

Case Report

Bilateral Simultaneous Central Retinal Vein Occlusion Secondary to COVID-19: A Case Report

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Keywords

COVID-19 · Central retinal vein occlusion · Thromboembolic complication

Abstract

Herein, we report a case of bilateral simultaneous central retinal vein occlusion (CRVO) secondary to coronavirus disease 2019 (COVID-19). A 48-year-old man, with hypertension, type 2 diabetes mellitus, and stage 4 chronic kidney disease, diagnosed with COVID-19 1 month ago presented to the ophthalmology department with blurred vision in both eyes for 2 weeks. Ocular examination revealed a classic clinical presentation of CRVO in both eyes. Optical coherence tomography revealed increased central macular thickness with intraretinal and subretinal fluid in both eyes. Laboratory data revealed elevated D-dimer and C-reactive protein (CRP) levels. The levels of other hypercoagulability markers were normal. The patient received intravitreal anti-vascular endothelial growth factor therapy in both eyes, followed by regular follow-up every month until complete resolution of symptoms and gradual improvement of the retinal vascular appearance. COVID-19 can cause a variety of coagulation abnormalities and thromboembolic complications such as bilateral simultaneous CRVO. Clinicians and patients should be aware of ocular symptoms and presentations that are probably associated with COVID-19.

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Introduction

Coronavirus disease 2019 (COVID-19) is caused by SARS-CoV-2 and has been declared a pandemic by the World Health Organization (WHO) on March 11, 2020 [1]. Pathogenesis of COVID-19 is not well understood, although there is increasing evidence that the virus causes

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excessive inflammation, endothelial dysfunction, and platelet activation, leading to coagulation abnormalities and thromboembolic complications [1, 2]. The most common clinical presentations of COVID-19 include fever, cough, dyspnea, and loss of taste and smell. Disease progression can result in septic shock, acute respiratory distress syndrome, and multi-organ failure [2].

To date, the known ocular manifestations associated with COVID-19 include conjunctivitis, uveitis, maculopathy, and optic neuropathy [3]. There are few reports regarding retinal vascular events secondary to COVID-19, such as central retinal artery occlusion, branch retinal vein occlusion, hemiretinal vein occlusion, and central retinal vein occlusion (CRVO) [3].

CRVO is a vision-threatening condition that predominantly occurs in older patients and usually results in unilateral vision loss. The development of CRVO is associated with age (90% of patients aged >50 years), hypertension, diabetes mellitus, hyperlipidemia, and glaucoma [4]. The occurrence of CRVO among individuals under 50 years of age is rare and is less than 1.5 cases per year in a single institution or 0.93 per 1,000 among individuals under 64 years of age [4, 5]. In a retrospective study, Chen et al. [5] have evaluated the risk factors for CRVO in young patients and found that some systemic diseases with hypercoagulable conditions, such as deep vein thrombosis, pulmonary embolism, antiphospholipid syndrome, antithrombin III deficiency, protein C and S deficiency, were significant risk factors associated with CRVO; however, hypertension and diabetes mellitus were not significant in young patients. Chen et al. [5] postulated that the atherosclerotic changes may be early, not clinically severe enough to result in significant total vein occlusion in young patients, although with time, progressive cumulative changes will cause CRVO in older patients. Patients with COVID-19 may have different coagulation abnormalities known as COVID-19-associated coagulopathy [6]. Therefore, the hypercoagulable state caused by COVID-19 should be associated with CRVO. Herein, we present a unique case of a 48-year-old patient who presented with simultaneous bilateral CRVO secondary to COVID-19 infection, possibly as a complication of COVID-19.

Case Report

A 48-year-old man diagnosed with COVID-19 1 month ago presented to the ophthalmology department with painless blurred vision in both eyes for approximately 2 weeks. He had 3 weeks of dry cough and musculoskeletal soreness, which ended about 2 weeks before the ocular symptoms. At the hospital, real-time reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 from a nasopharyngeal swab was performed again and was found to be positive with a cycle threshold value (Ct) of 32.25. He had underlying systemic diseases: hypertension, type 2 diabetes mellitus, and stage 4 chronic kidney disease that was under regular treatment and follow-up for several years. There was no personal or family history of thromboembolism. He had no history of ocular trauma or retinal diseases and had not undergone prior ocular surgeries. At initial evaluation, his best-corrected visual acuity was counting fingers at 1 m in both eyes. Intraocular pressure was normal. On slit-lamp examination, the anterior segment was normal in both eyes. Fundoscopic examination revealed diffuse flame-shaped retinal hemorrhage in all four quadrants, cotton-wool spots, dilatation, and tortuosity of all branches of the central retinal vein and macular edema (shown in Fig. 1). Optical coherence tomography of the macula showed increased central macular thickness (CMT) with intraretinal and subretinal fluids in both eyes (shown in Fig. 2).

Laboratory evaluation showed elevated D-dimer (1.05 mg/L) and C-reactive protein (CRP, 86.89 mg/L) levels. Other hypercoagulability markers such as prothrombin time (PT, 10.1 s), activated partial thromboplastin time (aPTT, 27.3 s), and international normalized

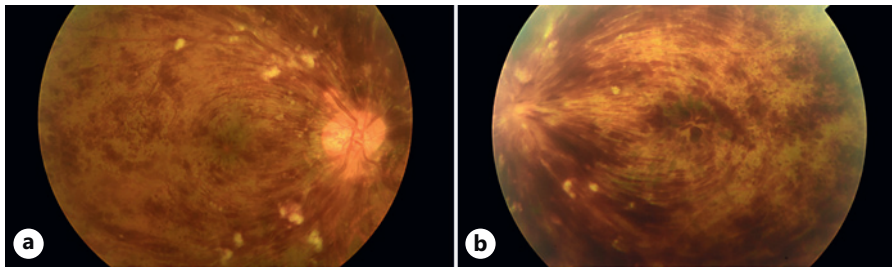


Fig. 1. Fundus photographs: right eye (a) and left eye (b). There is extensive retinal hemorrhage over all four quadrants, cotton-wool spots, tortuosity and dilatation of retinal vessels, and macular edema.

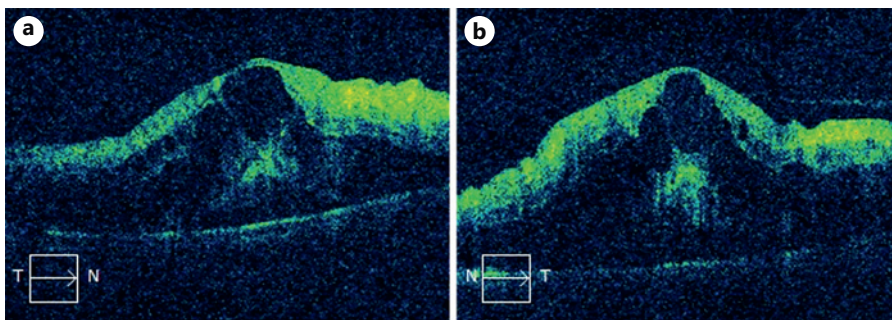


Fig. 2. Optical coherence tomography (OCT) for the macula showed increased central macular thickness (CMT) with intraretinal and subretinal fluid in both the right eye (a) and left eye (b).

ratio (INR, 1.01) were within the normal range. We also performed a systemic survey and found scattered embolic infarcts in the bilateral cerebral hemispheres on brain magnetic resonance imaging. Brain magnetic resonance imaging was performed because the patient had drowsiness, which occurred 2 weeks after the diagnosis of CRVO.

After the diagnosis of bilateral CRVO, the patient received intravitreal anti-vascular endothelial growth factor therapy in both eyes. After the treatment, CMT returned to normal range in both eyes (shown in Fig. 3). The patient underwent regular follow-ups every month until the complete resolution of symptoms and gradual improvement of the retinal vascular appearance.

Discussion

The prevalence of retinal vein occlusions in the developed world has been reported to be 5.2 per 1,000, and the prevalence of CRVO is 0.8 per 1,000 [4]. Similar to other thrombotic conditions, Virchow's triad (hypercoagulability, endothelial damage, and stasis) plays an important role in the pathogenesis of retinal vein occlusions [7]. Accordingly, both local and systemic conditions consisting of one of the three components should be considered risk factors for CRVO.

COVID-19 has been linked to hypercoagulability and thromboembolism that can lead to a variety of conditions involving almost all organ systems, including stroke, pulmonary embolism, deep venous thrombosis, and coronary thrombosis [8, 9]. Large- or small-vessel thrombotic events and abnormal coagulation tests can occur in up to 80% of patients with

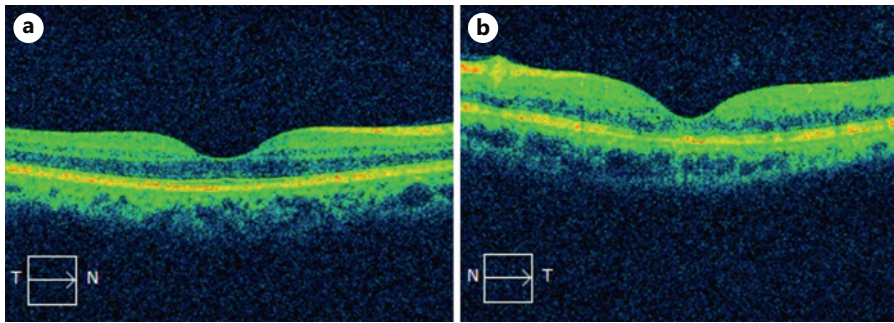


Fig. 3. Optical coherence tomography (OCT) for the macula showed central macular thickness (CMT) returned to normal range after receiving intravitreal anti-VEGF therapy in both the right eye (a) and left eye (b).

COVID-19 infection despite receiving treatment and are associated with a worse prognosis [8, 9]. Previous research shows COVID-19-related thrombotic syndrome is a unique thrombotic microangiopathy associated with viral invasion of cells expressing the angiotensin-converting enzyme 2 receptor as well as neighboring endothelial cells. This can trigger an excessive innate immune response with extensive activation of immune cells, the complement system, and proinflammatory cytokines [8]. Accordingly, COVID-19 may increase the risk of CRVO.

Ocular conditions associated with COVID-19 are relatively rare. More severe conditions related to retinal vessels, such as CRVO, has also been demonstrated, mainly as case reports [3]. There are speculations related to whether COVID-19 causes asymptomatic retinal capillary microvasculature changes. Szkodny et al. [10] did not detect significant differences between the recovered COVID-19 patients and healthy patients in terms of CMT or retinal nerve fiber layer (RNFL) thickness. However, Burgos-Blasco et al. [11] showed an increase in macular ganglion cell layer and peripapillary RNFL thickness in the recovered COVID-19 patients. In our case, significant increased CMT and peripapillary RNFL due to CRVO were detected at the first visit. After the treatment, both CMT and peripapillary RNFL returned to normal range.

Our patient had diabetes mellitus and hypertension, which are the traditional risk factors for the development of CRVO; however, in a study evaluating 10 CRVO patients with COVID-19 infection, the risk of acquiring CRVO secondary to COVID-19 persisted irrespective of age or the presence of traditional risk factors [12]. The ocular findings and symptoms in patients with CRVO secondary to COVID-19 are similar to those in patients with CRVO caused by other etiologies [12]. Our patient had classic ocular manifestations of CRVO, including extensive retinal hemorrhage over all four quadrants, cotton-wool spots, tortuosity and dilatation of the retinal vessels, and macular edema.

Elevated inflammatory markers and D-dimer levels have been found in 60% of patients with CRVO secondary to COVID-19 infection [12]. In our patient, laboratory data showed increased CRP and D-dimer levels, which indicated an increased risk of thrombosis, leading to CRVO. The patient's brain embolic infarcts should result from the same etiology as CRVO.

The prevalence rate of bilateral CRVO has been reported to be 0.41–7.7% of all CRVO cases [13]. Limited studies are reporting “bilateral” CRVO secondary to COVID-19 [14, 15]; however, we report a rare case of simultaneous bilateral CRVO secondary to COVID-19.

In conclusion, irrespective of the traditional risk factors, hypercoagulability associated with COVID-19 should be considered a factor in the development of CRVO. COVID-19 can cause various coagulation abnormalities and thromboembolic complications, such as simultaneous bilateral CRVO in our patient. Clinicians and patients should be aware of ocular

symptoms and presentations that are probably associated with COVID-19. The CARE Checklist has been completed by the author for this case report and is attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000529298).

Statement of Ethics

This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines. This report does not contain any personal information that could lead to the identification of the patient. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. The patient has consented to the submission of the case report to the journal.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Chien-Hung Lin conceived the study, analyzed the data, drafted, and revised the manuscript. I-Ting Sun reviewed and approved the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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