Annals of Case Reports
Anandh U and Bannur S. Ann Case Rep: 7: 842.
www.doi.org/10.29011/2574-7754.100842
www.gavinpublishers.com

Case Report

Nephrotic Syndrome Post COVID 19 Infection: Association or Mere Coincidence?

Urmila Anandh[1*], Sooraj Bannur[2]

[1]Senior Consultant Nephrology, Yashoda Hospitals, Secunderabad, India

[2]Registrar Nephrology, Yashoda Hospitals, Secunderabad, India

***Corresponding author**: Urmila Anandh, Senior Consultant Nephrology, Yashoda Hospitals, Secunderabad, India

Citation: Anandh U, Bannur S. (2022) Nephrotic Syndrome Post COVID 19 Infection: Association or Mere Coincidence?. Ann Case Report 7: 842. DOI: 10.29011/2574-7754.100842

Received: 09 May 2022; **Accepted:** 11 May 2022; **Published:** 13 May 2022

Abstract

Renal involvement is frequently recognised in patients with COVID 19 infection. Acute kidney injury and proteinuria are the two common manifestations. Renal biopsies during an ongoing COVID 19 infection reveal various types of glomerular injury, of which collapsing glomerulopathy is the commonest. We report three cases of nephrotic syndrome occurring four to six weeks after COVID 19 infection. The immunomodulatory nature of the SARS-CoV-2 virus makes us believe that there may exist an association between the viral infection and subsequent development of nephrotic syndrome.

Introduction

SARS-COV-2 infection has been shown to involve the kidney. Many studies have shown the presence of acute kidney injury with high grade proteinuria [1,2]. In a case series, nephrotic syndrome with AKI has been reported during an ongoing COVID -19 infection. Most of these patients were from African ancestry and the histopathological examination revealed podocytopathy and collapsing glomerulopathy [3]. Other studies have also alluded to the development of proteinuria secondary to COVID -19 infection. There are also increasing number of reports on the development/ relapse of glomerular disease following COVID -19 vaccination [4]. We report three cases of young adults who developed nephrotic syndrome four to six weeks following a COVID 19 infection.

Case Series

Case 1

An 18- year- old man from South Asian ancestry presented to our outpatient department with progressive swelling of his face and legs of two weeks duration. He had no history of any medical illness. He gave a history of fever and cough six weeks back. His evaluation revealed the presence of COVID -19 infection (rt-PCR positive). As he had mild symptoms, he was managed at home. His evaluation at our clinic revealed proteinuria, hypoalbuminemia and abnormal renal functions (Table 1). He underwent a renal biopsy which was reported as focal segmental glomerulosclerosis (NOS) (Figure 1). He was offered a trial of steroids (1 mg/kg daily). Over the next 6 months as his steroids were tapered, his

nephrotic syndrome relapsed. He was restarted on steroids again. We plan to start Tacrolimus when he achieves remission and taper steroids slowly.

Patient Details	Case 1	Case 2	Case 3
COVID 19 Infection Details	SARS-COV-2 positive Mild Symptoms Managed at home	SARS-COV-2 positive (rt-PCR) Mild symptoms At Home	SARS-COV-2 positive (rt-PCR) Cough, Fever anosmia Managed at home.
Temporal association of symptoms with COVID 19 Infection	Pedal oedema, facial puffiness 6 weeks after.	Pedal edema , facial puffiness, oliguria , weight gain after 4 weeks	Pedal edema, facial puffiness, weight gain after 6 weeks.
Clinical Features Facial Swelling Pedal Edema Abdominal Distention Oliguria Hypertension	Yes Yes Yes No No	Yes Yes Yes Yes No	 Yes Yes No Yes No

Laboratory Parameters			
Hemoglobin (g/dl)	13.4	16.7	12.6
Creatinine (mg/dl)	1.4	0.8	0.6
Serum Albumin (g/dl)	1.7	2.0	1.9
Urinalysis	Protein ++++ RBCs 4-5/hpf	Protein ++++ No RBCs	Protein +++ RBCs 15-20/hpf
Urine Protein Creatinine ratio	1.7	6.7	8.7
Ultrasound Abdomen	Normal sized kidneys.	Enlarged kidneys, ascites.	Normal sized , edematous kidneys
Renal Biopsy Histopathology	Focal segmental Sclerosis (NOS)	Normal	Focal segmental glomerulosclerosis(tip lesion) C3c positive
Immunofluorescence	Mesangial deposit of IgG, C3C, κ and Primary podocytopathy	None	Not done
Electron Microscopy	No deposits	Diffuse podocyte effacement	
ApoL1 genotype	G0/G0	G0/G0	G0/G0

Outcome	In clinical and biochemical remission for 3 months after completing 6 months of steroids. Relapsed on follow up, currently on tapering doses of steroids.	Taken steroids for 8 weeks. In clinical and biochemical remission .	On Tacrolimus, proteinuria in the sub-nephrotic range.

Table 1: Clinic revealed proteinuria, hypoalbuminemia and abnormal renal functions.

Case 2

A 20-year- old engineering student from rural South India presented to us with progressive weight gain and oliguria. Clinical examination revealed pedal oedema, facial puffiness and free fluid in the abdomen. He gave an history of COVID -19 infection 4 weeks back. He underwent a renal biopsy, which was essentially normal on histopathology and immunofluorescence. His electron microscopy revealed diffuse foot process effacement (Figure 2). A diagnosis of minimal change disease was made and he was started on steroids. He has completed 8 weeks of treatment and has achieved complete clinical and biochemical remission. His recent investigations after 3 months of follow up show normal renal function and a urine protein of 0.1 gram/day.

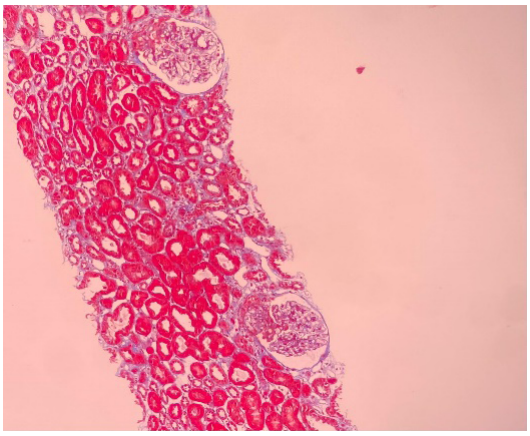

Figure 1: Histopathology showing FSGS (NOS) in case 1.

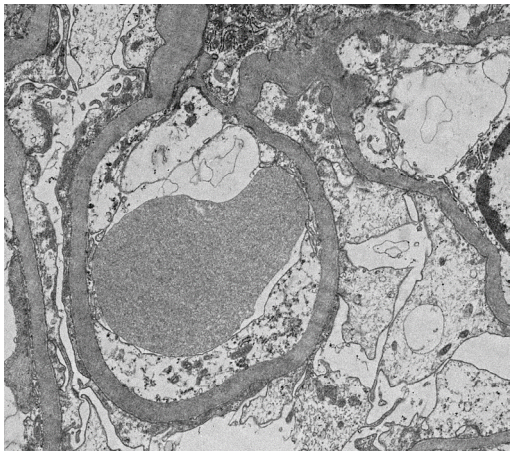

Figure 2: EM images showing diffuse podocyte effacement (Case 2).

Case 3

24 -year -old woman presented to us with facial puffiness, swelling of legs and abdominal bloating. She gave a history of symptomatic COVID 19 infection 6 weeks back. She was evaluated and found to have nephrotic syndrome. She underwent a renal biopsy, which revealed the features of focal segmental glomerulosclerosis (tip lesion) (Figure 3). She was started on steroids and was treated with tapering dose of steroids for three months. Her current urinary protein excretion is 1.8 grams /day. As she did not achieve complete remission, she was started on Tacrolimus. Currently she is on 0.1 mg/kg/day tacrolimus and her sub-nephrotic proteinuria persists.

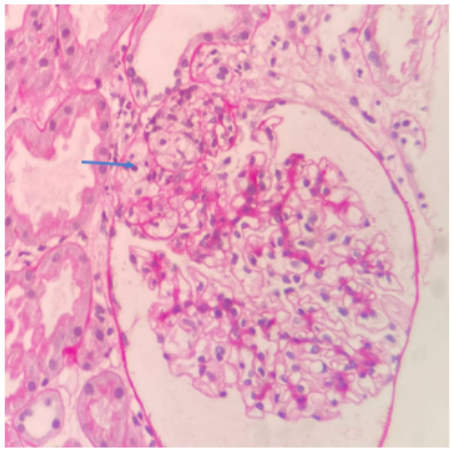

Figure 3: Renal biopsy showing focal segmental glomerulosclerosis (tip lesion) in Case 3.

Discussion

Acute kidney injury in COVID 19 infected patients requires immediate evaluation and therapeutic intervention, but what is often not highlighted is that proteinuria is an important and not so uncommon renal manifestation in COVID 19 infected patients [5]. In a biopsy series, glomerular involvement was noted in four out of ten patients. The patients in this series had features of collapsing glomerulopathy (CG) [6]. Collapsing glomerulopathy seems to be the common glomerular disease in patients with COVID 19 infection (Table 2) [7,8]. Also, there have been cases of new onset/relapse of nephrotic syndrome (NS) in children and young adults who developed COVID 19 infection. In most of these patients, biopsies were done during an ongoing COVID 19 infection [9,10,11]. Our patients are cases who developed NS four to six weeks after documented COVID 19 infection .All these young adults had relatively mild/asymptomatic COVID 19 infection. Focal segmental glomerulosclerosis was the histology in 2 out of 3 patients. None of them had histopathological evidence of collapsing glomerulopathy. None had evidence of high-risk ApoL1 genotype. The absence of CG may reflect the racial differences in extent and type of glomerular involvement in COVID 19 infection. The development of NS following COVID 19 infection may not reflect a causality but maybe considered as a chance association with SARS-CoV-2 infection. However, the immunomodulatory nature of the virus makes us speculate that there may exist some correlation with COVID 19 infection and development of NS [12]. Further studies are required to understand this unique propensity of the virus and its implication in the development of glomerular disease.

Published Reports	No of cases	Clinical Presentation	Histopathology	APOL1 Gene Testing
Kudose et al.[13]	32	AKI 22 Proteinuria -10	CG-23 FPE (incl. MCD) -7 Primary FSGS -2	16- positive 1- Negative *
Larsen et al.[14]	1	AKI Proteinuria	CG/ATN	Positive
Peleg et al. [15]	1	AKI Nephrotic proteinuria	CG/ATN	Positive
Kissling et al. [8]	1	AKI Nephrotic proteinuria	CG/ATN	Not available

Couturier et al [16]	2	AKI Proteinuria	CG	Positive (both cases)
Sharma et al. [6]	1	ATN	CG	Not Done
AKI-Acute kidney injury, ATN -Acute Tubular Necrosis, CG-Collapsing Glomerulopathy, FPE-Foot process effacement, FSGS-Focal Segmental Glomerulosclerosis, MCD-Minimal Change Disease. *Out of the 23 patients with CG, samples for APOL1 genetic testing were available in 17.				

Table 2: Reports in literature on collapsing glomerulopathy following COVID 19 infection.

Conclusion

Glomerular diseases are increasingly recognised in kidney biopsies of patients with COVID 19 infection. NS (new onset and relapse) is also described in literature. We report the development of nephrotic syndrome in three cases four to six weeks following a COVID 19 infection. Nephrotic syndrome have an underlying immunological mechanism and we speculate that the immunopathology engendered by COVID 19 infection might explain this association.

Data availability: All data pertaining to this submission is with the corresponding author and can be made available on reasonable request.

References

1. Pei G, Zhang Z, Peng J, Liu L, Zhang C, et al. (2020) Renal involvement and early prognosis in patients with COVID -19 pneumonia. J Am Soc Nephrol 31: 1157-1165.
2. Bruchfeld A. (2020) The COVID -19 pandemic: consequences for nephrology. Nature Rev .Nephrol 2020.
3. Shetty AA, Tawhari I, Safar-Boueri L, Seif N, Alahmadi A, et al. (2021) COVID-19 associated glomerular disease. J Am Soc Nephrol 32: 33-40
4. Kervella D, Jacquemont L, Chapelet-debout A, Deltombe C, Ville S. (2021) Minimal change disease relapse following SARS-CoV2 mRNA vaccine. Kidney Int. 2021.
5. Hirsch JS, Ng JH, Ross DW, Sharma P, Shah HH, et al. (2020) Northwell COVID 19 Research Consortium; Northwell Nephrology COVID 19 Research Consortium: Acute kidney injury in patients hospitalized with COVID -19 .Kidney Int. 98: 209-218.
6. Sharma P, Uppal NN, Wanchoo R, Shah Hh, Yang Y, et al. (2020) COVID -19 -associated kidney injury :A case series of kidney biopsy findings. J Am Soc Nephrol 31: 1948-1958.
7. Velez JCQ, Caza T, Larsen CP. (2020) COVAN is the new HIVAN:the re-emergence of collapsing glomerulopathy with COVID -19.Nature Reviews Nephrology 34: 279.
8. Kissling S, Rotman S, Gerber C, Halfon M, Lamoth F, et al. (2020) Collapsing glomerulopathy in a COVID -19 patient.Kidney Int.
9. Morgan KM, Imani PD. (2021) Case report: a 5 -year-old with new onset nephrotic syndrome in the setting of COVID-19 infection.BMC Nephrology 22: 323.
10. Alvarado A, Franceschi G, Resplandor E, Sumba J, Orta N. (2020) COVID 19 associated with onset nephrotic syndrome in a pediatric patient:coincidence or related conditions? Pediatric Nephrology.
11. Enya T, Morimoto Y, Oshima R, Miyazaki K, Miyazawa T, et al. (2020) Nephrotic syndrome relapse in a boy with COVID -19. CEN Case Reports 10: 431-434.
12. Tay MZ, Poh CM, REnia L, MacAry P, Ng LFP. (2020) The trinity of COVID 19:immunity, inflammation and intervention.Nat Rev Immunol.2020;Nat Rev Immunol. 20: 363-374.
13. Kudose S, Santoriello D, Bomback AS, Sekulic M, Batal I, Stokes M, et al. (2021) Longitudinal Outcomes of COVID 19 -associated collapsing glomerulopathy and other podocytopathies.JASN 32: 2958-2969.
14. Larsen CP, Bourne TD, Wilson JD, Saqqa O, Sharshir MA. (2020) Collapsing glomerulopathy in a patient with coronavirus disease 2019 (COVID 19). Kidney Int Rep 5: 935-939.
15. Peleg Y, Kudose S, D'AgatiV, Kisselev S, Gharavi A, et al. (2020) Acute kidney injury due to collapsing glomerulopathy following COVID 19 infection.Kidney Int nRep 5: 940-945.
16. Couturier A, Ferlicot S, Chevalier K, Guillet M, Essig M, et al. (2020) Indirect effects of severe acute respiratory syndrome coronavirus 2 on the kidney in coronavirus disease patients. Clin Kidney J 13: 347-353.