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ORIGINAL ARTICLE



## Panuveitis and Optic Neuritis as a Possible Initial Presentation of the Novel Coronavirus Disease 2019 (COVID-19)

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### ABSTRACT

**Objective:** To describe the ocular manifestations in a case of novel coronavirus disease 2019 (COVID-19).

**Material and methods:** A case of unilateral panuveitis and optic neuritis as initial presentation of COVID-19.

**Results:** As it is published, angiotensin-converting-enzyme-2 receptors can be found in many organs, such as the eyes, nerves, and vessels, so extrapulmonary involvement would be expected. According to current evidence and clinical characteristics of the patient, uveitis and optic neuritis could be produced by the virus.

**Conclusions:** It is fundamental to consider panuveitis and optic neuritis as an unusual presentation of ocular involvement in COVID-19 so proper care can be given to the patients.

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COVID-19; SARS-CoV-2; optic neuritis; uveitis; panuveitis

## Introduction

The new Severe Acute Respiratory Syndrome Coronavirus – 2 (SARS-CoV-2) is an RNA encapsulated virus that has caused more than 6.93 million cases worldwide to date.<sup>1</sup> SARS-CoV-2 binds to the angiotensin-converting-enzyme-2 (ACE2) receptor to enter the host cells.<sup>2</sup> The renin-angiotensin system, apart from its role in blood pressure regulation, has autocrine functions in other organs.<sup>2</sup> Some studies confirmed the presence of ACE2 receptors in conjunctiva, choroid, vascular endothelium, and nerves.<sup>2–8</sup> Regarding ocular manifestations of SARS-CoV-2, the main ocular involvement reported so far is conjunctivitis.<sup>4–6</sup> Currently, other systemic implications of its neuro and vascular endothelium tropism are being studied.<sup>2,3,7</sup> However, to the best of our knowledge, no cases of uveitis have been reported.

We describe a case of a Covid-19 patient in who panuveitis and optic neuritis presented at the very first manifestation of the disease.

## Clinical Case

A 60-years-old woman presented to the emergency with ocular pain, blurred vision, and redness in her left eye (OS). She referred a viral upper respiratory infection with sinusitis and follicular conjunctivitis 2 weeks before the presentation to our center. She denied any previous ophthalmological history.

Ocular examination showed a best-corrected visual acuity of 20/20 in the right eye (OD) and 20/200 in the

OS with a relative afferent pupillary defect in this eye. Slit-lamp examination revealed panuveitis, with 3+ cells in the anterior chamber<sup>8</sup> and focal posterior synechiae in OS. Funduscopy examination revealed vitritis, with 1+ vitreous haze, and optic nerve swelling with peripapillary subretinal fluid and peripapillary choroidal folds. Spectral domain Optical Coherence Tomography (SD-OCT) (Spectralis, Heilderberg Engineering, Heidelberg, Germany) confirmed these findings and showed edema of the retinal nerve fiber layer in OS (Figure 1). Neuroimaging and serologies for syphilis, toxoplasmosis, and HIV were negative, there were no symptoms of claudication or lower limb weakness and temporal arteries were normal. Although temporal arteritis, myelin oligodendrocyte glycoprotein-associated optic neuritis and optic neuromyelitis were included in the differential, those entities were ruled out on the view of the clinical characteristics, retinal imaging findings and laboratory test performed. Probable unilateral Vogt-Koyanagi-Harada (VKH) was suspected so treatment with oral prednisone (starting dose of 60 mg daily), hourly steroids drops, and mydriatics three times per day were started.

Ten days after, she developed dry cough and dyspnea. Blood tests showed lymphopenia ( $0.68 \times 10^3/\mu\text{l}$ ), neutrophilia ( $7.31 \times 10^3/\mu\text{l}$ ), platelet count ( $261 \times 10^3/\mu\text{l}$ ) and elevation of fibrinogen (635 mg/dl), D-Dimer (660 ng/ml), C-Reactive Protein (60.3 mg/l) and Lactate Dehydrogenase (755 UI/l) and Erythrocyte Sedimentation Rate (22 mm). Renal function was normal ( $>90 \text{ ml/min/1.73 m}^2$ ). A bilateral interstitial pulmonary pattern was seen in the chest X-ray. Polymerase chain



**Figure 1.** Examination with optic coherence tomography, spectral domain, spectralis, Heilderberg engineering, Heidelberg, Germany showing optic disk swelling in left eye with peripapillary subretinal fluid and choroidal folds at the moment of diagnosis.

reaction (PCR) for SARS-CoV-2 in nasopharyngeal exudate was positive and diagnosis of SARS-Cov-2 with bilateral pneumonia was made. Hydroxychloroquine (Dolquine®, Rubió, Barcelona, España) 400 mg twice a day for the first day and then 200 mg twice a day for 6 more days was given. After clinical worsening of her respiratory symptoms, she was admitted at our hospital and lopinavir-ritonavir (Kaletra®, AbbVie, Ludwigshafen, Deutschland) 400/100 mg twice daily was added until the disappearance of fever, 10 days after. Patient did not attend her follow-up visit due to the systemic disease and she was examined as an inpatient (15 days after beginning with oral steroids). In the visual acuity, anterior pole and fundus examination, no signs of uveitis, vitritis or papillitis were seen, patient visual acuity improved and oral steroids were then tapered. It was not possible to perform any ocular tests at that time due to the poor general condition of the patient.

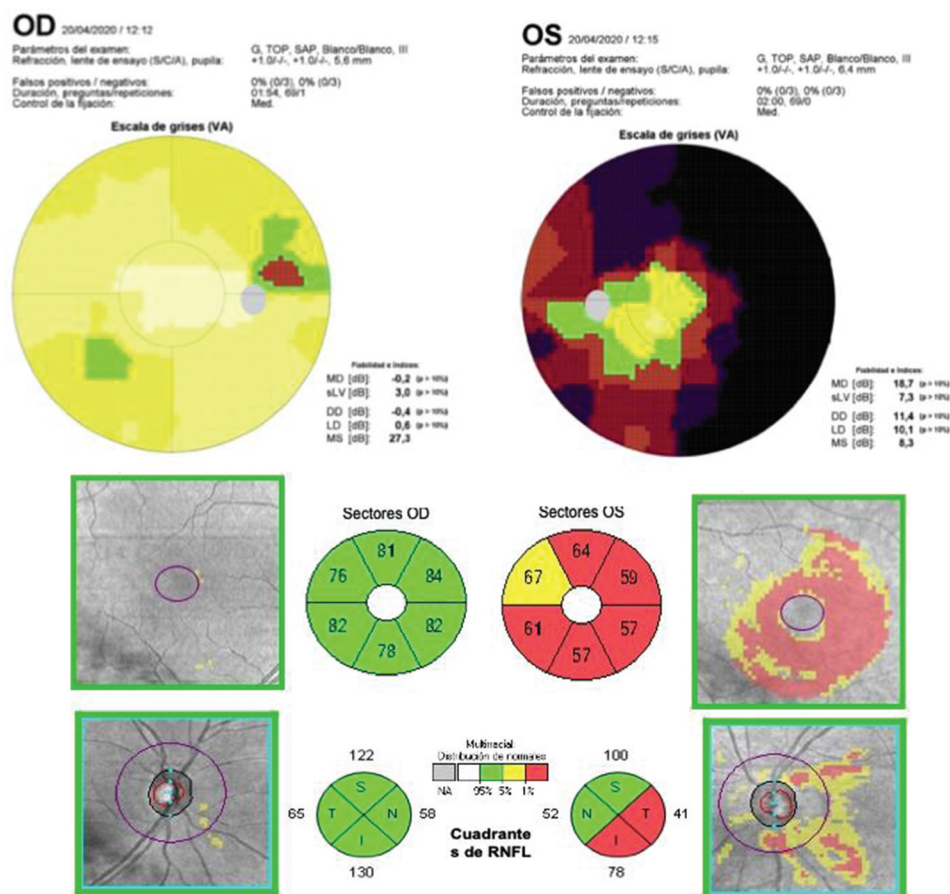
Once systemic symptoms improved and nasopharyngeal PCR became negative, patient was discharged. That day, the patients had undergone a complete ophthalmic examination. Visual acuity had improved (20/20 in OD and 20/40 in OS) and examination showed a cup/disc ratio of 0.3 OD and 0.7 OS, with optic disc pallor in the OS. Visual field (Octopus 900 Haag-Streit Diagnostics Koeniz Switzerland) and OCT (Cirrus HD-OCT 5000 Carl Zeiss Meditec AG Jena, Germany) were performed (Figure 2). Severe optic atrophy was revealed through the tests, with a retinal nerve fiber layer and ganglion cell layer decrease and its subsequent visual field defect in OS. Finally, a PCR for SARS-CoV-2 and other viruses (human herpes virus, cytomegalovirus, varicella-zoster virus, Epstein-bar virus, and

enterovirus) in aqueous humor was also performed that day, with a negative result.

## Discussion

We report a case of unilateral panuveitis and optic neuritis as the first manifestation of SARS-CoV-2 infection, before the onset of pulmonary symptoms. The initial clinical impression of unilateral VKH was ruled out due to the absence of bilateralization, meningism, and the existence of structural and functional damage at the level of the optic disc compatible with optic neuritis.<sup>9</sup> Other causes of optic neuritis were ruled out due to the clinical features of the patient, imaging, and laboratory tests. Although there is a possibility that the uveitis manifestation just preceded a SARS-CoV-2 infection, as patient visited several hospitals before showing pulmonary symptoms, it is likely that both diseases are related. Moreover, the timeline of the disease makes this hypothesis very likely. Furthermore, the conjunctivitis prior to the uveitis could have been an early manifestation of the infection, that even preceded the uveitis.

The existence of ACE2 receptors in the choroid is well known, and even have been used to develop new glaucoma drugs to reduce intraocular pressure.<sup>2</sup> CoV ocular infections have been well established in various animal models such as mice and cats. It is described in the literature that feline CoV (FCoV) and murine CoV mouse hepatitis virus (MHV) can produce uveitis and choroiditis, apart from retinal detachment, vasculitis, retinitis, retinal atrophy, and optic neuritis.<sup>2</sup> This evidence supports the assumption that the panuveitis could be caused by SARS-CoV-2.



**Figure 2.** Octopus 900 TOP 24-2 visual field showing defects on left eye. Ganglion cell layer loss and optic nerve atrophy in the same eye one month after acute symptoms, with spectral-domain optical coherence tomography cirrus HD-OCT 5000 Carl Zeiss meditec AG Jena, Germany.

Studies have shown that ACE2 receptors are also present in both neurons and vascular endothelium that would be the reason of the neuro and endothelium tropism of SARS-CoV-2.<sup>2,3,10,11</sup> SARS-CoV-2 has been detected in the nerves and neurons of patients in autopsies and associated thrombotic episodes have been described.<sup>3,10,11</sup>

The sequelae of the optic neuritis (atrophy) make other viral causes more unlikely,<sup>9</sup> as viral optic nerve neuritis usually resolves without sequelae.<sup>12</sup> So, the optic nerve atrophy could have been caused by an ischemic episode and SARS-CoV-2 has proved to have a prothrombotic effect due to its endothelium-tropism.<sup>3,11</sup> Whether the optic neuritis is true ischemic or inflammatory is difficult to determine. Equally, to determine if the inflammation is caused by direct infiltration of the virus in the ocular tissue, or it is a consequence of inflammation of the choroid further studies are warranted. Unfortunately, in our case, the PCR in the aqueous sample could only be done after patient discharge, when the PCR in the nasal swab was already negative and not active intraocular inflammation was present, so that could be the cause of the negative PCR.

Ocular manifestations of other CoV and the presence of ACE2 receptors in the eye, nerves, and endothelium have been already published.<sup>2</sup> In this case, panuveitis and optic neuritis could be initial features of SARS-CoV-2 infection, but this remains as a hypothesis. Further studies are warranted to

properly describe all the systemic manifestations of SARS-CoV-2 and to help ophthalmologists and other physicians in the detection of early cases, as early isolation seems to be the better option to control SARS-CoV-2 infection.

### Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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