Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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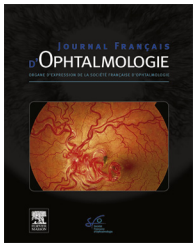

LETTER TO THE EDITOR

Mechanisms of retinal damage in patients with COVID-19☆

Atteintes rétiniennes chez les patients COVID-19 : mécanismes possibles

Recently, Marinho et al. used OCT to assess the retina in 12 patients infected by COVID-19. All patients showed hyperreflective lesions at the level of ganglion cells and inner plexiform layers more prominently at the papillomacular bundle in both eyes. OCT-angiography (OCT-A) and ganglionar cells complex analysis appeared normal. Authors suggested that ganglion cells and plexiform layer findings could be associated with CNS manifestations that have been described in animal studies and in COVID-19 neurological events [1].

These findings highlight the complexity of COVID-19 ocular involvements which are not limited to conjunctivitis. Multiples etiopathogenic pathways including microvascular thrombosis and autoimmune process can be evoked and should be assessed.

Although OCT-A appeared normal, the microvascular thrombosis mechanism cannot be formally excluded, because vascular microthrombus could have not been detected. Indeed, the two devices used by Marinho et al. were DRI-OCT Triton® Swept Source (Topcon, Tokyo, Japan) and XR Avanti® SD-OCT (Optovue, Fremont, CA, USA), which both have a transversal resolution of 20 μm in tissue [2]. Considering that diameter of second-order retinal arterioles is 14.7 ± 0.13 μm in young people and 16.1 ± 0.12 μm in old people [3], micro-occlusions in vessels less than 20 μm may not be detected in OCT-A. In addition, the vascular slowdown in these small diameter vessels becomes undetectable below a certain threshold, a fact that could make impossible the detection of micro-occlusions. This could explain why OCT-A examinations were normal in this series.

Recently, many papers reported that COVID-19 causes generalized endothelial damage and acute peripheral arterial thrombosis secondary to hypercoagulable state [4]. These microcirculation damages are more present in critically ill patients. In the series of Marinho et al. [1], no patient was hospitalized in intensive care and none had vasculitis manifestations. Assuming that retinal thrombosis is probably correlated with general thrombosis manifestations, this could be another explanation of OCT-A normality in the series of Marinho et al.

Data provided by experimental animal models brings additional arguments in favor of both microvascular occlusion and autoimmune pathways. Coronaviruses have been previously reported to be associated in animal models with retinal damages, such as retinal vasculitis, retinal degeneration, and blood-retinal barrier breakdown [5]. In experimental coronavirus retinopathy (ECOR), retinal damage is biphasic: in the early phase, there is retinal inflammation, infiltration of immune cells, and release of pro-inflammatory mediators; secondarily, after the first week of infection, viral clearance is achieved. However, subsequently retinal and RPE cell autoantibodies are produced, resulting in progressive loss of photoreceptors and ganglion cells as well as thinning of the neuroretina. These findings make surveillance in patients with COVID-19 essential to check the evolution and ensure that there will be no sequels [5].

Further investigations on larger series including patients with severe clinical manifestations are needed to assess the retinal lesions pathogeny. We suggest that it would be useful to perform OCT-A in patients with thromboembolic manifestations: it is likely that the retinal microvascular damage would be correlated with general thromboembolic events. In patients with extensive thromboembolic manifestations and often intubated and ventilated, retinal assessing with the mobile OCT-A Heidelberg SPECTRALIS® Flex device module (Heidelberg Engineering, Heidelberg, Germany) would be an interesting option. This device has already be successfully used for retinal imaging in unconscious and systemically unwell patients [6]. OCT-A will be useful to assess whether there is retinal hypoperfusion or not in patients with extensive thromboembolic manifestations.

As it has been reported that coronaviruses may be responsible for uveitis, choroiditis, and blood-retinal barrier breakdown in animal models [5], it is not excluded that the COVID-19 could be associated with intraocular inflammation. In the series of Marinho et al., none of the included 12 patients had clinically detectable inflammation [1]. Thus, we recommend performing a laser flare meter in patients with COVID-19 to detect infraclinical inflammation. In critically ill patients, laser flare meter is not feasible due to their general condition as long as there is no portable laser flare meter device yet; thus, the only possibility is to search for anterior segment inflammation. This could lead to a better comprehension of ocular involvement in patients with COVID-19.

☆ Refers to: Marinho PM, Marcos AAA, Romano AC, Nascimento H, Belfort R. *Retinal findings in patients with COVID-19. Lancet*. 395(10237)1610. DOI:10.1016/S0140-6736(20)31014-X. [PII: S0140-6736(20)31014-X. LANCET 8885].

Disclosure of interest

The authors declare that they have no competing interest.

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M. Chahbi[a], M. Bennani[b], N. Massamba[c], O. Sandali[d], R. Tahiri Joutei Hassani[e,*]
[a] *Casablanca eye clinic, 34, rue Mohamed El Yazidi-Ex Rhodes, 20100 Casablanca, Morocco*
[b] *Ophthalmology department, Rachidi clinic, 43, boulevard Rachidi, 20000 Casablanca, Morocco*
[c] *Department of ophthalmology and visual sciences, university of Chicago medical center, Chicago, IL, United States*
[d] *Ambulatory surgery department, Guillaume de Varye clinic, 210, route de Vouzeron, 18230 Saint-Doulchard, France*
[e] *Ambulatory surgery department, Avranches Granville hospital, 849, rue des Menneries, 50400 Granville, France*

* Corresponding author.
E-mail address: tjhr78@hotmail.com
(R. Tahiri Joutei Hassani)
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