Retinal vasoocclusive spectrum following COVID-19

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The coagulation abnormalities and thromboembolic complications of coronavirus 2 (SARS-CoV-2) are now a well-established fact. The hypercoagulable state, the tendency for thromboembolism, and a cytokine surge state have been the exclusive reasons for multiorgan failure and other morbidities that have been regularly reported in COVID-19 patients. Ocular involvement in patients with active disease and those who have recovered is uncommon but not rare. We report a case series of four patients with CRVO, BRVO, CRAO, and vitreous hemorrhage in patients with proven COVID-19 infection and no other systemic ailments. The case series also tries to correlate the elevated D-dimer values, which signify a plausible prothrombotic state with the vaso-occlusive phenomenon in the retina leading to significant visual morbidity.

Key words: Branch retinal vein occlusion, central retinal artery occlusion, central retinal vein occlusion, COVID-19, vitreous hemorrhage

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The novel coronavirus pandemic, which laid its roots in December 2019, has become one of the most devastating pandemics in the history of mankind, having major social and economic implications in addition to the disastrous implications on healthcare.[1] Few months into the pandemic, reports of post-COVID-19 infection complications surfaced, which included thromboembolic phenomenon and cardiovascular events. The proposed etiology for the above implications has been excessive inflammation, platelet activation, endothelial dysfunction, and stasis. D-dimer value has been found to be a predictive factor for venous thromboembolism. We report a case series depicting a spectrum of retinal vascular occlusive manifestations in individuals that developed within a span of

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1 month post moderate to severe infection with COVID-19. The aim of our series is to highlight and raise awareness regarding the post-COVID-19 thromboembolic inflammatory state in otherwise healthy individuals leading to various retinal occlusive sequelae.

Cases have been described in Table 1.

Discussion

The COVID-19 pandemic came with a lot of challenges. With time, a lot of information has been discovered about the virus. However, a lot more is yet to be discovered. To add to the burden, there has been an increase in the number of people reporting other symptoms post recovery from COVID-19. These symptoms can be as vague as a mild persistent headache, muscle pain fatigue, persistent cough, and/or chest pain. In addition, life-threatening and long-lasting effects on vital organs such as the heart, brain, and lungs, leading to heart failure, breathing problems, Güillain–Barre syndrome, and stroke are been frequently reported.

Systemic thromboembolic events and cardiovascular complications post infection with the novel coronavirus have been largely reported across the world.[2,3] Various studies have found that myocardial involvement was seen in around 20%–30% of hospitalized patients of COVID-19 with a raised level of troponin. The incidence of these events was found to be higher in patients with moderate to severe infection.

It was postulated that intense inflammation; platelet activation, and endothelial dysfunction were causative in inciting these potentially fatal events.[4,5]

Until recently, the association of post-COVID-19 complications in eyes was limited largely to conjunctivitis, the one being the presenting complaint found in up to 31% in certain studies.[6] In a study, 9.5% of hospitalized COVID-19 patients exhibited ocular signs and symptoms,[7] but it was inferred that the factors that lead to severe or worsening of COVID-19 status were not associated with the development of ocular symptoms. However, in recent times, reports of vaso-occlusive retinal disease have been on the rise [Figs. 1-4].

We encountered four cases of retinal vascular diseases post moderate to severe COVID-19 infection. The age of these patients ranged from 32 to 81 years. Both genders were found to be affected. Interestingly, none of the patients had any systemic risk factors that could be associated with retinal disease. All four patients gave a history of moderate to severe COVID-19 infection and were hospitalized for the same. None of the patients was vaccinated. On evaluating the records of these patients, we inferred that the ocular symptoms usually developed within a month post recovery. Three out of four patients except for case 2 experienced sudden onset diminution of vision. Case 2 was not sure about the onset of vision loss as he was intubated.

At the start of the pandemic, studies showed the non-association of ocular symptoms with the inflammatory markers. As the pandemic continued, the ocular involvement spectrum of COVID-19 was not limited to conjunctivitis or watery eyes.[7] The ocular spectrum expanded from non-vision-threatening findings such as red eye or cotton wool spots and increased tortuosity of vessels in the retina to more visually debilitating scenarios such as optic neuritis,[8] vasculitis, retinal artery occlusion,[9] and retinal vein occlusion.[8] These were linked to cytokine storm, breakdown of the blood–retinal barrier, and direct inflammatory infiltration of the retina.[8]

Table 1: Case Summary

Case Number	1	2	3	4
Age	81	63	32	41
Sex	Female	Male	Male	Female
Chief complaint	DOV for 1 day	DOV	DOV for 14 days	DOV for 3 weeks
Systemic history	Asthma +	Nil	Nil	Nil
Duration since recovery post COVID-19 in days	15	21	21	21
Severity of COVID-19 infection	Severe	Severe	Moderate-Severe	Severe
History of ICU admission	Yes	Yes	No	Yes
D-dimer values	0.9	1.8	1.1	0.9
Serum ferritin	-	982	-	-
LDH	-	1200	-	-
Vision in the affected eye	HMCF	HMCF PR+	FC2M	3/60
Vision in the other eye	6/18	6/6	6/6	6/6
Anterior segment finding	Cataract Both eyes	Normal	Normal	Normal
Posterior segment finding	No view due to vitreous hemorrhage	Cherry-red macula	Flame-shaped hemorrhages Tortuous vessels in the supero-temporal quadrant CME NSD	Flame-shaped hemorrhages in all quadrants Tomato splash CME
Diagnosis	Vitreous hemorrhage [Fig. 1]	CRAO [Fig. 2]	BRVO [Fig. 3]	CRVO [Fig. 4]
Management	Conservative	HBOT	Intravitreal Anti-VEGF	Intravitreal Anti-VEGF
Investigations	USG: S/O VH	OCT: Marked CNP	OCT: CME NSD	OCT: CME

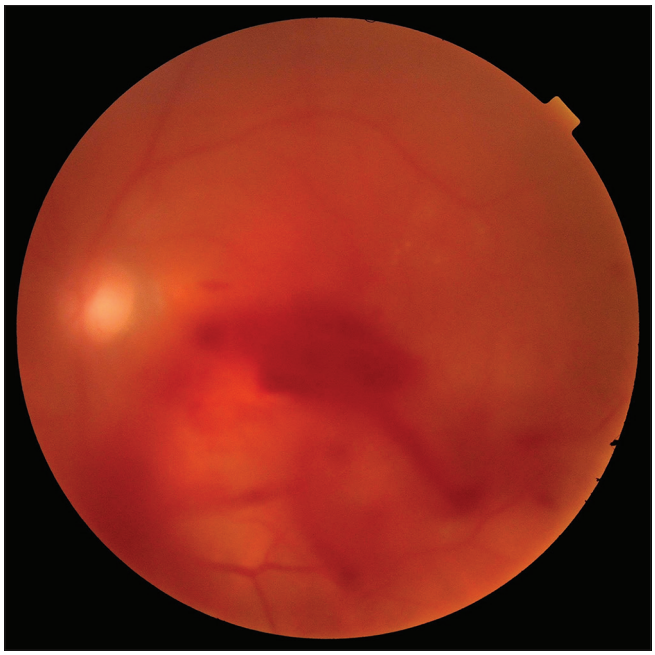

Figure 1: Color fundus photograph showing suspended vitreous hemorrhage

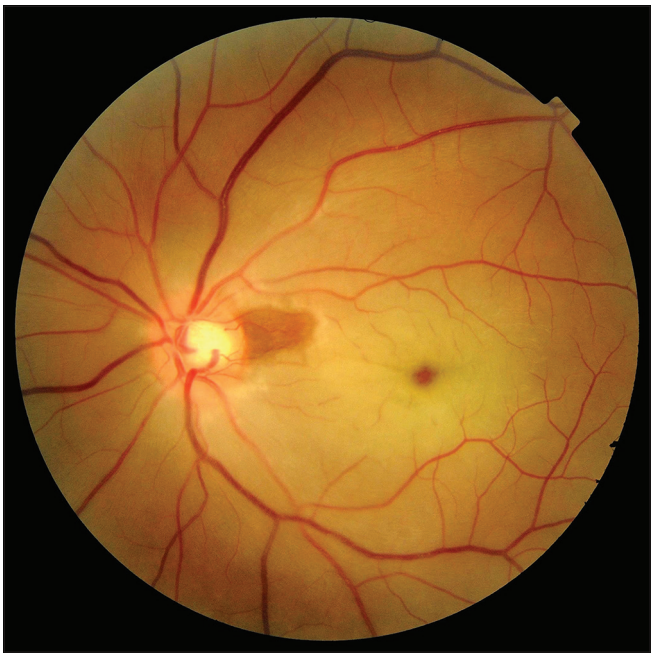

Figure 2: CRAO left eye showing retinal whitening with a cherry-red spot at the macula

Figure 3: BRVO left eye showing flame-shaped hemorrhages, dilated tortuous veins in the supero-temporal quadrant, and cystoid macular edema

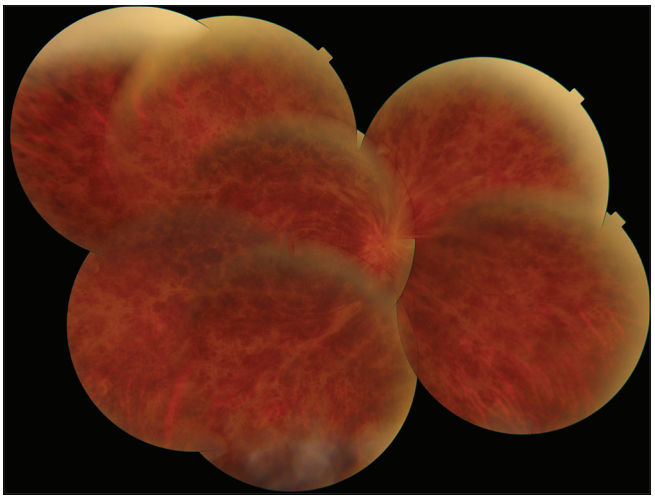

Figure 4: CRVO RE showing flame-shaped hemorrhages in all quadrants, giving a tomato splash appearance with cystoid macular edema

D-dimer is one of the end fragment products when fibrin is acted on by the plasmin enzyme. D-dimer is found to increase in patients with deep-vein thrombosis, arterial thrombosis, and disseminated intravascular coagulation. Its production is based on the degradation of fibrin or its production. After the emergence of COVID-19, D-dimer has been established as one of the inflammatory and prognostic biomarkers. The investigation records of our patients were suggestive of deranged inflammatory parameters. All four patients had a high D-dimer value, with the mean being 1.17 μg/mL. The patients were treated with intravenous antiviral, corticosteroids, and anticoagulants in addition to the supportive symptomatic treatment for their systemic manifestations of COVID-19.

Although the number of cases reported in our series is small, it is pertinent to highlight the strong association between the D-dimer levels and the retinal vaso-occlusion that were encountered. This series focuses on raising awareness regarding the ocular thromboembolic phenomenon, especially in patients who have been admitted in the intensive care unit. It is likely that the CRAO patient had an ocular embolic event while he was admitted in for severe COVID-19 infections and realized the ocular morbidity post discharge. There is a need for setting up a proper screening protocol for moderate to severe COVID-19 patients or patients who have elevated D-dimer levels so that the ocular embolic events can be recognized and managed at an early stage in a more efficient manner.

It is important to understand the need to screen out patients who are at risk of ocular comorbidities based on inflammatory biomarkers to prevent significant visual loss.

Conclusion

COVID-19 infection has been associated with delayed systemic complications associated with increased inflammatory tendency. This case series demonstrate ocular complications associated with this particular entity. A high level of suspicion and newer protocols for early screening of patients with severe COVID-19 infections may help curb this problem.

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Conflicts of interest

There are no conflicts of interest.

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