on admission progressively increasing to 2.44 mg/dL. We obtained 24-h urine collection for protein and creatinine and measured 13 g proteinuria. Renal sonogram showed right and left kidneys measuring 10 cm, with increased echogenicity without any evidence of hydronephrosis. ANA screen was negative and C3, C4 levels were not depressed. No monoclonal proteins were identified on electrophoresis & Free kappa lambda ratio was within normal limits. Additionally, Hepatitis panel and HIV were negative. Renal biopsy was performed showing focal segmental glomerulosclerosis in the setting of IgA nephropathy (Oxford classification: Mesangial hypercellularity 0, Endocapillary Hypercellularity0, Segmental glomerulosclerosis 1, Tubular atrophy/Interstitial fibrosis 2, Crescents 0) with moderate to severe tubulointerstitial scarring, mild arteriosclerosis and arteriolar hyalinosis and severe

arteriolosclerosis. Based on discussion with renal pathologist, the biopsy showed numerous FSGS lesions in the setting of a minimally proliferative IgA nephropathy. (Up to 16 glomeruli per section were seen, 1 of which (6%) were obsolescent (see Figs. 1–4). There was diffuse mesangial expansion with focal and segmental mild hypercellularity. Crescents, fibrin or necrosis were not appreciated). FSGS can arise in the setting of IgA nephropathy, however, a primary form of Podo cytopathic injury cannot be excluded on histologic grounds alone. Correlation with trajectory of proteinuria suggested including whether proteinuria and COVID-19 were coincident.

In addition to optimizing blood pressure control, patient was treated with immunosuppressive therapy with systemic glucocorticoids as the patient was deemed to be at high risk of disease progression using the International IgAN (IgA Nephropathy) Prediction Tool. She was started on prednisone 60 mg/day for 2 months followed by a slow taper over the next 4–6 months. Her weight on discharge was 108 kgs.

After 2 months of prednisone 60 mg/day, her dipstick proteinuria improved to 1+, UPCR improved to 1.2 g/g creatinine. Prednisone dose was reduced to 40 mg/day at that point, with slow taper over the next 4 months, treatment was completely stopped on April 18, 2021. Her proteinuria continued to improve down to 0.3 g/g creatinine on UPCR and creatinine level stabilizing/improving down to 1.4–1.5 range from a peak of 2.84. Her clinical status continued to improve with optimal blood pressure control, progressive improvement of edema, and her weight down to 99.7 kg. Proteinuria maintained between 0.3 and 0.4 g/g creatinine.

2.1. Laboratory findings

Lab findings are reported in the table below.

3. Discussion

Acute kidney injury is a frequent complication of COVID-19 infection. Underlying pathogenesis causing renal dysfunction is unclear, but many possible mechanisms have been proposed. One of the proposed mechanisms includes direct renal injury as viral nucleoproteins have been demonstrated in the renal tubules.[4] Renal tubular cells express angiotensin converting enzyme receptor 2 which acts as a port of entry for the virus and affects the kidney.[5] Cytokine storm demonstrated in severe COVID infection is another explanation leading to kidney injury.[4]

Most common pathology noted on renal biopsy is acute tubular necrosis.[6] Glomerulopathies have been demonstrated to be associated with COVID-19 and most cases are collapsing glomerulopathy. There are only a handful of reported cases of IgA nephropathy due to COVID-19 infection.[7]

IgA nephropathy is usually seen after respiratory infection. It usually presents within 5 days of respiratory infection, hence it is also sometimes referred to as synpharyngitic. An interesting presentation in our case is patient presented with symptoms of IgA nephropathy weeks after the COVID diagnosis. Though at the time of diagnosis patient had 3+ proteinuria in the urinalysis, she had no clinical symptoms suggestive of renal pathology.

Most cases of IgA nephropathy usually present as hematuria. Only about 5% cases present with nephrotic syndrome or rapidly progressing glomerulonephritis. IgA nephropathy can rarely present as malignant hypertension.[8] As in our case, patient presented with elevated blood pressure of 211/76, but it is unclear if the presentation is due to IgA nephropathy, or it was just a mere coincidence.

Few case reports of IgA vasculitis have been reported secondary to COVID 19 presenting with arthralgia, skin rash and kidney injury which was not seen in our patient.[9] There are also several

Lab values	Feb 2017	Jan 2020	Aug 2020 (COVID diagnosis)	10/09/2020 (Day of hospital admission)	10/21/2020 (during peak creatinine)	11/09/2020 (outpatient follow up)	04/15/2021 (outpatient follow up)	10/12/2021 (outpatient follow up)
BUN mg/dL	N/A	15	22	21	38	61	33	44
Creatinine mg/dL	N/A	1.07	1.37	1.98	3.49	1.87	1.75	1.36
EGFR mL/min/m^2	N/A	>60	46	28	14	30	33	44
Serum albumin mg/dL	N/A	N/A	3.5	2.2	N/A	2.9	3.2	3.5
Urine protein	Negative	12, 753	>300	>300	N/A	N/A	N/A	N/A
Urine RBC Per hpf	Negative	N/A	Negative	TNTC	N/A	N/A	N/A	N/A
UPCR	N/A	N/A	N/A	N/A	3.1	N/A	0.6	0.3
U24 protein mg/24 h mg/mg	N/A	N/A	N/A	N/A	12, 753	4.1	N/A	N/A

N/A-not available, TNTC Too Numerous to Count.

published case reports of COVID-19 vaccination leading to IgA nephropathy.

Renal biopsy of our patient showed FSGS in the setting of minimally proliferative IgA nephropathy. The biopsy specimen was not tested for viral nucleoproteins. In summary, we described a case of IgA nephropathy likely resulting from a recent COVID-19 infection. In our case, the patient was deemed to be at high risk of disease based on International IgAN Prediction Tool and was started on steroids. The International IgAN Prediction Tool is a resource to quantify risk of progression and inform shared decision-making with patients, using clinical and histologic data at the time of biopsy.[10] The initial management guidelines per KDIGO for all patients with persistent proteinuria include lifestyle modification (smoking cessation, weight control, regular exercise, dietary sodium restriction), blood pressure control and maximally tolerated RAAS (Renin Angiotensin Aldosterone System) blockade.[11] Our patient was on enalapril, but was held when AKI progressed and was resumed later when creatinine improved. In special situations like IgA nephropathy with nephrotic syndrome, it is unclear whether this is a specific podocytopathic variant of IgAN or the existence of MCD/FSGS (Minimal Change disease/ Focal Segmental glomerulosclerosis) in a patient with IgAN. In those patients with IgA nephropathy with high risk of progression after maximal supportive care, immunosuppression may be considered and used with extreme caution. We had used prednisone in our patient which appeared to be efficacious.

Declaration

This article has not been presented at any conference. It has not been submitted to any other journal. No Funding/support has been received for writing this article.

Conflicts of interest

Authors have no conflict of interest.

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