



Case Report

Coronavirus Disease 2019 (COVID-19)- Associated central retinal vein occlusion: A case report and literature review

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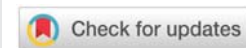
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Abstract

Coronavirus Disease 2019 (COVID-19) is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) that is associated with several inflammatory and vascular endothelial complications. Ocular vascular occlusive events were reported in COVID-19 patients including both Central Retinal Vein Occlusion (CRVO) and Central Retinal Artery Occlusion (CRAO). We report a case of a 34-years-old patient with right CRVO after 14 days of COVID-19 infection presenting with decreased vision. In addition, we provide a summary of both CRVO and CRAO reported in the literature.

Introduction

Late in December 2019, a novel coronavirus was identified to be responsible for unidentified pneumonia outbreaks and sporadic human infections. The virus was labeled as SARS-CoV-2 causing COVID-19 which was declared by the World Health Organization (WHO) as a pandemic in March 2020 affecting millions of people worldwide [1]. COVID-19 has been associated with different types of complications mainly vascular in nature where retinal occlusive vascular events, both venous and arterial were described and reported [2].

In this manuscript, we describe a case of central retinal vein occlusion in a 34-year-old male in the settings of COVID-19 infection. In addition, we review and summarize the reported cases of COVID-19 associated retinal occlusive vascular events in the literature.

Case report

A 34-year-old male with type 1 diabetes mellitus since the

age of 8 years on exogenous insulin, currently 55 International units (IU)/day, with controlled Hemoglobin bA1c and no previous ocular history (no previous diabetic retinopathy on previous ocular exams) developed fever and cough and tested positive for SARS-CoV-2 by Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) assay with mild pneumonia on chest imaging. The patient blood glucose level remained stable and well-controlled on the same insulin dose without the need for any changes. His symptoms were very mild for which he received only supportive treatment until symptoms resolved. Two weeks following the positive test, the patient presented with sudden decreased visual acuity and distorted vision in the right eye. In the clinic, his visual acuity was 20/20 in both eyes and the right and left intraocular pressures were 19 mmHg and 18mmHg respectively. Slit-lamp examination of the anterior segment was normal bilaterally. Similarly, dilated fundus examination of the left eye was unremarkable. However, the fundus of the right eye showed diffuse intraretinal hemorrhages, retinal vein tortuosity and dilatation

typical for (CRVO), but no evidence of macular edema. Optical Coherence Tomography (OCT) of the right eye was normal with a central retinal thickness of 247 μ m (Figure 1). Optical Coherence Tomography Angiography (OCTA) was done and showed no neovascularization (Figure 2).

Diagnostic workup blood pressure, complete blood count, lipid panel, Hemoglobin bA1c, glucose level, C-reactive protein, erythrocyte sedimentation rate, anti-cardiolipin, lupus anti-coagulant, B2 glycoprotein 1 IgM and IgG antibodies, homocysteine and thrombophilia panel were unremarkable. The patient has no family history of thrombophilia and thrombosis. Based on what as mentioned above the patient was diagnosed with right central retinal vein occlusion and was followed up with monitoring. One month later, he reported worsening of his decrease in vision in the right eye with visual acuity of 20/25 and his repeat OCT showed the appearance of Cystoid Macular Edema (CME) with associated mild subretinal fluid (Figure 3) for which he was started on intravitreal antivascular endothelial growth factor (anti-VEGF) injections of aflibercept. One a month after the initiation of the injection, his visual acuity improved in the right eye to 20/20, and his OCT showed resolution of the macular edema (Figure 4).

Discussion

Retinal vein occlusion is a retinal vascular condition characterized clinically by engorgement, dilatation and tortuosity of retinal blood vessels that can progress if not treated into macular edema, intra-retinal bleedings, ischemic retinal areas, optic disc swelling, and reduced visual acuity.

Several medical conditions including hypertension, diabetes, vasculitis, and thrombophilia are the most common factors to be associated with retinal vascular events [3]. COVID-19-associated coagulopathy and hypercoagulability have been documented and investigated since the onset of the pandemic, demonstrating hallmark diffuse small vessel thrombosis and vascular endothelial lesions induced mainly by inflammation [4].

Hypercoagulability is a major risk factor for CRVO and it is essential to rule out other causes of CRVO in an otherwise healthy

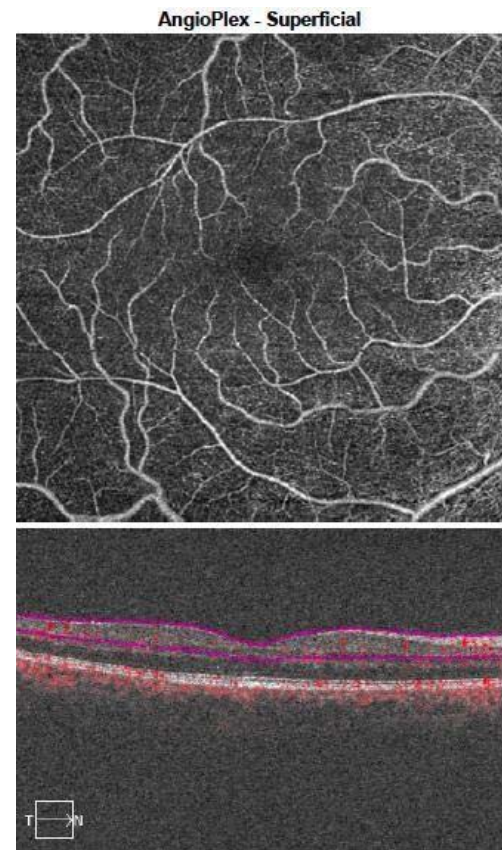


Figure 2: Right eye OCTA on presentation.

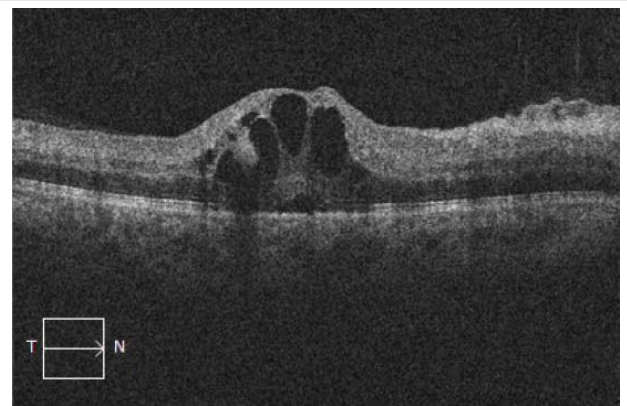


Figure 3: Right eye OCT after 1 month of presentation.

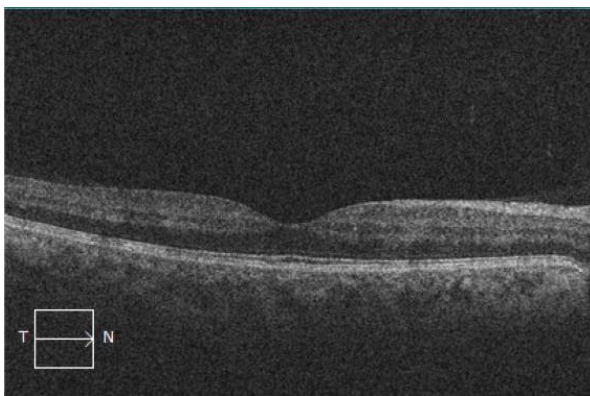


Figure 1: Right eye OCT on presentation.

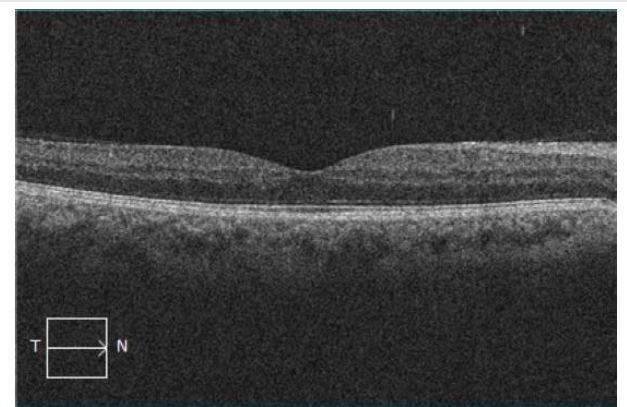


Figure 4: Right eye OCT 1 month after intravitreal injection treatment.



patient. Our patient is young and his diabetes is well controlled, with negative hypercoagulable studies which are similar to many of the reported cases in the literature [5]. In addition, it was shown that COVID-19 can cause a hyperinflammatory state that induces an increased risk of Venous Thromboembolism (VTE) in different sites and organs. However, the accurate mechanism is still not fully understood [4]. COVID-19 is believed to induce CRVO through either a VTE or by promoting retinal vasculitis secondary to thrombo-inflammatory cascade due to a cytokine-storm immune response through the excessive secretions of cytokines and chemokines by antigen-presenting cells and T-cells. Both mechanisms can lead to endothelial cell dysfunction and breakdown in the inner blood-retinal barrier leading to the development of macular edema due to increased capillary permeability [6]. Macular edema secondary to CRVO has been treated with different modalities in the literature. The use of intraocular steroids, systemic steroids and even antiplatelet medications were reported. However, as in our case, the most common treatment that is currently used is via blocking intraocular VEGF by injecting intravitreal anti-VEGF agents such as aflibercept, bevacizumab or ranibizumab [6,7].

Reviewing the literature, we found multiple articles reporting cases of COVID-19-associated CRVO; however, only 8 cases reported documented CRVO, 5 of whom are males and 3 are females with a period of time between COVID-19 symptoms and ocular symptoms ranging from 5 to 21 days except for one case of 60 days by Sanchez, et al. and an unknown period by Venkatesh, et al. as shown in (Table 1). Moreover, the first possible case of COVID-19 vaccine-induced non-ischemic CRVO was reported [8].

CRVO was not the only ocular vascular event in COVID-19, where central retinal artery occlusion (CRAO) was also

documented in the settings of COVID-19 infection. CRAO is an ophthalmic an emergency that resembles myocardial infarctions to cardiologists and strokes to neurologists where the outcome can be a permanent vision loss [9]. CRAO was correlated with the predisposition to arterial thrombosis where the inflammatory state in COVID-19 induced changes in homeostasis leading to thrombotic disease in the arterial system as well as in the venous circulation [10].

Moreover, the available treatments of CRAO and their efficacies are still controversial and they include the use of thrombolytic agents and maneuvers such as ocular massage, use of intraocular hypotensive agents and anterior chamber paracentesis to dislodge the blood clot [9]. While a significant visual improvement is expected and observed with CRVO post-treatment, the visual recovery after CRAO is often very poor due to the lack of a definitive therapy [11]. Six cases of COVID-19-associated CRAO were reported and are summarized in (Table 2).

Conclusion

We present this interesting case of COVID-19-associated CRVO in order to shed the light on one of the emerging vascular complications of this disease. It was shown that COVID-19 infection can affect the vascularity of any organ through its hypercoagulability and hyperinflammatory state. In addition, we discussed the presence of CRAO and the current possible treatments of both entities.

This helps the physicians dealing with COVID-19 patients to manage complications and to follow up closely on any ocular manifestations based on the reported durations for early diagnosis and appropriate management leading to better outcomes.

Table 1: Reported cases of COVID-19 associated Central Retinal Vein Occlusion.

1	Sheth, et al. [5]	52/M	None	Sudden painless decreased vision in the left eye	Inferior hemiretinal vein occlusion with superonasal branch retinal vein occlusion	10 days
2	Gaba, et al. [3]	40/M	Hypertension Morbid Obesity	Painless blurred vision bilaterally but worse in the Left eye	Bilateral central retinal vein occlusion	5 days
3	Raval, et al. [4]	39/M	None	Decreased vision and floaters in the Right eye	Right central retinal vein occlusion	8 days
4	Cuadros Sanchez, et al. [2]	32/M	None	5-days photopsia, in the Right eye with blurred vision and cephalaea	Right central retinal vein occlusion	60 days
5	Venkatesh et al. [6]	56/F	Diabetes type 2	Decreased vision in Left eye	Left central retinal vein occlusion	Unknown
6	Walinjkar, et al. [12]	17/F	Polycystic Ovaries	Decreased vision in Right eye	Right central retinal vein occlusion	21 days
7	Yahalomi, et al. [13]	33/M	None	Blurred vision in Left eye with flashes of light	Left central retinal vein occlusion	14 days
8	Rego Lorca, et al. [14]	30/F	Maturity-Onset Diabetes of the Young	Bilateral blurred vision and Myodesopsias	Bilateral central retinal vein occlusion	14 days
9	Current case	34/M	Diabetes type 1	Sudden decreased vision and distorted vision in the Right eye	Right central retinal vein occlusion	14 days

**Table 2:** Reported cases of COVID-19 associated Central Retinal Artery Occlusion.

Case No.	Author(s)	Age	Medical History	Symptoms	Diagnosis	Duration
1	Montesel, et al. [10]	59/M	Hypertension Hyperuricemia	Sudden painless vision loss in the left eye	Left central retinal artery occlusion	22 days
2	Acharya, et al. [9]	60/M	Hypertension Dyslipidemia CAD, COPD	Sudden painless vision loss in the Right eye	Right central retinal artery occlusion	12 days
3	Alam, et al. [15]	59/M	Hypertension	Sudden painless vision loss in the Right eye	Right central retinal artery occlusion	-
4	Bapaye, et al. [16]	42/M	None	Sudden painless vision loss in Both eyes	Bilateral central retinal artery occlusion	13 days
5	Larochelle, et al. [17]	68/M	Atrial Fibrillation Cirrhosis Hypertension	Profound vision loss in the Right eye with eye movements abnormalities	Right central retinal artery occlusion	4 days
6	Ucar, et al. [11]	54/M	None	Sudden painless vision loss in the Right eye	Right central retinal artery occlusion	21 days

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