

Central retinal vein occlusion secondary to varicella zoster retinal vasculitis in an immunocompetent individual during the COVID-19 pandemic - A case report

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We report the occurrence of unilateral central retinal vein occlusion (CRVO) in a young yoga enthusiast who presented amidst the COVID-19 pandemic. Subtle signs of uveitis when systemically investigated revealed a multitude of causes, but ocular fluid polymerase chain reaction was positive for varicella

zoster virus (VZV). The prompt initiation of antivirals resulted in a good visual outcome. Our case describes the rare presentation of VZV retinal vasculitis as CRVO in a young healthy individual and highlights the importance of early antiviral therapy for favorable outcomes.

Key words: Central retinal vein occlusion, COVID-19, polymerase chain reaction, retinal vasculitis, varicella zoster virus infection, yoga

Ocular infection with varicella zoster virus (VZV) can have a varied presentation ranging from herpes zoster ophthalmicus to acute retinal necrosis (ARN) and progressive outer retinal necrosis.^[1] Central Retinal Vein Occlusion (CRVO) secondary to VZV is rare, with reports of occurrence in an individual with HIV infection^[2] and in elderly people with cardiovascular morbidity.^[3] It has also been reported in association with varicella zoster dermatitis.^[4,5] We describe the case of a young immunocompetent male who presented with features of CRVO but was detected to have an underlying retinal vasculitis due to VZV.

Case Report

A 23-year-old male from coastal Karnataka was referred as a case of CRVO in November 2020. He presented with a history of sudden onset rapidly worsening painless loss of vision in the right eye (RE) for 3 days. He denied a history of fever or skin

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lesions preceding the onset of visual complaints. He also gave us a history of practicing the yoga “headstand” pose (*Sirsasana*) regularly. Apart from having chickenpox 4 years earlier, his past medical history was unremarkable. On ocular examination, best-corrected visual acuity was 6/24, N8 in the (RE) and 6/6, N6 in the left eye (LE). Few fine keratic precipitates were noted with grade 2+ cells in the anterior chamber in the RE, which were absent the previous day when examined by the referring consultant. The pupillary reactions were normal in both eyes. Intraocular pressure measured by Goldmann applanation Tonometry was 14 and 18 mmHg in the RE and LE, respectively. The RE fundus revealed an edematous optic disc with dilated and tortuous retinal veins. There was extensive vascular sheathing with hemorrhages alongside the retinal vasculature [Fig. 1a]. On indirect ophthalmoscopy, grade 1 vitreous haze was noted and the peripheral retina showed few hemorrhages without retinitis or vascular sheathing. LE exam was unremarkable. Optical coherence tomography (OCT) in the RE showed features of macular edema and one focal perivascular area of disruption of the inner layers of the retina with shadowing, suggesting the possibility of evolving retinitis [Fig. 1b]. The OCT-angiography showed tortuous veins and areas of reduced perfusion in the superficial and deep capillary plexus with a well-maintained foveal avascular zone.

Initial investigations, including a complete blood picture and peripheral smear, were within normal limits. Serum Homocysteine was elevated [32 umol/L]. The subsequent signs of uveitis prompted an investigation into the possible inflammatory and infectious etiologies. His serology for HIV, Mantoux test, and Interferon Gamma Release Assay for Tuberculosis was negative. However, the Serum ACE level was elevated [96 U/L] and Toxoplasma IgG was positive.

An aqueous humor sample from the RE sent for polymerase chain reaction (PCR) [TaqMan Real-Time PCR probe] analysis was positive for VZV. Oral valacyclovir 1 gm thrice a day was initiated, with clinical improvement being noted in 3 days [Fig. 1c]. Subsequent therapy with oral prednisolone 60 mg once a day, topical ciprofloxacin (0.3% w/v), and dexamethasone (0.1% w/v) in tapering doses resulted in further improvement of signs, including a resolution of macular edema with the appearance of a macular star. After a total of 6 weeks of antiviral and steroid therapy, his best-corrected vision in the RE improved to 6/6, N6 with marked improvement in fundus findings, and was maintained till 3 months of follow-up [Fig. 1d].

Discussion

Our case presented a diagnostic dilemma with an unusual clinical picture and lab diagnoses. In the general healthy population, CRVO is more common than ARN.^[6,7] Hence, CRVO secondary to vasculitis due to viral retinitis may be easily missed in early cases. Moreover, with CRVO being described in patients performing yoga and in COVID-19 infection, other treatable infective causes are likely to be overlooked.

Shah *et al.*^[8] reported a case of central retinal vein occlusion following *sirsasana*, also called the “headstand” posture in yoga, which was regularly performed by our patient. However, unlike their report, the younger age, absence of history of previous thromboembolic phenomenon, and systemic co-morbid illnesses made this diagnosis less likely in him. The presentation in the backdrop of the prevailing pandemic also suggested the possibility of retinal vein occlusion due to COVID-19 itself.^[9] Our patient had denied any clinical symptoms or contact with an infected case to warrant the need for investigation of COVID-19,

Table 1: Summary of the various reports of Varicella zoster-induced Central retinal vein occlusion

Authors, Year	Age (y), Gender	Ocular presentation	Duration of complaints	Systemic disease	PCR for VZV from ocular fluid	Treatment	Outcome (Visual Acuity), recurrence
Biswas J <i>et al.</i> , ^[2] 2001	40, Male	(RE) CRVO	15 days	HIV, HZO	NA (Aqueous immunofluorescence for VZV negative)	Intravenous acyclovir, oral steroids	Poor (No PL), Nil
Kang S <i>et al.</i> , ^[4] 2001	54, Male	(LE) CRVO and CRAO Subsequently, (RE) Acute Retinal Necrosis	12 days	Varicella dermatitis on forehead 8 weeks earlier	NA (decreasing serum IgG titers against varicella zoster over 3 months)	Intravenous acyclovir, oral steroids, aspirin	Poor (Perception of Light)
Yeh S <i>et al.</i> , ^[3] 2012	66, Male	(LE) CRVO and CRAO	7 days	Coronary artery disease	Positive	Intravenous Aciclovir, Oral Valacyclovir, Intravitreal Foscarnet	Poor (No PL)
Bansal R <i>et al.</i> , ^[5] 2017	15, Male	(LE) CRVO and CRAO	15 hours	Varicella dermatitis	Negative	Intravenous and oral acyclovir; oral steroids	Poor (No PL)
Murdock J <i>et al.</i> , ^[12] 2017	58, Male	(RE) CRVO and CRAO; (LE) multiple BRVO	1 day	Chickenpox with systemic vasculitis	NA (serum IgM for VZV positive)	Intravenous Aciclovir, Intravenous and oral Steroids	Poor (PL, HM)
Sarpangala S <i>et al.</i> , 2021 [Present case]	23, Male	(RE) CRVO	3 days	Nil	Positive	Oral Valaciclovir, oral steroids	Good (6/6)

RE: Right eye; LE: Left eye; CRVO: Central Retinal Vein Occlusion; CRAO: Central Retinal Artery Occlusion; BRVO: Branch Retinal Vein Occlusion; HIV: Human Immunodeficiency virus; HZO: Herpes Zoster Ophthalmicus; NA: Not available; VZV: Varicella zoster virus; PL: Perception of Light; HM: Perception of Hand movements

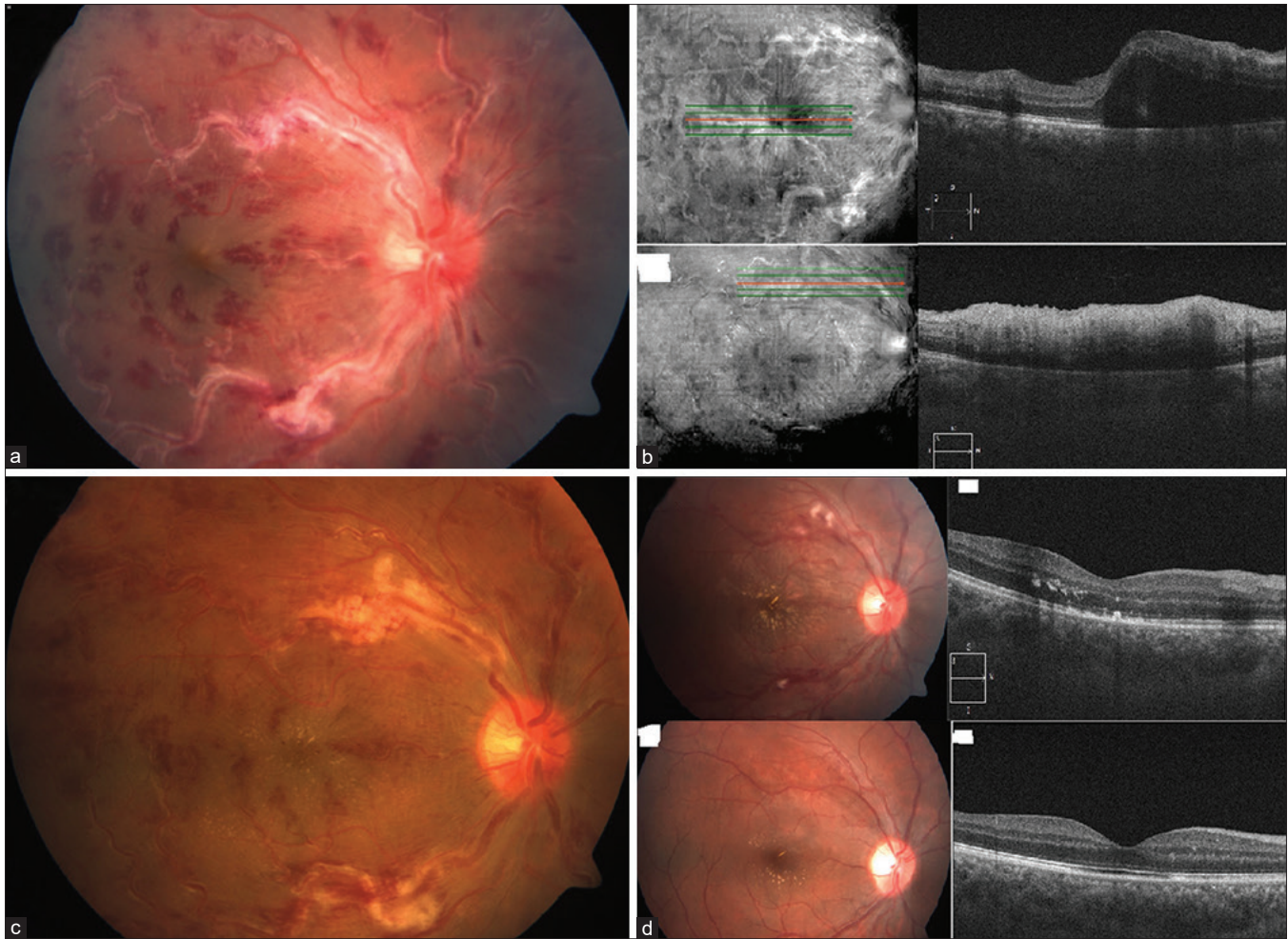


Figure 1: (a) Fundus photograph (FF) depicting dilated retinal veins with sheathing and hemorrhages, “frosted branch” appearance. (b) Optical Coherence tomography (OCT) on presentation showing macular edema and focal area of loss of demarcation of retinal inner layers with shadowing, suggestive of retinitis. (c) Resolving retinal vasculitis, 72 hours after initiation of oral valacyclovir, prior to starting oral steroids. (d) FF and OCT of macula during follow-up after 4 weeks and 3 months, showing resolution of retinal vasculitis and macular edema

which was bound by regulatory guidelines. However, subclinical SARS-CoV2 infection has been implicated in cases of Herpes zoster appearing during the pandemic.^[10] Among the inflammatory causes, Toxoplasmosis is a common cause of posterior uveitis in the young. Although serology revealed toxoplasma IgG to be positive, there was no evidence of active or old chorioretinitis suggestive of toxoplasmosis. Sarcoidosis is another important cause of retinal vasculitis. However, in our case, the absence of peripheral exudative vasculitis and choroiditis made the diagnosis less likely despite a raised serum ACE. Apart from the predominantly hemorrhagic form of vascular sheathing and an acute presentation, there were almost no clinically evident signs pointing toward Varicella zoster infection. The subtle OCT features of retinitis and the positive VZV DNA in PCR made it the most likely etiology. As vascular occlusion may precede ARN,^[3] antiviral therapy was the first line of management implemented. The favorable outcome of this early intervention further substantiates our diagnosis. Oral valacyclovir 1000 mg 8th hourly was started based on reports of its efficacy being nearly equal to intravenous acyclovir therapy in the treatment of ARN.^[11]

Varicella zoster has been implicated as a cause of CRVO due to retinitis, retinal vasculitis, and optic perineuritis [Table 1]. Our case had a better visual outcome than the other described

cases, probably due to isolated central retinal venous occlusion, without arterial involvement. Early identification of the causative organism, younger age of presentation, absence of comorbidities, and early initiation of antiviral therapy may also have contributed to the better outcome.

Conclusion

CRVO may be the initial presentation of varicella zoster-induced retinal vasculitis in a young immunocompetent individual. A strong clinical suspicion aided by ocular fluid analysis and early initiation of antiviral therapy can prevent progression to sight-threatening complications such as ARN.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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