Response to comments on: Retinal vein occlusion in COVID 19: A novel entity

Dear Editor,

We thank the authors[1] for taking interest in our case report[2] and giving us an opportunity to clarify the fundamentals of diagnosing Uveitis and its associated spectrum of presentations.

Characterizing retinal vasculitis is a challenging task. It needs meticulous clinical evaluation and interpreting multimodal imaging based on recommendations laid down by the "Standardization of Uveitis Nomenclature Working group".[3] To quote from the 'Results of the First International Workshop of SUN', "Achieving consensus on which retinal vascular changes constituted retinal vasculitis was more problematic. Although the group provisionally agreed to consider perivascular sheathing and vascular leakage or occlusion on fluorescein angiogram as evidence of retinal vascular disease for the classification of retinal vasculitis, there was consensus that the definition of retinal vasculitis required more work".[3] Although the authors state that "vascular staining and posterior pole leak" as seen in our case can occur in retinal vein occlusions,[1] one important pointer towards an inflammatory etiology is the additional presence of leakage of optic disc and vessel wall in our patient.[2] Moreover, perivascular sheathing or cuffing has been reported in only around 64% of cases with retinal vasculitis.[4] Hence the notion of the authors that absence of perivascular exudates, cuffing or sheathing rules out vasculitis is incorrect. Furthermore, in occlusive retinal vasculitis secondary to other viral infections such as dengue and chikungunya, it is uncommon to see these clinical findings of perivascular exudations or sheathing.[5,6] Though retinal vasculitis in COVID-19 has not been described earlier, it may have similar pathogenesis as dengue and chikungunya viruses.

The authors correctly point out that COVID-19 related vasculopathy has been described in literature, including a solitary case of central retinal artery occlusion (CRAO).[7] We have reported a case of retinal vein occlusion (RVO) secondary to COVID-19 and its successful management, which has not been reported in literature.[2] Regarding the role of biomarker in COVID-19, a diverse range have been evaluated including C-reactive protein, D-Dimer, IL-6, platelet count, cardiac troponin, lactate dehydrogenase (LDH), white cell count (WCC) and so on.[8] Of these, the utility of CRP and D-Dimer levels is most useful for predicting clinical outcomes.[9] Additionally, CRP is the earliest biomarker to be elevated and studies have shown it to be more reliable than even computer tomography (CT) scan for earliest identification of disease severity.[10] Nonetheless, studies have shown these biomarkers to be normal in mild to moderate cases. In our case, D-dimer levels were not tested but the CRP levels were within normal limits, which has been mentioned in the case report.[2] This is suggestive of mild-moderate disease systemically, as evident by his discharge from the COVID hospital in stable condition three days prior to presenting for the retinal disease. With regards to the details of the patient's one-week course during hospital admission, we were unable to incorporate it in the original manuscript[2] due to paucity of word limit based on the journal guidelines. For the information of the readers, the patient was admitted for one week with symptoms of fever which was treated with oral paracetamol 500 mg QID. Additionally, he received supplementary medications in the form of vitamin C (2000 mg daily), vitamin D (5000 IU daily) and zinc (22 mg). His vitals, including heart rate, blood pressure and SPO2 levels remained stable throughout his hospital stay. There were no complications and he was discharge in stable condition at the end of one week.

The authors state that since there is absence of other features of systemic vasculitis, COVID-19 cannot be an etiology of RVO. In literature, cases of solitary involvement of a particular organ being affected by COVID-19 has been distinctly illustrated, including CRAO, Vestibular Neuritis and urticaria.[7,11,12] Hence it is not uncommon to have an isolated organ damage due to COVID-19 as seen in our case. Lastly, the authors claim that temporal association is unlikely a causative reason for vasculitic RVO. We have only claimed an association, which may or may not be causal. However, we cannot rule out causality and more cases need to be studied. Furthermore, we would like to inform the readers that ocular involvement such as retinitis/retinal pigment epithelitis/vasculitis/uveitis are common after viral fever.[13] Hence to question temporal association between COVID-19 and RVO within an interval of ten days, and in the absence of any other plausible etiology, is indeed surprising.

In the letter, the authors demonstrate ambiguity by initially pointing to a COVID-19 related vasculopathy rather than vasculitis as an etiology, and later refuting association with COVID-19 altogether.[1] It would be interesting to know the etiology which the authors propose for a case of retinal vasculitis developing within 10 days of a viral infection (COVID-19) with the best part of potential causative factors being ruled out.

We would like to conclude by highlighting key points:

1. Presence of vessel wall staining, with leakage at posterior pole, from the vessel walls and optic disc are important attributes of vasculitis.
2. Clinical findings such as perivascular sheathing, cuffing and exudates may not always be present in vasculitis; rather FFA is crucial to confirm retinal vasculitis.
3. It is not uncommon to observe posterior segment involvement post-viral fever; a temporal association is frequently noted after ruling out other common etiologies.
4. Whether the COVID-19 related vasculitic RVO is due to direct involvement of viral particles or secondary to an immune mediated thromboembolic event remains a conjecture, unless we perform a thorough histopathological evaluation.

We would like to reiterate to our colleagues and readers to view this case report from a broader perspective of the COVID-19 pandemic. Subsequent to this case, we have come across an expanding array of posterior segment involvement due to COVID-19 such as isolated retinal hemorrhages, optic neuritis, and third nerve palsy (Unpublished data). We have now included RT-PCR analysis for COVID-19 in workup protocol for all cases of young vasculitis, or other posterior uveitic/occlusive pathologies. Although much remains to be known about the COVID-19 virus and its ocular involvement, we are optimistic that our initial work in this area would encourage other researchers to undertake comprehensive studies in this field.

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Conflicts of interest

There are no conflicts of interest.

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