Response to Comment on; Newly Diagnosed Glomerulonephritis During COVID-19 Infection Undergoing Immunosuppression Therapy, a Case Report

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Dear Editor,

I have read the article entitled "Comment on; Newly Diagnosed Glomerulonephritis During COVID-19 Infection Undergoing Immunosuppression Therapy, a Case Report." By Mubarak *et al.*, I want to congratulate the authors for this successful editorial letter, and make some contributions.

In this comment Mubarak *et al.* have been noted some point that we clarify them in the following:

1- Mubarak *et al.* mentioned that our case did not have any respiratory symptoms related to glomerulonephritis (GN), but it is notable that our case had diffuse alveolar hemorrhage in his computed tomography report and it could related to systemic vasculitis.[1]

2- It is a reality that differentiation between these two entities (crescent & pseudocrescent) can be very hard and challenging, but not in our case which reveals clear crescentic features of gloms in figures.

The term crescent is used for a lesion consisting of extracapillary hypercellularity, composed of a variable mixture of cells. Fibrin and fibrous matrix may be present; 10% or more of the circumference of Bowman's capsule should be involved.[2] In our case parietal epithelial cells show proliferation and make cellular crescent, although in some glom's podocyte hyperplasia is seen also and it's not in conflict with the diagnosis of crescentic GN.

True crescents and pseudocrescents even may coexist in the same glomerulus.[3]

The presence of fibrinoid necrosis, karyorrhexis, glomerular basement membrane rupture and red blood cell casts to be helpful indicators of crescent formation while the absence of these findings with the presence of protein resorption droplets admixed with the hypertrophied and hyperplastic podocytes, significant tubular intracytoplasmic protein resorption drops, microcystic tubular dilatation, thyroid type tubular atrophy and a predominance of solidified or disappearing-type global glomerulosclerosis suggests collapsing glomerulopathy.[4]

In contrast with your comment, there were no protein resorption droplets in our pictures and also cellular vacuolation was not specific for pseudocrescent formation.

The glomeruli in the case also show capsular rapture (Figure 1A), fibrinoid necrosis (Figure 1B), and karyorrhexis (Figure 1C); which define the diagnosis of crescentic GN.

Collapsing lesions are more commonly global than segmental and are often accompanied by severe tubulointerstitial injury with microcysts and hypertrophic tubular epithelial cells swollen.[5]

Many various IHC markers like CD68, CK, Nestin, CD44, WT1, and ki67 can be helpful in challenging case for differentiation between crescent and pseudo crescent,[3,4,6] but in this case the diagnosis was clear by morphology and IHC study just achieved for responding your comment and as expected, confirmed our diagnosis.

In collapsing glomerulopathy, hyperplastic podocytes showed complete loss of normal podocyte phenotype utilizing known markers of podocytes (CALLA, GLEPP1, Podocalyxin, Synaptopodin, WT1, P27, and p57) were decreased while Cyclin D1, Cyclin E, Cyclin A, Ki-67, Desmin, Cytokeratin, and CD68 were increased.[4,7]

We use the markers of cytokeratin, CD68, and Ki67 (Figure 2) and no accentuated staining compatible for hyperplastic podocytes was seen. Usually in true crescents, no cell expresses cytokeratin and numerous CD68-positive hyperplastic dysregulated podocytes in a glomerulus showing a pattern of collapsing GN.[3]

It should be mentioned that contrary to previous reports, podocytes are indeed involved in human