

Central Retinal Vein Occlusion as a Post COVID-19 Complication

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Abstract

Purpose: To present an interesting case report of a healthy 34-year old female who presented to our ophthalmology clinic with unilateral non ischemic central retinal vein occlusion, two months after she was tested positive for SARS-CoV-2.

Case Presentation: We present a 34-y old female who was referred to our ophthalmology clinic with blurred vision in her right eye, without other systemic symptoms. She was diagnosed as COVID-19 two months before onset of her visual symptoms. Further investigation ruled out any medical disease or any other known etiological factor related to hypercoagulable state.

Results: During eye examination BCVA was 6/6 on both eyes. The anterior segment was without pathological changes, normal pupillary light reflex and intraocular pressure. On fundus examination, the right eye showed presence of dot-blot and flame-shaped hemorrhages in all quadrants, dilated and tortuous veins and mild swollen optic disc. Fluorescein angiography showed delay in arteriovenous transit time, perivenous fluorescein staining of dilated tortuous veins and retinal hemorrhages were masking the retinal capillary bed, confirming non ischemic central retinal vein occlusion. OCT imaging did not show macular edema and therefore the patient was only observed.

Conclusion: The hypercoagulable state induced by COVID-19 may be associated with CRVO. This may implicate awaring of COVID-19 related thromboembolic phenomena as a cause of CRVO. We hope that our case report that illustrate CRVO as a complication of COVID-19 will allow us to increase more our knowledge about various possible ocular manifestations of COVID-19 disease. Further studies and case reports should be reported to better understand the connectivity between Covid-19 and retinal vascular diseases.

Keywords: Ocular Manifestations of Covid-19; Central Retinal Vein Occlusion; Sars-Cov-2

Abbreviations

ACE: Angiotensin Converted Enzyme; BCVA: Best Corrected Visual Acuity; BRVO: Branch Retinal Vein Occlusion; CRVO: Central Retinal Vein Occlusion; DIC: Disseminated Intravascular Coagulation; COVID-19: Coronavirus Disease 2019; OCT: Optical Coherence Tomography; PT: Prothrombin Time; RPE: Retinal Pigmented Epithelium

Introduction

The World Health Organization (WHO) has declared that COVID-19 infection, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as a pandemic disease since March 2020 [1]. Universally, as of 12 November 2021, there have been more than 250 million affirmed cases of COVID-19, including more than 5 million passings, detailed to WHO [2]. Patients with COVID-19 have varying degrees of symptoms. They may be asymptomatic or experience fever, body aches, myalgia and generalized fatigue, headache and dry cough. Severe symptomatic cases have pneumonia and severe dyspnea which require hospitalization and intensive care. The less frequent manifestations include tastelessness, diarrhea, hemoptysis, rhinorrhea, liver and kidney damage, nausea, and vomiting. SARS-CoV-2 has an incubation period from 2 to 14 days in symptomatic cases [3]. The disease severity and progression depends mainly on the cellular immune responses to the viral antigens and the inflammatory cytokine storm evident in recent studies [4]. Critically ill patients with high mortality rate have been referred to coagulopathy and disseminated intravascular coagulation (DIC) as a serious complication of COVID-19 infection [5]. COVID-19 may lead to thromboembolic vascular events due to severe inflammation, endothelial dysfunction, platelet activation, and stasis [6]. Various ocular manifestations have been noticed in patients with COVID-19. This includes conjunctivitis, retinal microvascular changes such as retinal microangiopathy, cotton wool spots, retinal vascular tortuosity and microhaemorrhages, acute middle maculopathy and less commonly Papillophlebitis and acute macular neuroretinopathy [7]. Retinal vein occlusion is reported as one of the vascular complications of COVID-19 infection. The severity of the disease is not related to the incidence of vein occlusion among COVID-19 patients. Elevated D-dimer, fibrinogen, cytokines, prothrombin time (PT) and activated partial thromboplastin time (aPTT) promotes the coagulation in the circulation of COVID-19 Patients even in healthy young adults with no chronic diseases [7]. Retinal vein occlusion is a common cause of visual impairment in the elderly population with commonly associated arteriosclerotic diseases [8]. The rate of CRVO has been reported to be less than 1.5 cases/year at a single organization [9]. The most commonly associated medical condition with CRVO in young adults has been found to be dyslipidemia [10].

Case Report

In our article we present a 34-y old female who was referred to our ophthalmology clinic with blurred vision in her right eye, without other systemic symptoms. She was diagnosed as COVID-19 two months before the onset of her visual symptoms. Further investigation ruled out any medical disease or any other known etiological factor related to hypercoagulable state. Complete blood analysis were done, including risk factors for hypercoagulability and we found relative lymphopenia, increased C-reactive protein and high erythrocyte sedimentation rate. We also evaluated D-dimer that in our case was within normal limits.

During eye examination BCVA was 6/6 on both eyes. During examination the anterior segment was without pathological changes, normal pupillary light reflex and intraocular pressure.

On fundus examination, the right eye showed presence of dot-blot and flame-shaped hemorrhages in all quadrants, dilated and tortuous veins and mild swollen optic disc (Figure 1). Fluorescein angiography showed delay in arteriovenous transit time, perivenous fluorescein staining of dilated tortuous veins and retinal hemorrhages were masking the retinal capillary bed, confirming non ischemic central retinal vein occlusion (Figure 2). OCT imaging did not show macular edema and therefore the patient was only observed (Figure 3).



Figure 1: Fundus photography of the left eye showing presence of dot-blot and flame-shaped hemorrhages in all quadrants, dilated and tortuous veins and mild swollen optic disc.

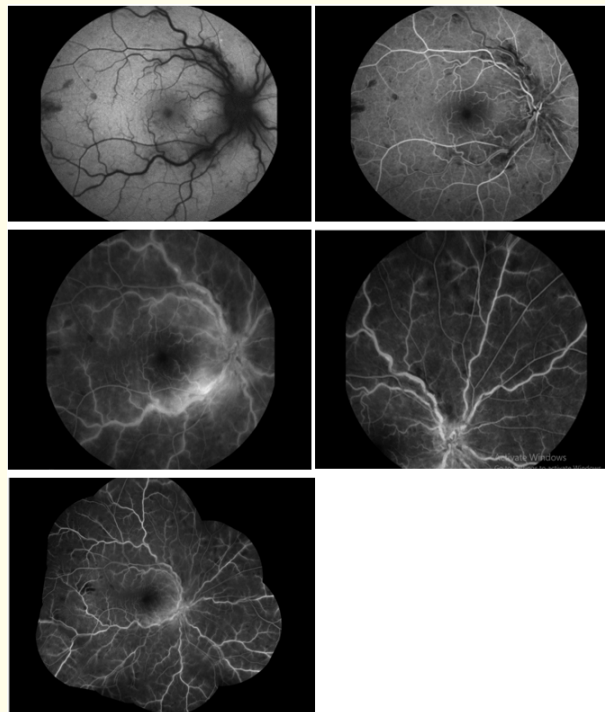


Figure 2: Fluorescein angiography showed delay in arteriovenous transit time, perivenous fluorescein staining of dilated tortuous veins and retinal hemorrhages were masking the retinal capillary bed.

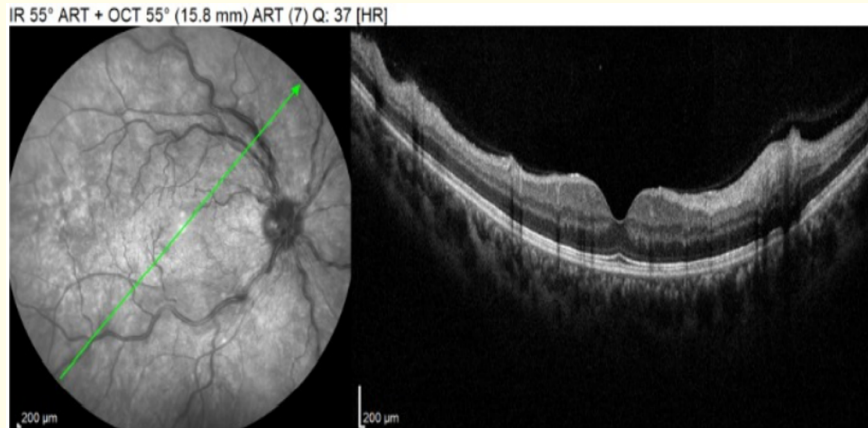


Figure 3: Optical coherence tomography (OCT) of the macula within normal limits.

The patient was followed-up monthly till complete resolution of symptoms and gradually improvement of the retinal vascular appearance.

Discussion

The rapid development of the Coronavirus disease 2019 (COVID-19) pandemic has faced the world with significant challenges, especially healthcare professionals around the world [11]. Changes in immune and coagulation systems and possible viral spread through the blood–brain barrier have been described in SARS-2 infection [2].

Clinical ocular manifestations in patients with Covid-19, particularly retinal involvement, indicate that retinal involvement is not a coincidence but rather a consequence of disease. COVID-19 can cause significant changes in the retina, mainly as a result of blood coagulation disorders or inflammation affecting the blood vessels of the retina as well as its layers [12]. Such clinical changes are directly related to the severity of the disease. But the authors cannot determine whether such changes are a direct response to the virus or an immune response of the host [13].

In Covid-19 patients the most important event is endothelial damage and thromboembolic events affecting different body organs [14].

A recent paper by Zhang, *et al.* [15] showed that responsible in the pathogenesis of damage of the blood vessels in patients with COVID-19 is complement-mediated thrombotic microangiopathy (TMA) that damages the endothelium of the retinal blood veins resulting in their closure. Immunohistochemical analyzes have confirmed the presence of ACE receptors in the ciliary body, choroid, retina and retinal pigment epithelium (RPE) [16]. Because COVID-19 can attack vascular pericytes that express ACE-2 receptors, viral infection can lead to complement-mediated endothelial dysfunction, vascular damage, and thus involvement of ocular microcirculation [17].

Mostly retinal findings in patients with COVID-19 published last year were retinal microhaemorrhages, cotton wools-like lesions, dilated veins and tortuous vessels as well as inner retinal OCT hyperreflective spots [18], probably as common signs of retinal microvasculopathy [19].

Also, in patients with COVID-19, 30 days after the onset of infectious symptoms was found that the blood vessels of the retina, both arteries and veins had a larger diameter than in persons not exposed to COVID-19. In addition, in the most severe clinical cases, the retinal veins showed more dilatation indicating an association with the time to onset of disease symptoms [20]. Therefore, retinal vein diameter can be an important parameter to assess the inflammatory response and vascular endothelial damage in COVID-19, as well as for the management of COVID-19 complications.

Using optical coherence tomography (OCT) the authors also described subtle retinal changes in the inner layers of retina like hyper-reflective lesions, cotton-wool spots, as well microhemorrhages have also been reported [21].

Marinho, *et al.* analyzing OCT also reported retinal findings in post COVID-19 patients, possibly associated with COVID-19 infection as hyperreflective lesions at the level of the ganglion cell and inner plexiform layers of the retina or signs of cotton wool exudates and microhaemorrhages along the retinal vascular arcade [22]. No signs of intraocular inflammation were detected.

No clear conclusion can be reached whether these changes in the retina are due to COVID-19 or just a random findings. The authors did not find a clear correlation between the presence of these retinal signs and concomitant diseases, but it is possible that the inflammatory response induced by this infection or the treatment of the disease may had a stronger effect in patients with an already fragile microvasculature. due to their basic conditions.

In many viral retinal diseases that affect the retina can occur many pathologic alterations of the retina due to a direct effect of the virus on retinal neurons [23] or secondary when the virus damages the endothelium like in HIV retinopathy [24]. SARS-CoV-2 is able to infect endothelial cells of blood vessels [25] and also has been detected in the blood vessels of the retina [1]. In fact it is important evaluating of the fundus in all COVID-19 patients, to can find the correlation between these retinal signs and presence of COVID-19.

Coagulopathy disorders and disseminated intravascular coagulation (DIC) have been considered as important complications of severe COVID-19 and also may be regarded as the most common causes of death [26]. COVID-19 patients may be predisposed to thromboembolic events, both in the arterial and venous blood vessels, due to excessive inflammation, endothelial dysfunction, platelet aggregation, and stasis [26].

Two main possible mechanisms may explain vascular damage in COVID-19 disease, firstly a pseudo-vasculitis condition as a result of a viral infiltration of endothelial cells and secondly, a hypercoagulable condition, characterized by a disseminated intravascular coagulation-like (DIC-like) [27]. These mechanisms may explain the association between the impact of COVID-19 disease on retinal circulation and the occurrence of retinal vascular diseases such as BRVO or CRVO presented in our case.

Blood coagulation disorders have also been reported in patients with COVID-19, especially in those with severe disease. Studies conducted in China showed elevated D-dimer in 46,4% of covid patients which was pronounced more in severe cases [28].

Another retrospective study in China showed elevated D-dimer levels, prothrombin time (PT) and partial thromboplastin time prolongation levels that were higher on admission among patients requiring ICU support [29].

Conclusion

The hypercoagulable state induced by COVID-19 may be associated with CRVO. This may implicate awaring of COVID-19 related thromboembolic events as a cause of CRVO.

We hope that our case report that illustrate CRVO as a complication of COVID-19 will allow us to increase more our knowledge about various possible ocular manifestations of COVID-19 disease. Further studies and case reports should be reported to better understand the connectivity between Covid-19 and retinal vascular diseases.

Conflict of Interest

Authors have no financial interest.

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