



Ocular Venous Thrombosis as the Main Manifestation of an Otherwise Pauci-Symptomatic COVID-19

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Abstract

The clinical impact of SARS-CoV-2-induced disease (COVID-19) recognizes different severity in adults. SARS-CoV-2 infection also involves the eyes, and acute conjunctivitis represents the most frequently ocular manifestation currently reported. We present a clinical case of ocular venous thrombosis observed in a healthy woman affected with a pauci-symptomatic COVID-19, occurred during the pandemic peak. SARS-CoV-2 infection was confirmed by nasopharyngeal swab and IgG serology. Further to acute conjunctivitis, venous thrombotic events should be included in the list of possible ocular COVID-19 manifestations. COVID-19 -induced viral tissue damage, hypercoagulability, and dysregulation of immune response likely represent the main pathogenetic determinants of this severe ocular complication.

Keywords: COVID-19; Atypical manifestations; Eyes; Conjunctivitis; Ocular venous thrombosis

Introduction

SARS-CoV-2 is a zoonotic RNA beta coronavirus rapidly spreading all over the World and causing a pandemic [1,2]. The clinical impact of SARS-CoV-2-induced disease (COVID-19) has different severity in adults, from benign manifestations to fatalities (pneumonia, ARDS, multi-organ failure) [3,4]. Transmission is described as occurring via close contacts through the small droplets emitted during talking, coughing or sneezing, and reaching mucosal surfaces, namely the mouth, the nose, the eyes [1-4].

In humans, further to typical symptoms (mainly respiratory), COVID-19 can also develop atypical signs which sometimes may not be immediately ascribed to the SARS-CoV-2 infection, such as: Cardiovascular; embolic; neurological; gastrointestinal; hemorrhagic; olfactory and gustatory; psychiatric; cutaneous signs) [5].

SARS-CoV-2 also involve the eyes, even if only a few reports are available on ocular disorders occurring during COVID-19 [6,7]. Ocular manifestations include conjunctivitis, anterior uveitis, retinitis, and optic neuritis [5,8], being acute conjunctivitis, the most frequently ocular manifestation currently reported in the literature [9,10].

Case Presentation

It is the case of a 73-year-old Italian, non-smoking healthy woman, blood group A positive, without any significant comorbidity, and Leiden factor V negative who claimed red eyes, tearing, foreign-body sensation, photophobia, and increased secretions on 20th March, 2020, followed three days later by mild fever (37.6°C) associated to diarrhea (both lasting only one day), and Dysgeusia for 5 days. Ocular symptoms were assumed as due to acute conjunctivitis and self-managed at home (because in the pandemic peak) for five days with anti-inflammatory+anti-histamine eye wash medications (three times daily), but without any significant improvement. These symptoms persisted unchanged after the pharmacological treatment. As a blurred vision complicated the original clinical picture, she underwent an ophthalmologic consultation on March 25th: The conjunctivitis was confirmed by slit lamp examination, while the fundus oculi examination and the Spectral Optical Coherence Tomography (OCT) were absolutely normal (Figure 1A). Moreover, visus was 20/20, and the eye pressure 14 mmHg.

To note that her husband was admitted for severe COVID-19 pneumonia and ARDS on 28th March, and the lady was then quarantined (home isolation), even if in the absence of any other

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Figure 1A: The basal OCT picture on March 25.

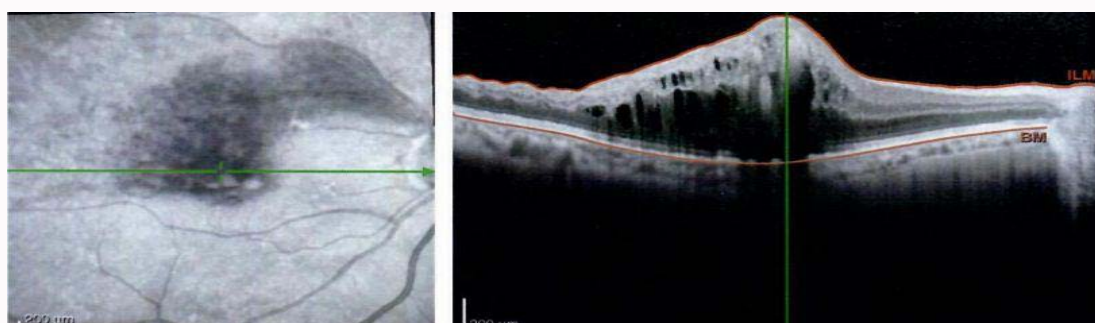


Figure 1B: The OCT picture on May 28: Evidence of macular edema due to BRVO.

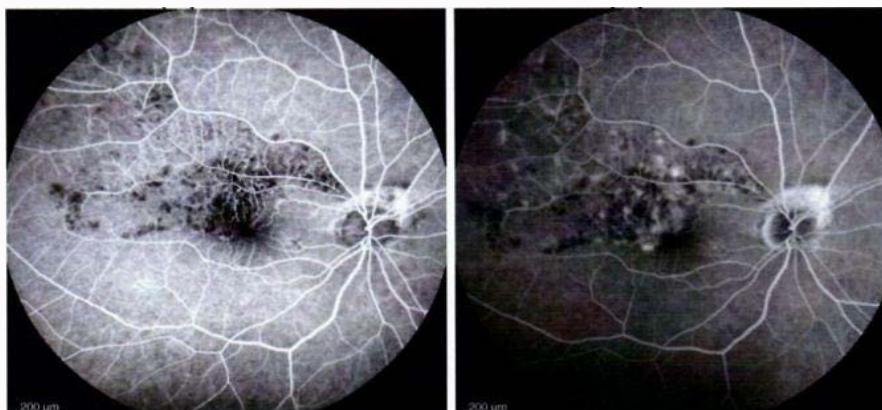


Figure 2: The fluorangiographic picture on May 28 confirmed the recent BRVO occurrence, with macular edema and minimal ischemia.

extra-ocular manifestation.

Due to the peak of the national pandemic context (actually, pauci-symptomatic conditions were absolutely disregarded), her RT-PCR nasopharyngeal swab was delayed to twenty days later: When tested, the swab proved positive, although by a low viral load. Plasma SARS-CoV-19 serology (namely, IgG plasma level) proved highly increased (8.35 Index (S/C; $nv < 1.4$; by Chemiluminescence Method, Abbott C8200) in the same days, thus confirming the occurrence of the previous SARS-CoV-2 infection and the substantial expression of specific acquired immunity. Two swabs repeated four weeks later were negative.

On May 28th (namely, as soon as possible after the strict lockdown), a sub-acute Branch Retinal Venous Occlusion (BRVO) was found in the right eye by ophthalmoscopy, associated with a macular edema. The visus showed the loss of 3 lines of visual acuity in the right

eye. A second OCT examination and the retinal fluoroangiography confirmed the diagnosis (Figure 1B and 2).

The macular edema was treated with intravitreal administration of dexamethasone 700 mcg (Ozurdex 700), and the OCT picture proved improved significantly after eight weeks (Figure 3).

Discussion

At present, conjunctivitis is the ocular disorder most frequently related to COVID-19 [11]. Its occurrence has been reported in more than 30% of cases with confirmed SARS-CoV-2 infection, and in about 20% of subjects with positive RT-PCR from pharyngeal and conjunctival swabs [8,10].

Conjunctivitis was also frequently described as the initial symptom of SARS-CoV-2 infection, and its role in tears-mediated transmission of viral particles was progressively emphasized, together

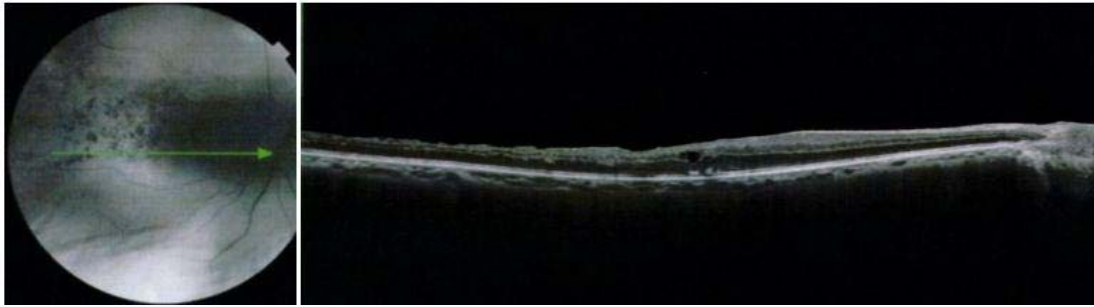


Figure 3: The OCT picture was improved 8 weeks after the intravitreal treatment.

with its value for early diagnosis of COVID-19 new cases [9,12-14].

It was also stated that the eye is rarely involved in human SARS-CoV-2 infection and that the eyes do not represent a preferred portal for the infection spreading [15]. Nevertheless, the ocular tropism of respiratory viruses had been already demonstrated in the past [16], while the SARS-CoV-2 RNA has been found in conjunctival scrape samples of COVID-19 patients with conjunctivitis [9,17], although in the absence of any typical symptom of COVID-19 [18].

Furthermore, ACE2 receptors, namely the specific binding sites for SARS-CoV-2 spike proteins, that are widely expressed on the cell membranes of different human tissues, have also been found in the retina, and in choroid and conjunctival epithelia [19-21], thus leading to the suggestion that various ocular manifestations might occur during COVID-19.

On the other hand, the aggressive inflammatory response due to the cytokine storm is a significant component of the pathophysiology of SARS-CoV-2 infection, together with the intravascular coagulation disorders [4]. Actually, it was also suggested that the huge formation of IgM and IgG immunocomplexes in these circumstances may contribute substantially to these events [4,11-22], and in defining COVID-19 patients as “at higher risk” to develop venous thromboembolic complications.

The present clinical report concerning the occurrence of an ocular thrombotic event during a pauci-symptomatic COVID-19 is particularly challenging for different reasons: 1) COVID-19-induced ocular venous thrombosis was never previously described in the literature; 2) the role of conjunctivitis has been once more confirmed as one of the earliest symptoms of SARS-CoV-2 infection [9]; 3) it has been emphasized for the first time the putative role of conjunctivitis in signaling the possible occurrence of severer and more dangerous ocular events (thrombotic in the case), otherwise misdiagnosed. On the other hand, it should be emphasized that COVID-19 manifestations have been described even in asymptomatic infected individuals with low viral loads in their nasopharyngeal swabs [23,24].

In conclusion, although not frequent as acute conjunctivitis, venous thrombotic events should also be included in the list of possible ocular COVID-19 manifestations, likely being viral tissue damage, hypercoagulability, and dysregulation of immune response the main pathogenetic determinants of this severe vascular complication of SARS-CoV-2 infection.

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