BANTAO Journal 2021; 19(2): 67-71

BJ

BANTAO Journal

Short communication

Focal Segmental Glomerulosclerosis and Collapsing Glomerulopathy after Covid 19 Infection

Vesna Ristovska[1], Pavlina Dzekova Vidimliski[1], Vlatko Karanfilovski[1], Zaklina Sterjova-Markovska[1], Aleksandra Canevska-Taneska[1], Igor Nikolov[1], Galina Severova[1], Lada Trajcevska[1], Panche Zdravkovski[2] and Gordana Petrusevska[2]

[1]University Clinic for Nephrology, [2]Institute of Pathology, Medical Faculty, University Sts. Cyril and Methodius, Skopje, N. Macedonia

Abstract

Introduction. Focal segmental glomerulosclerosis (FSGS) is defined as an increase in the mesangial matrix in some glomeruli with obliteration of capillary lumens, sclerosis, hyalinosis, foam cells, and adhesions to the Bowman's capsule. Collapsing glomerulopathy is a morphologic variant of focal segmental glomerulosclerosis (FSGS) characterized by segmental and global collapse of the glomerular capillaries, marked hypertrophy and hyperplasia of podocytes, and severe tubulointerstitial disease. Actually secondary collapsing glomerulopathy is a heterogeneous group including numerous causes: viruses, toxins and drugs such as heroin and pamidronate.

Case reports. We report on two cases with glomerular disease after COVID-19 infection. The first patient, 53 years old male, with nephrotic syndrome and histopathologic features of glomerular capillary collapse. He was admitted in our department with nephrotic syndrome and renal failure. Several months ago, he had COVID-19 infection and was treated for COVID-19 pneumonia, but he had not symptoms for any renal disease. In following months, the patients manifested symptoms such as nausea, dysuria and light malleolar edema. Laboratory findings presented increased values of BUN 27mmol/l, creatinine 453 μmol/l, with proteinuria 4,6 g/24h. In order to identify the cause for these results, renal biopsy was performed with diagnose of collapsing glomerulopathy. The patient was followed up for a period of 6 months and treated with corticosteroid therapy. The values for creatinine were decreased to 195 μmol/l, with proteinuria 1 g/24h. After that the patient was stable, but with slowly increasing values for creatinine up to 242μmol/l and proteinuria 0,61 g/24h, for a period of the next several months.

Second case was a patient 58 years old, male with pulmo-renal syndrome, with bilateral pneumonia and acute kidney injury. COVID 19 infection was established with BUN 36 mmol/l and serum creatinine up to 586 μmol/l. Several weeks the patient was treated with hemodialysis. After that the patient was stable, the values for BUN and serum creatinine were still higher but without necessity for dialysis treatment. Proteinuria of 1,98 g/24hours still remained and renal biopsy was performed. Focal segmental glomerulosclerosis was diagnosed. The follow up in next several months included therapy with corticosteroids, after that with cyclosporin, with effect on improved kidney function with BUN 14 mmol/l, creatinine 156 μmol/l and values for proteinuria of 0,96 g/24hours.

Conclusion. SARS-CoV-2 associated renal disease seems to have different outcome and follow up despite the treatment. Renal biopsy may be crucial along with the molecular testing for COVID 19.

Keywords: focal segmental glomerulosclerosis, collapsing glomerulopathy, COVID 19 infection, kidney injury

Introduction

Cases of even mild symptomatically COVID 19, are accompanied by acute kidney injury or heavy proteinuria and glomerulopathy. Although acute kidney injury was seen among most of them, uncommon pathology such as collapsing glomerulopathy were detected and most of these patients progressed to irreversible kidney injury and dialysis [1-3].

Collapsing glomerulopathy is a morphologic variant of focal segmental glomerulosclerosis (FSGS) characterized by segmental and global collapse of the glomerular capillaries, marked hypertrophy and hyperplasia of podocytes, and severe tubulointerstitial disease [3-5]. Actually secondary collapsing glomerulopathy is a heterogeneous group including numerous causes: viruses, toxins and drugs such as heroin and pamidronate.

The data suggest that collapsing glomerulopathy is clinically, pathologically, and epidemiologically different from noncollapsing FSGS. Although collapsing glomeru-

Correspondence to: Vesna Ristovska, University Clinic for Nephrology, Vodnjanska 17, 1000 Skopje, N. Macedonia; E-mail: v.ristovska@yahoo.com

lopathy resembles HIV-nephropathy both pathologically and clinically, it differs clinically by having no evidence for associated HIV infection and other viruses such as COVID 19, and differs pathologically by lacking endothelial tubuloreticular inclusions. Patients with repeated renal biopsy showed transition from minimal change disease to collapsing focal segmental glomerulosclerosis [6].
COVID-19 has been associated with acute kidney injury and published reports of native kidney biopsies have reported diverse pathologies [4,7-9].

Case report 1

We report on patient, 53 years old, male with nephrotic syndrome and histopathologic features of glomerular capillary collapse. He was admitted in our department with nephrotic syndrome and renal failure. Several months ago, he had COVID 19 infection and was treated for COVID pneumonia, but he had not symptoms for any renal disease. In following months, the patient manifested symptoms such as nausea, dysuria and light malleolar edema. Laboratory findings presented increased values of BUN 27mmol/l, creatinine 453μmol/l, CRP 1,7, total protein 62g/l, albumin 33 g/l, with proteinuria of 4,6 g/24h. In order to identify the cause for these results, renal biopsy was performed. The histopathologic findings presented 3 completely ischemic collapsing glomeruli and segmental sclerosing changes in 3 of the glomeruli, with fibrous thickened Bowman membrane. The tubulointerstitial compartment exhibits acute tubular injury with areas of tubular atrophy (Figure 1). TEM analysis showed one completely collapsed glomerulus, and another one with segmental sclerosis. Ultra-structurally, we revealed ischemic collapsed basal membrane with huge subendothelial deposition of collagenous fibrils, some associated with glomerular basement membrane spikes like (Figure 2). Tubular epithelium revealed ischemic lesions. In one segment the basal membrane showed relatively preserved contour with edema of the endothelial cells. Tubular basement membrane revealed ischemic collapsing changes with ischemic lesion of the tubular epithelial changes. There are neutrophils, lymphocytes and histiocytes in the interstitium. Some structures suspicious for virus inclusions were seen on high magnifications, such was x200.000, with location in the endothelial cells. Some of these structures showed spikes typical for COVID 19 viral morphology (Figure 3).
The patient was followed up for a period of 6 months and treated with corticosteroid therapy. The values for creatinine were decreased to 195 μmol/l, with proteinuria of 1 g/24h. After that the patient was stable, but with slowly increasing values for creatinine up to 242 μmol/l and proteinuria 0,61 g/24h, for a period of the next several months.

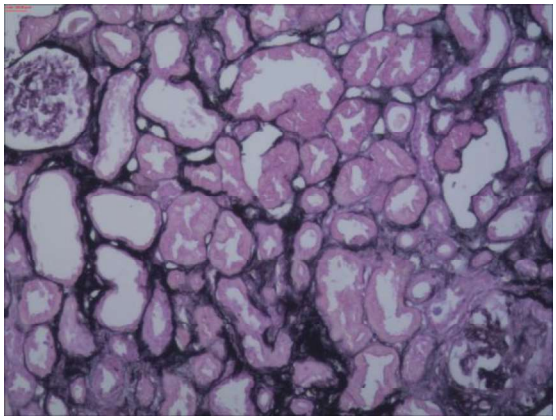

Fig. 1. Collapsing glomerulopathy after COVID 19 infection. Tubulointerstitium exibit acute tubular injury with areas with tubular atrophy

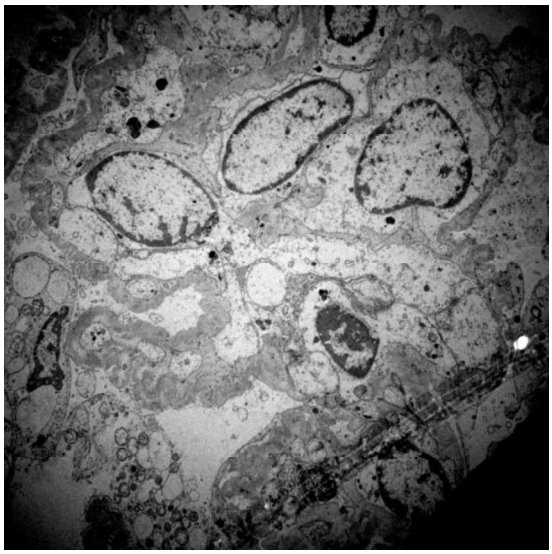

Fig. 2. Collapsed basal membrane with subepithelial deposition of collagenous fibrils

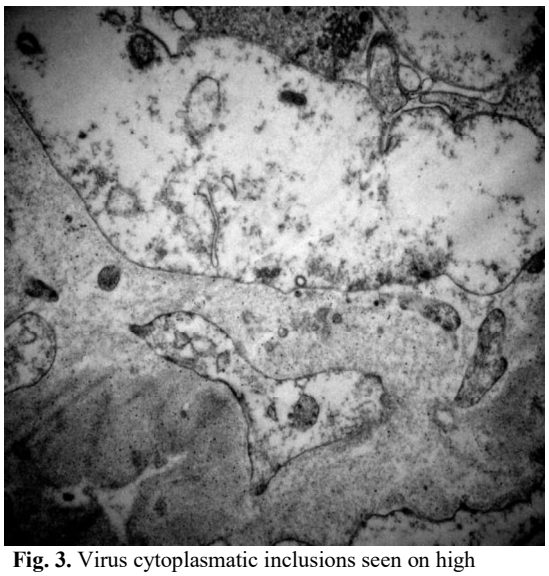

Fig. 3. Virus cytoplasmatic inclusions seen on high magnification

Case report 2

Second case was a patient, 58 years old, male with pulmo-renal syndrome, with bilateral pneumonia and acute kidney injury. COVID 19 infection was established with BUN 36 mmol/l and serum creatinine up to 586 µmol/l. Several weeks the patient was treated with hemodialysis. After that the patients was stable, although the values for BUN and serum creatinine were still higher, but without necessity for dialysis treatment. Proteinuria of 1,98 g/24hours still remained and renal biopsy was performed and focal segmental glomerulosclerosis was diagnosed. The histopathological findings revealed 3 glomeruli with relatively preserved structure, with slightly enlargement of the mesangial matrix. The other 6 glomeruli showed different grades of focal and segmental glomerulosclerotic lesion (Figure 4). In tubules there were erythrocyte cylinders with focal tubular atrophy and interstitial fibrosis. On semithin section analysis there was increased number of mesangial cells and mesangial matrix with opened capillary lumina.

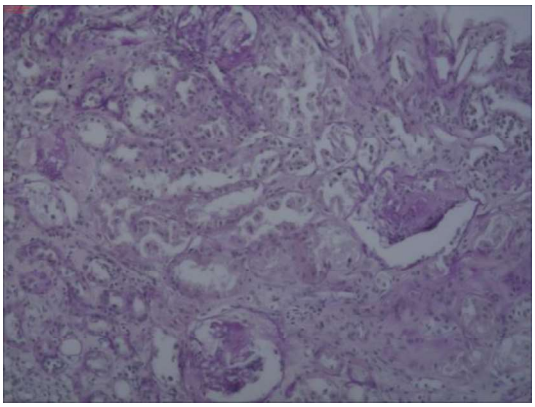

Fig. 4. Different grades of focal and segmental glomerulosclerotic lesions after COVID 19 infection

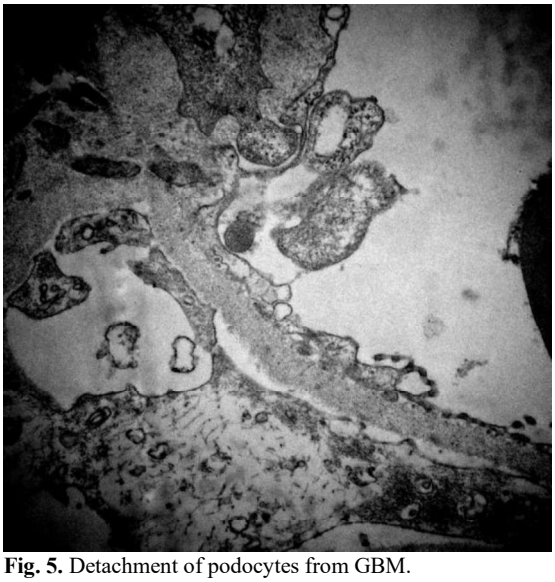

Fig. 5. Detachment of podocytes from GBM.

There were synechiae between visceral and parietal cells. Ultra-structurally the glomerular basement membrane had regular thickness with obvious segmental fusion of podocytes. There were found osmiophylic lipid inclusions in the visceral epithelial cells. In one segment detachment of the visceral epithelium from the GBM was seen (Figure 5). In some areas there were found GBM ischemic lesions with capillary intraluminal lymphocytes and histiocytes. There were some structures which were with morphologic characteristics of viral particles with present spikes like structures in the endothelial cell's cytoplasm and in lymphocytes. Some of them were included in membrane structures as cytoplasmatic inclusions (Figure 6).

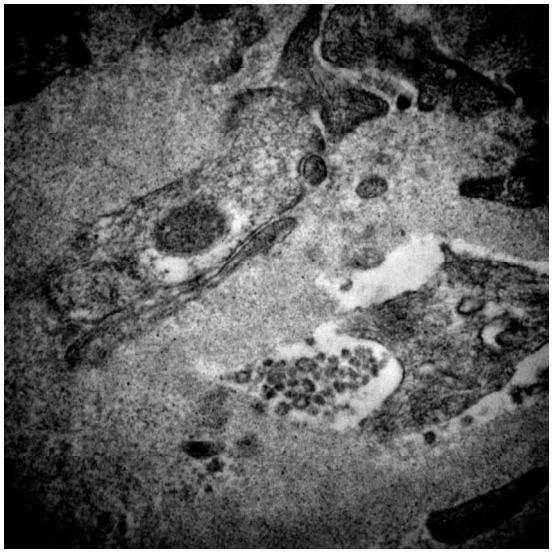

Fig. 6. Viral inclusions in endothelial cells of the glomeruli

The follow up in the next several months included therapy with corticosteroids, after that with ciclosporin, with effect on better kidney function with BUN 14 mmol/l, creatinine 156µmol/l and values for proteinuria 0,96g/24hours.

Discussion

The incidence of acute kidney injury associated with COVID-19 is variable depending on the geographic regions, and occurs in approximately 25-30% of patients admitted to hospitals [8,10]. The most common injury observed in autopsy and biopsy findings is acute tubular injury [8]. In a recently published studies, authors reported SARS-CoV-2 causing specific manifestations of proximal tubule dysfunction [11,12]. Histopathology showed proximal tubular injury, acute tubular necrosis, intraluminal debris, marked decrease in megalin expression in the brush border and electron microscopy evidence of particles resembling coronaviruses in cisternae of the endoplasmic reticulum in proximal tubule cells

[11]. Reports also indicate that rhabdomyolysis occurs in 7-20% of patients with COVID-19 acute kidney injury.
Infection with SARS-CoV-2 has been associated with cytokine release syndrome, a cytokine storm which contributes to hypoperfusion related injury of renal tubules [8]. Viral infection in alveolar cells, leads to massive recruitment of immune cells causing cytokine-mediated acute kidney injury [8-10].
Over the past several decades various pandemics have highlighted the different mechanisms by which viruses cause kidney disease [7,11-13]. With the novel coronavirus pandemic which has so far affected 96 million people as of January 2021 a new cohort of patients with kidney injury has been reported. The high infectivity causing rapid spread of this virus among the global population can have a significant long-term kidney complication than prior pandemics. Although there have been several publications over the past few months with attempts to identify the exact mechanism of kidney injury in these patients, the exact pathophysiology of COVID-19, the kidney injury remains unclear. The absence of viral particles demonstrated an alternate mechanism for renal injury explained in part by a dysfunctional immune response leading to a cytokine storm causing a cascade of renal injury including acute tubular injury, interstitial inflammation, microangiopathy, proteinuria, and possible glomerulopathy. As in the case of the hepatitis viruses and HIV-associated kidney disease, we may be seeing the start of a new disease entity as recently described of COVID-19-associated nephropathy (COVAN) along with increased chronic kidney disease in patients with COVID-associated kidney injury in the future [9,14]. Patients with COVID-19 develop a wide spectrum of glomerular and tubular diseases. Indications for kidney biopsy were recorded as any combination of acute kidney injury, even superimposed on chronic kidney disease, nephrotic-range proteinuria, or nephrotic syndrome, as previously described. The biopsy series reveal diverse kidney pathology in SARS-CoV-2-infected patients [9, 12]. The findings highlight the potential for viral infection to influence on immune responses that trigger new glomerular disease. Acute tubular injury is common and likely multifactorial and develops in up to 37% of hospitalized patients with COVID-19 and its pathophysiology has not been fully elucidated [15]. The lack of definitive virus in kidney cells argues against direct viral infection as the major pathomechanism [14].
Our findings provide two cases of focal segmental glomerulosclerosis, and its rare variant manifested as collapsing glomerulopathy, with evidence for the presence of at least some viral particles of COVID 19, mostly in the endothelial cells of the glomerular structures. In our cases we found different findings, but with clinical feature for chronic kidney injury. Renal biopsies were processed by standard techniques for light microscopy, immunofluorescence, and electron microscopy. The findings presented 2 variants of glomerular disease, but with similar clinical feature, manifested with proteinuria and edema, followed by the decrease of the renal function. The follow-up for several months presented well response on the therapy with corticosteroids and cyclosporine. After that period the patient with focal segmental glomerulosclerosis was stable with improvement of the renal function, but the patient with collapsing glomerulopathy as a variant of focal segmental glomerulosclerosis, had poor prognosis with progression of the disease to chronic renal failure.

Conclusion

We can say that SARS-CoV-2 associated renal disease has different outcome and follow up despite the treatment. The necessity for renal biopsy with extensive ultrastructural analysis as well molecular testing for COVID 19 positivity is obvious for diagnosis of the renal injury. That fact is important for the further follow up and treatment of these patients, after COVID 19 infection.

Conflict of interest statement. None declared.

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