Bilateral posterior ischemic optic neuropathy following COVID-19: a case report and literature review

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Background: Multiple cases of ischemic optic neuropathy following infection from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been documented. The most described entity is anterior ischemic optic neuropathy, although rare cases of posterior ischemic optic neuropathy have been reported, mostly in the setting of severe disease. We present the first report of posterior ischemic optic neuropathy involving both eyes and following uncomplicated coronavirus disease 2019 (COVID-19). Relevant literature is analyzed and discussed.

Case Description: A 65-year-old man presented with severe painless visual loss beginning in the lower hemifield of the right eye and involving both eyes in the span of 24 hours. Visual acuity in the right eye was reduced to no light perception and to uncertain light perception in the left eye. He had recently recovered from COVID-19 which had manifested with mild respiratory symptoms that did not require medical treatment. Complete ophthalmological evaluation revealed no anomalies except for non-reactive pupils. As radiological investigations including contrast magnetic resonance and computer tomography did not reveal acute events bilateral posterior ischemic optic neuropathy was hypothesized. As giant cell arteritis is an important cause of sequential ischemic neuropathy, high dose steroid treatment was carried out until temporal biopsy ruled out vasculitis. Steroid treatment was then slowly tapered over the course of 45 days. The patient had a history of carotid stroke and thrombophilia and blood pressure monitoring after the event revealed hypotensive episodes which led to the suspension of antihypertensive medication. At one-month follow-up, a slight improvement in visual functioning was observed, with the patient being able to count fingers with both eyes. This improvement was confirmed at two months. Fundus examination revealed pale optic discs, which confirmed the diagnosis of posterior ischemic optic neuropathy.

Conclusions: COVID-19 can induce vascular occlusion through endothelial dysfunction. Additionally, we propose that lowering of systemic blood pressure, as reported following infection, might also contribute to or even instigate optic nerve ischemia.

Keywords: Coronavirus disease 2019 (COVID-19); ischemic optic neuropathy (ION); posterior ischemic optic neuropathy (PION); case report

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Introduction

Posterior ischemic optic neuropathy (PION) is a rare disease that can lead to severe vision loss and blindness. Ischemic optic neuropathy (ION) more commonly involves the vascular supply of the head of the optic nerve [anterior ION (AION)]. Rarely, the retrobulbar portion of the optic nerve is affected and PION develops. In both cases, the patient experiences sudden, painless visual loss, sometimes upon awakening. Compared to AION, which always presents with optic nerve head edema, in PION the fundus initially appears normal, as the retrobulbar region of the optic nerve cannot be directly visualized. Based on etiology, ION can be classified into arteritic and non-arteritic. Arteritic ION develops from vasculitis of orbital arteries in the setting of giant cell arteritis. Non-arteritic anterior ION (NAION) is associated with small vessel disease and systemic vascular disorders wich might impair autonomic regulation, such as diabetes, atherosclerosis, hypertension and nocturnal hypotension (1). While NAION has extensively been described following coronavirus disease 2019 (COVID-19) (2-10), only a few cases of monocular PION have been reported (11-13).

We present the case of a patient who suffered from bilateral PION a few weeks after pauci-symptomatic COVID-19. Relevant literature is reviewed and etiopathogenic hypotheses are discussed, with the aim to highlight the need to monitor for systemic changes following infection as they might lead to devastating effects. We present this article in accordance with the CARE reporting checklist (available at https://amj.amegroups.com/article/view/10.21037/amj-23-105/rc).

Highlight box

Key findings

- Severe bilateral posterior ischemic optic neuropathy may follow uncomplicated coronavirus disease 2019 (COVID-19).

What is known and what is new?

- Posterior ischemic optic neuropathy has only been reported in the setting of complicated COVID-19.
- Uncomplicated COVID-19 may induce posterior ischemic optic neuropathy through thromboembolic and/or hemodynamic mechanisms.

What is the implication, and what should change now?

- Ophthalmologists should evaluate vascular risk factors including post COVID-19 vasculopathy when dealing with ischemic optic neuropathy.

Case presentation

A 65-year-old man presented because of severe loss of vision in the right eye, beginning in the lower hemifield of the right eye on waking up and evolving to no light perception in the span of a few hours. The following day the left eye was also involved with visual acuity reduced to light perception. He denied any other symptoms, such as ocular pain, pain on eye movement or headache. Recent history was significant for COVID-19, for which he had been tested because of mild respiratory symptoms and a fever of up to 37.5 ℃, which he had developed 11 days before presentation. He denied the use of any medication and had tested negative to nasopharyngeal swab two days before the onset of visual symptoms. He had been vaccinated against COVID-19 with two doses. He was on statins, anti-hypertensive and antiplatelet medication because he had suffered an ischemic stroke from left internal carotid artery occlusion seven years earlier. Additionally, he was on haematological follow-up because of polyglobulinemia and hyperhomocysteinemia.

At presentation, ophthalmic examination was, besides non-reactive pupils, unremarkable. Optical coherence tomography and angiography showed a slight thickening of the nerve fiber layer with faint fluorescein staining of the optic disks, but no optic disk edema. The macula and remaining retina and choroid were within limits (*Figure 1*).

Radiological investigations including contrast and angio-magnetic resonance and computed tomography showed long-standing complete occlusion of the left internal carotid artery and late ischemic changes in the left parietal and precentral regions. No acute hemorrhagic or ischemic events were detected.

Considering the severe loss of vision in the face of negative imaging findings and having excluded other causes of visual loss, a diagnosis of PION was made.

Because of the bilateral and sequential involvement, the patient was started on intravenous methylprednisolone (1,000 mg/day for five days, followed by oral prednisone 1 mg/kg), on suspicion of giant cell arteritis, although the patient denied any systemic symptoms and erythrocyte sedimentation rate and platelets were within range. Slight subjective improvement was noted in the left eye after a few days and in the right eye after one week. Temporal artery biopsy was negative for giant cell arteritis and steroid therapy was gradually reduced. Systemic work-up including lumbar puncture did not show infective involvement. As 24-hour pressure monitoring showed recurrent episodes of asymptomatic hypotension, hypertensive medication

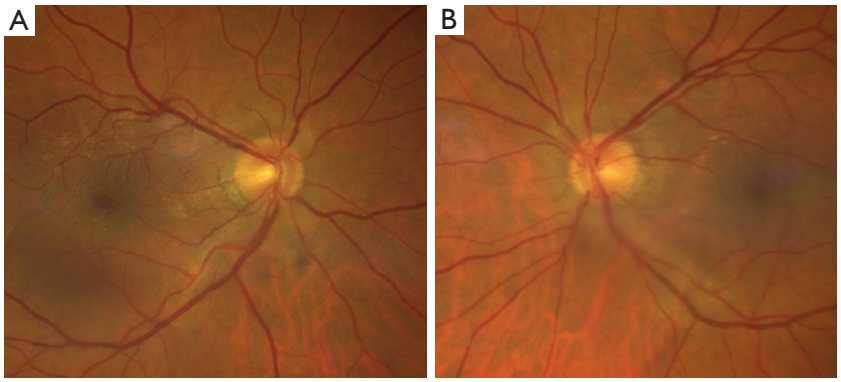

Figure 1 Color fundus photo of the right (A) and left eye (B) at presentation. Posterior pole is within limits, and optic nerve head appears normal, with well-defined margins.

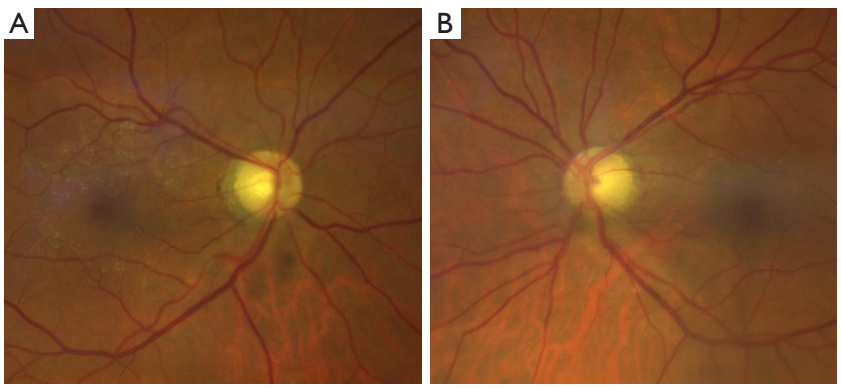

Figure 2 Color fundus photo of the right (A) and left eye (B) at two-month follow-up. Macular region is within limits, however, pallor of the optic discs is now apparent. The violet spots are artifacts from the camera lens.

was stopped. On discharge, the patient's immediate family and social services were involved in helping the patient adjust to blindness. At two-month follow-up, visual acuity had stabilised to count finger at 50 cm in the right eye and count finger at one meter in the left eye. Whitening of the optic nerves and ganglion cell loss was observed, which was compatible with chronic changes in PION (*Figure 2*). *Figure 3* summarizes the timeline of events. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

The differential diagnosis for visual loss in the face of normal ophthalmological exam is not extensive. Central artery occlusion and choroidal ischemia may not always be apparent upon fundus examination, but they can readily be identified with optical coherence tomography and fluorescein angiography. Detection of impaired pupillary reflex to light is very useful as it rules out malingering and suggests optic nerve disease. Retrobulbar optic neuritis is a common cause of acute neuropathy, although in this case it was considered unlikely, as it usually associated with pain on eye movement and affects individuals between the ages of 20 and 40 years. Failure to improve significantly with steroid treatment and unremarkable magnetic resonance

Physical examination		Investigations	Interventions
Fever (max 37.5 ℃) with mild respiratory symptoms	**11 days before**		
	9 days before	Positive nasopharyngeal swab for COVID-19	
Resolution of systemic symptoms	**5 days before**		
	2 days before	Negative nasopharyngeal swab for COVID-19	
03:00 PM **Loss of vision in the lower hemifield of the right eye upon awakening** 06:00 PM Complete loss of vision to the right eye (no light perception) Left eye: normal vision		Imaging: no evidence of acute cerebral events	Methylprednisolone 1 g endovenous for 5 days
04:00 PM Right eye: no light perception **Reduction of visual acuity to uncertain light perception in the left eye**	**Day 2**	Systemic work-up including lumbar puncture: negative for infective/inflammatory disease	
	Day 3		
Right eye: no light perception Left eye: improvement of visual acuity to light perception	**Day 5**	Blood pressure monitoring: asymptomatic hypotensive episodes (systolic pressure <100 mmHg)	Oral prednisone
			Antihypertensive
Right eye: improvement to light perception Left eye: improvement of visual acuity to counting fingers at 1 m	**Day 10**		
	Day 20	Temporal artery biopsy results: negative for giant cells	Began prednisone tapering
Right eye: improvement to count finger at 50 cm Left eye: count fingers at 1 m Fundus oculi: pale optic discs	**Month 1**		
	Day 45		Prednisone stopped
Final visit: Right eye: count fingers at 50 cm Left eye: count fingers at 1 m Fundus oculi: pale optic discs	**Month 2**		

Figure 3 Timeline of the patient's clinical course. COVID-19, coronavirus disease 2019.

of the optic nerve also assisted in excluding neuritis. Brain and orbit imaging are also indicated as lesions along the optic pathway can cause visual loss without ocular changes. In this case, PION was considered the most likely diagnosis (14). ION results from vascular insufficiency to the optic nerve. It can be of vasculitic origin, in the setting of Giant Cell Arteritis, or non-arteritic. In NAION, the anterior part of the optic nerve—that is, the optic nerve head—is affected, which manifests as visible optic disk edemа at fundus examination. Likely risk factors are crowded optic disk and nocturnal hypotension: reduced blood flow in the optic nerve head results in ischemia and axonal swelling which, in a small disk, compresses capillaries and induces vascular dysfunction with visual loss, usually discovered upon awakening (1). Thrombophilia can be found in younger patients with NAION without cardiovascular risk factors (15).

PION involves the retrobulbar part of the optic nerve. It is rarer than AION. As it is not associated with optic nerve head edema or any other ocular signs apart from pupillary reflex defects it is a diagnosis of exclusion, although disk pallor can be noticed after 6 to 8 weeks. The blood supply of the posterior portion of the optic nerve is most often superficial, from a plexus of peripheral

capillaries that surrounds the optic nerve, with no axial blood supply. Because of this, the internal part is more vulnerable to ischemia, which results in central visual field loss. As in NAION, generic risk factors such as diabetes, hypertension, carotid and peripheral vascular disease have been identified, but also more specific causes which suggest a role for optic nerve hypoperfusion, such as migraine and severe nocturnal hypotension. Perioperative PION has also been described, which is associated with anemia and hypovolemic hypotension during or immediately after surgery (1).

Currently, NAION in association with COVID-19 has been described in nine patients (*Table 1*), of which seven presented with monocular involvement (2-6,8,9) and two with bilateral disease (7,10).

The majority of patients experienced visual loss after recovering from the infection, more commonly within the first two weeks.

Two cases of monocular PION in the setting of severe disease and COVID-19 have also been reported: in association with orbital mucormycosis (12) and following blood loss from hemothorax in a patient who had previously suffered from NAION (13). One single case report exists of monocular PION in a hypertensive woman with uncomplicated COVID-19, although the patient spontaneously recovered, and no relative afferent pupillary defect was described (11).

In most of these works, vascular occlusion from endothelial dysfunction has been proposed as the causative mechanism and, indeed, multifocal vascular damage accompanied by complement activation was found in the brain tissue of patients that died with COVID-19 (16). Additionally, impairment of the capillary peripapillary plexus has been demonstrated in patients who have recently healed from COVID-19 (17).

Literature analysis, however, shows that, excluding one case, no patient had a history of thrombophilia or tested positive when screened. Indeed, as discussed, ION is not purely a thromoboembolic disease, rather, it is often associated with a transitory hypotensive state (18).

Interestingly, COVID-19 can also have hemodynamic effects. Angiotensin II antibodies have been found in the sera of COVID-19 patients and blood pressure dysregulation has been described after severe COVID-19 (19). In a study of patients hospitalised for COVID-19 at the beginning of the pandemic, 75% had to discontinue anti-hypertensive medication because of lowering of blood pressure (20). A small case series focusing on geriatric patients also detected hypotension during 24-hour monitoring following COVID-19 (21).

Among the reports of ION in COVID-19 some patients were given intravenous steroid treatment (6-8,10). It is unclear whether this might influence visual recovery. In patients aged 50 or older Giant Cell Arteritis should always be ruled out if ION is diagnosed. As definitive diagnosis can only be made with temporal artery biopsy, steroid treatment is indicated if suspicion is high, as it may prevent visual loss in the fellow eye (which occurs in up to 95% of cases in untreated) and systemic complications of vasculitis (14). While widespread, the use of corticosteroids in non-arteritic optic neuropathy is not supported by clinical trials (22), rather, studies on NAION have demonstrated spontaneous improvement in 40% of patients (1). As discussed, post COVID-19 ischemic neuropathy could partially be linked to vasculopathy of suspected inflammatory nature (16)—suggesting a role for the immunosuppressive effect of steroids. However, only a very modest improvement in visual acuity was noted in the patient described in this report, while either worsening (8) or stable function (6,7,10) is described in already published case reports.

As this is a single observation, no generalized conclusions can be reached regarding casualty or suggested treatment, and this is the main limitation of this study. Additionally, vitamin D deficiency, which has been linked to endothelial dysfunction (23), was not investigated in this patient. Another limitation is that multiple risk factors (thrombophilia, carotid vasculopathy and hypotension) co-existed in this patient and, as such, it is uncertain the exact measure in which they might have contributed to the final outcome. We believe it is important to report, as PION is a very rare entity and the knowledge on COVID-19 is ever expanding. While evaluating vasculopathy during recovery may not be feasible in all patients, blood pressure monitoring and treatment modification can easily be carried out.

Conclusions

This work adds to the existing literature which links COVID-19 with optic nerve ischemia, although more studies are needed to investigate its exact role. Treating clinicians should monitor cardiovascular state closely in the weeks following COVID-19 infection and ophthalmologists should inquire about recent COVID-19 disease when dealing with ION.

Table 1 Published works featuring non arteritic ischemic optic neuropathy in patients with COVID-19

Authors	Diagnosis	Age (years)	Days from COVID-19 diagnosis to visual symptoms	Hospitalised	Baseline VA	Visual field defect	Steroids?	Evolution	Concomitant disease	Thrombophilia screening?
Rho *et al.* (2)	AION	43	14	No	20/30	Inferior defect	No	NA	DM, hyperlipidemia	Yes, negative
Yüksel *et al.* (3)	AION	72	13	No	20/63	Inferior defect	No	Worsening	DM, HTN	No
Moschetta *et al.* (4)	AION	64	42	Yes	20/20	Inferior defect	No	Improvement	None (HTN after onset)	Yes, negative
Golabchi *et al.* (5)	AION	52	14	Yes	Hand motion	Central and nasal scotoma	No	NA	None	No
Babazadeh *et al.* (6)	AION	67	0	Yes	20/800	Superior defect	Yes	Stable	CAD, HTN	Yes, negative
Sanoria A *et al.* (7)	Bilateral sequential AION	45	30	No	RE: 20/20; LE: 20/80	RE: inferior defect; LE: concentric scotoma	Yes	Stable	DM, HTN	Yes, negative
Romozzi *et al.* (8)	AION	61	0	No	20/25	Concentric scotoma	Yes	Worsening (after vaccine)	None	No
Sitaula *et al.* (9)	AION	60	1	No	20/200	Inferior defect	No	Improvement	None	No
Shahri *et al.* (10)	Bilateral AION	57	18	No	RE: LP; LE: no LP	NA	Yes	Stable	DM, AAGC	Yes, negative
Selvaraj *et al.* (11)	PION	50	7	No	Unable to CF	Inferior, superotemporal defect	No	Improvement	HTN; hyperlipidemia	No
Kaushik *et al.* (12)	AION and PION	73	0	Yes	No LP	NA	NA	Stable	Mucormycosis, DM	No
Chen *et al.* (13)	PION	81	14	Yes	CF	Generalized depression	No	NA	Blood loss, vasculopathy, hypotensive status, HTN	Yes, negative
Mambretti *et al.* (present case)	Bilateral PION	65	9	Yes	RE: no LP; LE: LP	NA	Yes	Improvement	RE: CF; LE: CF	HHcy, polyglobulinemia

COVID-19, coronavirus disease 2019; VA, visual acuity; AION, anterior ischemic optic neuropathy; NA, not available; DM, diabetes mellitus; HTN, hypertension; CAD, coronary artery disease; RE, right eye; LE, left eye; LP, light perception; AAGC, acute angle closure glaucoma; PION, posterior ischemic optic neuropathy; CF, count fingers; HHcy, hyperhomocysteinemia.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://amj.amegroups.com/article/view/10.21037/amj-23-105/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://amj.amegroups.com/article/view/10.21037/amj-23-105/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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