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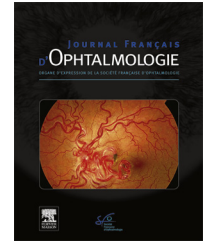


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## LETTER TO THE EDITOR

### Non-arteritic anterior ischemic optic neuropathy as an atypical feature of COVID-19: A case report



*Neuropathie optique ischémique antérieure non artéritique comme manifestation atypique de COVID-19 : un rapport de cas*

#### Introduction

Coronavirus disease 2019 (COVID-19), an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused a major global outbreak [1]. Most cases of COVID-19 are associated with fever and respiratory tract symptoms. This infection can also occur with various neurological, gastrointestinal, olfactory, ocular, cutaneous, and cardiac manifestations. Ocular manifestations of COVID-19 are usually rare [2]. It was important to note that ocular findings may present the infection's presenting picture. According to the first reports of complications of COVID-19 infection, the most typical and significant ocular manifestations are conjunctival infection, epiphora, and conjunctivitis [3]. Here, we present a patient with COVID-19 with non-arteritic anterior ischemic optic neuropathy (NAION).

#### Case report

A 67-year-old woman was admitted to the ward with decreased vision in the left eye, preceded by a two-day headache. She had a headache primarily in the frontal and left temporal zones and a blurred vision with a scotoma mainly at the superior eye field. Although there was no orbital pain, she complained about eye discomfort. She reported that the symptoms are primarily present in the morning. Her past medical history was coronary artery disease (CAD), for which she received a percutaneous coronary intervention (PCI) 7 years ago, and uncontrolled high blood pressure. No redness, discharge, epiphora, photophobia, foreign body sensation suggesting conjunctivitis, and scleritis were evident. She had no tenderness on temporal bones.

Ocular examination revealed decreased visual acuity without nystagmus, ophthalmoplegia, and related pupillary defect. Fluorescein angiography showed filling defects around the left optic disc. The anterior chamber appeared normal while examining under the slit-lamp. However, a mild cataract in the right eye and a dense posterior subcapsular cataract in the left side was detected, due to which fundus and optic disk examination were not feasible. Her

best-corrected visual acuity (BCVA) was estimated to be 20/20 and worse than 20/800 in the right and left eyes, respectively. However, no color vision diminution was found. Goldmann's perimetry showed a superior left visual field defect, with no visual field abnormalities in the contralateral eye.

Moreover, the tonometry result was indicative of normal intraocular pressure (IOP). Optical coherence tomography (OCT) observations were normal, without papillary edema or macular damage. Neurologic examination revealed left eye visual acuity of hand motion without Marcus Gunn's pupils and intact ocular movements. Also, coordination gait and limb forces were normal, with symmetrical nasolabial folds and no focal neurological deficits.

Her routine laboratory tests were normal. Electrocardiography showed T-wave inversions at I, II, III, aVL, aVF, and precordial leads. Echocardiography was performed because of the suspected underlying cardiovascular decompensation that showed a 45% ejection fraction with mild to moderate aortic valve regurgitation. She was receiving antiplatelet anticoagulant and antihypertensive medications, along with brimonidine eye drops. According to the neurologist's recommendation, immediate high-dose corticosteroid treatment was required. Magnetic resonance imaging (MRI) of the brain and optical nerves was requested to exclude acute cerebral lesions, findings of which were not significant. Doppler examination of carotid arteries showed no obstruction. Thus, unilateral non-arteritic anterior ischemic optic neuropathy (NAION) was suspected based on clinical and paraclinical findings.

The venereal diseases research laboratory (VDRL), human immunodeficiency virus (HIV) antibody, hematological, rheumatological, and immunological tests were inconclusive. Furthermore, concerning metabolic disorders to be significant risk factors for the development of NAION, diabetes mellitus, hyperlipidemia, and thyroid disorders have been excluded with the corresponding necessary laboratory tests.

Then, two days following admission, the patient developed a low-grade fever and a mild to moderate dyspnea, fluctuating oxygen saturation (SpO<sub>2</sub>) between 88–92% on room air. Nevertheless, due to the current pandemic, the pulmonary assessment appeared reasonable. Lung computed tomography (CT) scan demonstrated several small subpleural nodules at the posterior segments of her right upper lobe, suggesting the early stages of COVID-19. A reverse transcriptase-polymerase-chain reaction (RT-PCR) test for SARS-CoV-2 was performed, which was positive. She was treated lopinavir/ritonavir (Kaletra), corticosteroid pulse therapy, and high-flow nasal oxygen. Unfortunately,

her visual acuity did not improve after two weeks of follow-up.

## Discussion

It has been noted that ophthalmology manifestations can be a challenging clinical presentation of COVID-19. Different studies reported various prevalence rates of ocular problems (0.8% to 31.6%) in hospitalized patients with this disease, with the most prevalent ocular manifestation reported being conjunctivitis [4]. Nonetheless, nearly all ophthalmic engagements related to this infection resolve spontaneously without intervention.

Ischemic optic neuropathy (ION) is acute optic nerve ischemia, occurring primarily in patients over 60 years old. It is classified as posterior and anterior ischemic optic neuropathies [5]. Anterior ischemic optic neuropathy (AION) is a common eye disease leading to vision loss. It occurs as a result of optical nerve infarction predominantly in the elderly. AION is classified into two distinct categories: 1) arteritic anterior ischemic optic neuropathy (AAION), which is most commonly seen with giant cell arteritis (GCA); and 2) non-arteritic anterior ischemic optic neuropathy (NAION), associated with diabetes mellitus, coronary artery disease, hypertension, hyperlipidemia, hypercoagulability states, and migraine. As mentioned earlier, AION is more common in elderly individuals. Therefore, diagnosis in young patients could be a sign of underlying small-vessel cerebrovascular diseases, such as diabetes, hyperlipidemia, hypertension, high body mass index (BMI), and connective tissue diseases. The typical patient complaint is a sudden unilateral visual loss, often immediately after waking up in the morning. AION is usually accompanied by optic disc inflammation with hemorrhages and sometimes adjacent cotton-wool exudates [6]. Jaw claudication and neck pain are potentially helpful clinical clues for GCA-induced AION [7].

Non-arteritic anterior ischemic optic neuropathy (NAION) is usually unilateral, painless condition. During the ocular examination of a NAION patient, a decreased visual acuity, afferent pupillary defect, optic disk edema, dyschromatopsia, and peripapillary splinter hemorrhage could be observed classically associated with a defect in the inferior altitudinal visual field. However, our patient had left-eye superior hemianopia, familiar with advanced glaucomatous optical neuropathy. Therefore, tonometry was performed, indicating a normal IOP. The difference between AAION and NAION in the funduscopic examination is the pale color of the optic nerve disc in the AAION and the hyperemic and swollen one in the NAION [8]. Unfortunately, the funduscopic examination was inconclusive due to our patient's dense and severe cataract. In NAION, visual acuity differs from normal vision to no light perception.

Nonetheless, the degree of visual impairment is more often less severe than the AAION. A left eye visual acuity of hand motion without Marcus Gunn's pupils was observed on neurologic examination. The current patient's condition did not seem compatible with AAION since giant cell arteritis was unlikely due to the absence of other accompanying symptoms, such as headache, scalp and temporal tenderness, or jaw claudication.

In general, visual field loss occurred in ION, maybe classic, arcuate, central, or altitudinal, and is associated with the optical nerve affected part [9]. However, the most common presentation is altitudinal vision loss, usually in the inferior field. In addition, our patient was involved with superior hemianopia in the left eye, which is a relatively uncommon finding in NAION. Laboratory tests and paraclinical measures can help with confirming the diagnosis. For example, elevated erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and platelet count suggest GCA or AION [10], all of which were normal in our patient contrary to the diagnosis of AION. Since this condition is predominantly neurological, thrombotic events may have been a predisposing factor rather than an ophthalmic complication. Therefore D-dimer would be an excellent marker to confirm her hypercoagulability state and prognosis [11], which was normal in our patient. Fluorescein fundus angiography may be a practical test for detecting thrombosis in AAION [12]. Due to the different pathogenicity of NAION, this diagnostic procedure may not have been of similar utility to our case. Nonetheless, our patient carried out no conclusive result indicating any occlusion in the posterior ciliary artery (PCA).

There has been no definitive treatment for NAION until now, and almost half of the cases recover spontaneously. Most of the recommended treatments are intended to prevent thrombosis or reduce the edema of the optic disk. Also, timely diagnosis of the underlying cause of sudden vision loss is vital. In other words, early receiving of corticosteroids in the case of GCA leads to significant improvement and prevention of blindness. Except for a few studies where systemic corticosteroids have improved vision, corticosteroids are not routinely suggested for NAION [13–16]. However, some studies have reported the beneficial corticosteroid effect in NAION. In the context of COVID-19, the benefits of steroids have not been fully explored. Based on the thromboembolic basis of NAION, some neurologists and ophthalmologists suggest that NAION patients take aspirin. On the other hand, being aware of other severe thromboembolic complications such as pulmonary thromboembolism, cerebrovascular accidents, and disseminated intravascular coagulation is needed. For this reason, our patient began taking these medications to avoid potential squeals.

## Conclusion

Since patients with COVID-19 are prone to thromboembolic and ischemic events, there would be an increased rate of ophthalmic vascular complications. Therefore, ophthalmologists and neurologists should carefully evaluate COVID-19 patients with new-onset ocular complaints about recent attributable COVID-19 from the current epidemic.

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#### Disclosure of interest

TTS reports that he provides strategic and scientific recommendations as a member of the Advisory Board and speaker for Novocure, Inc. and also as a member of the Advisory Board to Galera Therapeutics, which are not in any way associated with the content or disease site as presented in this manuscript. All other authors have no relevant financial interests to be declared.

#### References

- [1] Javanian M, Bayani M, Shokri M, Sadeghi-Haddad-Zavareh M, Babazadeh A, Ghadimi R, et al. Risk factors for mortality of 557 adult patients with COVID 19 in Babol, Northern Iran: a retrospective cohort study. *Bratisl Lek Listy* 2021;122:34–8.
- [2] Karimi S, Arabi A, Shahraki T, Safi S. Detection of severe acute respiratory syndrome Coronavirus-2 in the tears of patients with Coronavirus disease 2019. *Eye (Lond)* 2020;34:1220–3.
- [3] Emparan JPO, Sardi-Correa C, Lopez-Ulloa JA, Viteri-Soria J, Penniecook JA, Jimenez-Roman J, et al. COVID-19 and the eye: how much do we really know? A best evidence review. *Arq Bras Oftalmol* 2020;83:250–61.
- [4] Wu P, Duan F, Luo C, Liu Q, Qu X, Liang L, et al. Characteristics of ocular findings of patients with Coronavirus disease 2019 (COVID-19) in Hubei Province. *China. JAMA Ophthalmol* 2020;138:575–8.
- [5] Hayreh SS. Management of ischemic optic neuropathies. *Indian J Ophthalmol* 2011;59:123–36.
- [6] Hoorbakht H, Bagherkashi F. Optic neuritis, its differential diagnosis and management. *Open Ophthalmol J* 2012;6:65–72.
- [7] Chacko JG, Chacko JA, Salter MW. Review of Giant cell arteritis. *Saudi J Ophthalmol* 2015;29:48–52.
- [8] Inanc M, Tekin K, Budakoglu O, Ilhan B, Aydemir O, Yilmazbas P. Could platelet indices and neutrophil to lymphocyte ratio be new biomarkers for differentiation of arteritic anterior ischemic neuropathy from non-arteritic type? *Neuroophthalmology* 2018;42:287–94.
- [9] Atkins EJ, Bruce BB, Newman NJ, Bioussé V. Treatment of nonarteritic anterior ischemic optic neuropathy. *Surv Ophthalmol* 2010;55:47–63.
- [10] Kermani TA, Schmidt J, Crowson CS, Ytterberg SR, Hunder GG, Matteson EL, et al. Utility of erythrocyte sedimentation rate and C-reactive protein for the diagnosis of giant cell arteritis. *Semin Arthritis Rheum* 2012;41:866–71.
- [11] Linkins LA, Takach Lapner S. Review of D-dimer testing: good, bad, and ugly. *Int J Lab Hematol* 2017;39:98–103.
- [12] Littlewood R, Mollan SP, Pepper IM, Hickman SJ. The utility of fundus fluorescein angiography in neuro-ophthalmology. *Neuroophthalmology* 2019;43:217–34.
- [13] Gungor I, Konuk GE, Sullu Y, Ariturk N. Papillophlebitis: treatment of vision loss due to subretinal fluid with intravitreal Ranibizumab. *Neuroophthalmology* 2014;38:336–9.
- [14] Rehder D. Idiopathic intracranial hypertension: review of clinical syndrome, imaging findings, and treatment. *Curr Probl Diagn Radiol* 2020;49:205–14.
- [15] Graves J, Balcer LJ. Eye disorders in patients with multiple sclerosis: natural history and management. *Clin Ophthalmol* 2010;4:1409–22.
- [16] Hayreh SS, Zimmerman B, Kardon RH. Visual improvement with corticosteroid therapy in giant cell arteritis. Report of a large study and review of literature. *Acta Ophthalmol Scand* 2002;80:355–67.

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