DOI: 10.1002/jmv.26290

JOURNAL OF MEDICAL VIROLOGY WILEY

Optic nerve analysis in COVID-19 patients

To the Editor,

We read with great interest the recent article of Baig and Sanders[1] regarding the neurological manifestations and the possible neuroinvasive routes opted by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We congratulate the authors for their excellent review.

Similarly to the brain,[2] there is evidence of SARS-CoV-2 detection in retinal biopsies of deceased patients with coronavirus disease 2019 (COVID-19).[3] Hence, the virus may reach the eye through the optic nerve or affect it by other mechanisms, such as systemic inflammation.

Optical coherence tomography (OCT) is a noninvasive imaging technique that measures the retinal nerve fiber layer thickness (RNFLT), providing a comprehensive analysis of the optic nerve. OCT has been used in multiple diseases and could give insight on SARS-CoV-2 neurotropism. We aim to report changes in RNFLT in COVID-19 patients.

Of a study of 17 patients examined after COVID-19 infection, we present the data of the only five patients who had baseline OCT due to previous ophthalmological exams. All patients had been examined at the Emergency Department for COVID symptoms and had tested positive for SARS-CoV-2. Patients underwent optic nerve analysis with Spectralis-OCT (Heidelberg Engineering, Heidelberg, Germany) 4 weeks after diagnosis. All peripapillary RNFLT measurements were made using a circular scan pattern centered on the optic nerve. The eye-tracking system allows any subsequent OCT scan to be scanned at exactly the same location as the prior scan. The Spectralis-OCT software calculates the average RNFLT for the overall global (360 degrees).

Of the eight eyes included, seven eyes showed an increase in RNFLT (mean: 4.3 μm) compared to previous examinations (Table 1). The only patient's eye that showed a decrease had glaucoma, which accounts for this thinning. The other eyes included in the series were healthy and had previous OCT due to routine exams. All patients had fever, asthenia, and cough, and three patients also presented with neurological symptoms (anosmia, ageusia, headache, or dizziness). None reported changes in vision. Four were treated with hydroxichloroquine and one of these patients with lopinavir/ritonavir too.

Marinho et al[4] have recently described hyperreflective lesions at the ganglion cell and inner plexiform layers, but results of the retinal layers appeared normal. However, without previous quantitative values from prior exams, it is difficult to identify quantitative changes in RNFLT. For this reason, we analyzed patients with previous OCT examinations.

Normative databases of RNFL thickness values are normally used to interpret the measurements. Decreases in RNFLT have been described with age in healthy individuals with a mean decrease of 0.365 μm/year.[5] Increases in RNFLT can be due to optic nerve inflammation.

On the other hand, coronavirus is known to cause retinitis and optic neuritis in animal models, being viral-induced inflammation the most likely etiology.[6] This inflammation of the optic nerve could be detected with an increase of RNFLT.

Change can also be caused by the relative hypoxia of tissues due to various reasons such as pneumonia and dyspnea. However, murine models with 48 hours of systemic hypoxia (10% O_2) have shown glial dysfunction, but no neural changes.[7] Interestingly, it has been

TABLE 1 Clinical characteristics and peripapillary optical coherence tomography findings

Patient	Sex	Age	Neurological symptoms	Clinical severity	Eye	Previous mean RNFLT (μm)	Time since previous OCT (months)	Mean RNFLT after COVID-19 (μm)	Increase (μm)
1	Female	64	Headache	Mild	R	96	15	100	4
2	Male	66	Anosmia ageusia	Severe	R	99	15	103	4
					L	103	15	111	8
3	Male	65	···	Moderate	R	87	48	89	2
					L	81	48	72	−9
4	Male	66	···	Moderate	L	96	61	99	3
5	Female	66	Anosmia, ageusia	Mild	R	86	34	87	1
					L	89	34	97	8

Abbreviations: COVID-19, coronavirus disease 2019; OCT, optical coherence tomography; RNFLT, retinal nerve fiber layer thickness; R: right eye; L: left eye.

suggested that the asymptomatic hypoxemia presented by some COVID-19 patients with severe pneumonia is related to a dysfunction of cortical, and is associated with neuroinvasion of the virus. Hence, brainstem involvement could play a role in respiratory failure.[8,9]

COVID-19 treatment may also be a possible mechanism for these RNFLT changes. However, no changes in RNFL have been described with hydroxychloroquine, and we found no reports of changes associated with lopinavir/ritonavir.[10] Therefore, neither physiological age-related changes nor COVID-19 treatment appear to be responsible for our findings.

For the moment, it is not known whether these changes represent a residual inflammation of the acute illness or transient changes, and the clinical significance of these findings is unknown. To the best of our knowledge, this is the first report in the literature of changes in the RNFLT possibly associated with COVID-19 infection. OCT is a reliable and reproducible method for measuring RNFLT and detects changes in RNFLT with high accuracy. Further research is warranted to establish the consequences of COVID-19 on the optic nerve.

ACKNOWLEDGMENTS

We thank Javier Martin-Sanchez and Juan Gonzalez-Armengol.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

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