

## Comment: Newly Diagnosed Glomerulonephritis During COVID-19 Infection Undergoing Immunosuppression Therapy, a Case Report

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We read with great interest the case report article by Moeinzadeh *et al*, entitled “newly diagnosed glomerulonephritis during COVID-19 infection undergoing immunosuppression therapy” published in a recent issue of IJKD.<sup>1</sup> The authors presented a case of a 25-year-old male with no known co-morbidities who presented with weakness and arthralgia to coronavirus clinic. Initial work up revealed severe anemia (hemoglobin [Hb] of 5.2 g/dL) and renal impairment (serum creatinine [SCr] of 3.7 mg/dL). He was admitted to the hospital, where further investigations showed worsening of renal function (SCr 4.2 mg/dL) with active urinary sediment and a further decline in Hb concentration (4.5 g/dL). High-resolution computed tomography (HRCT) of the chest demonstrated ground glass opacities (GGO) with a differential of diffuse alveolar hemorrhage and possible coronavirus infection. Patient received three days pulse of steroid [1 gram of Methylprednisolone/day] with presumed diagnosis of rapidly progressive Glomerulonephritis (RPGN). Serology and secondary work up were sent out and renal biopsy was obtained. The patient subsequently underwent plasmapheresis and three doses of intravenous immunoglobulin (IVIG), 20 g each time for alveolar hemorrhage. Renal biopsy was later reported as diffuse crescentic GN. Meanwhile, his coronavirus test was found to be positive and hydroxychloroquine in addition of levofloxacin was initiated.

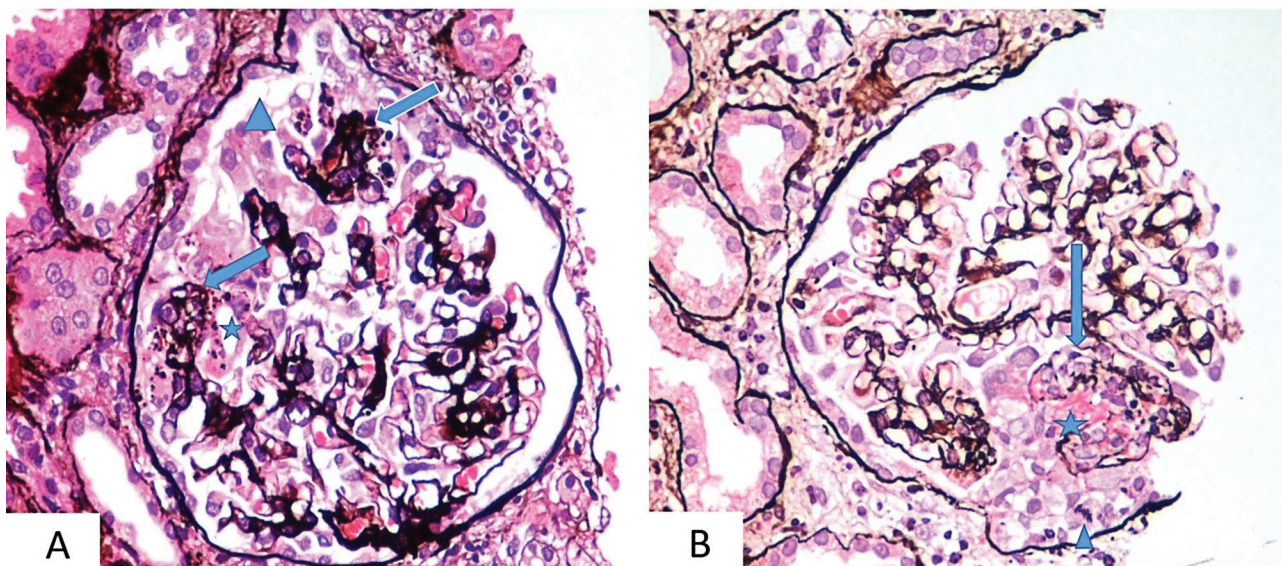
The above case adds yet another dimension to the expanding spectrum of renal pathological lesions seen in patients of COVID-19 disease, particularly one based on renal histopathology. We would like to take this opportunity to highlight some points pertaining to kidney involvement in COVID-19, in general, and in this particular case. Clarification of the following items by the authors will further improve the understanding of the kidney pathology in this disease.

- 1- The data of kidney involvement in COVID-19 infection has started to accumulate but the results are conflicting.<sup>2</sup> Renal involvement in COVID-19 is common and has been shown to correlate with in-hospital deaths.<sup>3</sup> However, biopsy based studies are scarce.<sup>4</sup> Most reports suggest tubulointerstitial involvement in this disease, but more recently, a number of case reports have reported glomerular involvement, particularly, collapsing glomerulopathy (CG), especially in persons of African ancestry.<sup>5-7</sup> This suggests a possible role of APOL1 high risk alleles in predisposing these patients to the development of CG in COVID-19 infection, and the viral illness serving as second-hit in its pathogenesis.<sup>8-10</sup>
- 2- The case presented by Moeinzadeh *et al* was diagnosed and treated in the lines of primary GN coexisting with COVID-19 infection. The patient was treated for both conditions and there is also some overlap in the treatment of COVID-19 disease and primary GN. The major cause of morbidity in this case, according to authors, seems to be autoantibody-mediated vasculitis, manifesting as pulmonary renal syndrome. However, lack of any respiratory symptoms with this degree of involvement in vasculitis is unusual. Regarding renal biopsy findings, it is important to note that renal biopsy was obtained on completion of induction treatment of RPGN and no detailed pathology description was given. The authors only provided representative images of one or two abnormal glomeruli. All the three images show segmental obliteration of capillary lumina with segmental collapse of capillary loops and associated florid extracapillary proliferation of cells, which appear to be visceral epithelial cells (podocytes). These cells either surround the segmentally sclerosed

tuft (with a cleft-like space between the parietal epithelial cell layer) or fill the urinary space resembling a cellular crescent (pseudo-crescent). There is focal vacuolization and a few hyaline droplets in the cytoplasm of some of these proliferating cells. No evidence of glomerular necrosis, such as influx of leukocytes, necrotic cell debris or accumulation of fibrin is visible. No immunofluorescence or electron microscopy findings are given. A right approach would have been to consider both pseudo-crescents and true crescents in the differential diagnosis. All the features noted above, in our view, favor pseudo-crescents and hence CG should have been considered in the differential. It is well known that sometimes it is difficult to differentiate among these two forms of extracapillary proliferative GN and this case represents one of those examples. We take the liberty to illustrate this point in Figure 1, where preliminary view shows striking homology between the two conditions; however, more critical review shows tangible differences between these. The authors could utilize some immunohistochemical markers or electron microscopic study to differentiate between the two. Additionally, other known causes of CG,

such as HIV status, parvovirus B19 infection, and others should be considered and clinically ruled out. If it turns out to be CG, this will be a significant finding as almost all previous cases of CG in association with COVID-19 infection have been reported in African Americans.

- 3- The results of the primary and many subsequent investigations were not correctly presented. His hemoglobin (Hb) is stated to be 5.2 g/L at presentation, which should be in g/dL. Similarly, SCr is given as 3.7 g/dL, which should be 3.7 mg/dL. C-reactive protein (CRP) is given as 2+, which is not a correct presentation of this result. Titer of c-ANCA given as 1/50 (positive) is incomprehensible. What method of ANCA testing was used?
- 4- The authors state that they discharged the patient with stable creatinine value of 5.5 mg/dl. With just one value of SCr, how can they claim that the function was stable, when all previous readings showed a continued rise?
- 5- The authors also did not establish definitive recovery from COVID-19 in this case according to Iran Ministry of Health and Medical Education COVID-19 guidelines. The reason put forward was the critical condition of the patient. This is



It shows morphological features of true crescent and pseudo-crescent. A) Medium-power view of a glomerulus showing collapse of two tufts with overlying podocyte hyperplasia and hypertrophy forming focal pseudocrescents over the involved tufts (arrows). Note: There are numerous protein resorption droplets in the cytoplasm of podocytes. These also show cytoplasmic vacuolization (asterisk). There is no fibrin or capillary wall rupture. Moreover, an irregular cleft-like space (arrowhead) separates this mass of proliferating podocytes from parietal epithelial layer (Jones silver stain,  $\times 200$ ). B) A glomerulus with focal true crescent formation (arrow). Note the rupture of capillary walls of the tuft at 5 O'clock position with exudation of fibrin into the Bowman's space and nuclear debris (asterisk). Note that the proliferating cells in the extracapillary space are originating from the parietal epithelium, which is showing a mitotic figure (arrowhead). There is no space between true crescent and parietal epithelium in this case. (Jones silver stain,  $\times 200$ ).

contradictory with their subsequent statement, in which, they claim that the patient was discharged healthy.

In summary, the authors need commendation on presenting the above case for increasing the awareness of nephrology and pathology community regarding expanding spectrum of pathological lesions in COVID-19 disease. We think this critique will further improve the understanding of many aspects of this interesting case.

### Competing interests

The authors declare that they have no competing interests.

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