

Case Report

Unusual presentation of a multiple sclerosis case involving central retinal artery occlusion

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Abstract

The term intermediate uveitis (IU) refers to a subgroup of uveitis in which the vitreous is the site of greatest inflammation. Patients with multiple sclerosis (MS) have a greater frequency of IU compared with the general population.

The IU associated with MS is characterized by the presence of pars planitis (occasionally accompanied by anterior uveitis) and the presence of peripheral retinal vasculitis in the form of periphlebitis (venous sheathing) in 6–26% of patients.

We present a patient with an unusual initial presentation of MS involving central retinal artery occlusion (CRAO) in the right eye (RE).

Although retinal vascular changes are asymptomatic in the majority of MS patients, the spectrum of impairment ranges from simple peripheral retina periphlebitis to the presence of peripheral occlusive retinal vasculitis in 6.5% of patients.

This atypical case may represent an extreme of the spectrum of retinal vasculitis associated with demyelinating disease.

Keywords: Central retinal artery occlusion, Retinal vasculitis, Multiple sclerosis, Intermediate uveitis, Periphlebitis

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Introduction

The term intermediate uveitis (IU) refers to a subgroup of uveitis in which the vitreous is the site of greatest inflammation. When IU is accompanied by snowbanks or snowballs, the condition is referred to as pars planitis.¹

Patients with IU may present with inflammation in the anterior chamber (which is generally minimal) and peripheral vascular sheathing.^{1,2}

Patients with multiple sclerosis (MS) have a greater frequency of IU compared with the general population. According to the publications we consulted, between 0.4% and 26.9% of patients with MS develop uveitis, and between 7.8% and 14.8% of patients with IU develop MS.^{1,3} However, other diseases are associated with IU, including Lyme disease, syphilis, cat scratch disease, and sarcoidosis.¹

We present a patient with an unusual initial presentation of MS involving central retinal artery occlusion (CRAO) in the right eye (RE). This highly atypical case may represent one extreme of the retinal vasculitis spectrum associated with demyelinating diseases.

Case report

We present a 46-year-old woman who was admitted to the emergency room in 2010 with a sudden decrease in the RE visual acuity (VA), which had an onset several hours prior. She had mild pain with eye movement. The patient did not have a relevant medical history and was medicated only with oral contraceptives.

In the emergency room, the blood pressure was 101/67, and the examination revealed a VA of 6/200 in the RE and

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20/20 in the left eye (LE). The intraocular pressure was 15 mmHg in the RE and 14 mmHg in the LE.

The pupils were isochoric and normoreactive to light and accommodation, but with the presence of a relative afferent pupillary defect in the RE. The slit lamp revealed RE conjunctival ciliary injection and the presence of mild inflammation, 1+ cells, and flare in the anterior chamber. There were no posterior synechiae.

Conspicuous in the fundus of the eye was a hyperemic, slightly elevated optic disk, with ischemic pallor of the retina at the posterior pole that was compatible with acute CRAO and a preserved cilioretinal artery (Fig. 1A). Likewise, there was vascular sheathing and vitritis with snowballs.

The fluorescein angiogram showed mild signs of retinal vasculitis, retinal arterial filling delay, diffuse retinal capillary non-perfusion in the posterior pole compatible with CRAO. Preservation of the retinal circulation around the cilioretinal artery was visible, as was contrast leakage from the optic disk in the subsequent frames (Fig. 1B–C). The macular optical coherence tomography (OCT) showed increased retinal reflectivity consistent with CRAO (Fig. 2).

Given the presence of typical periventricular demyelinating lesions (some showing contrast uptake) in the cranial and orbital MRI, as well as slight enhancement of the optic nerve after contrast injection, it was believed that the patient might have had optic neuritis in addition to uveitis (Fig. 3). Consequently, treatment was initiated with intravenous methylprednisolone, 1 g every 24 h for three days (single dose), followed by a tapered oral dose (1 mg/kg tapered gradually in 2 weeks). Likewise, topical treatment was initiated using a corticosteroid in the RE (prednisolone acetate drops three times a day, gradually reducing the dose in 4 weeks).

Upon ophthalmologic examination two months later, the VA was 20/50 in the RE and 20/20 in the LE. There was no inflammation in the anterior chamber, and the fundus of the RE displayed global pallor of the optic nerve with retinal arteriolar attenuation at the posterior pole. The neurological examination was normal. The VA improvement was believed to be caused by the decreased in macular thickening or optic neuritis improvement after corticosteroid treatment.

The requested blood analyses, which included C-reactive protein (CRP), Anti-nuclear Ab (ANA), Anti-DNA, Treponema pallidum hemagglutination assay (TPHA), Rapid Plasma Reagin (RPR), Angiotensin converting enzyme (ACE), serum Lysozyme, and coagulation risk profile, were all within normal limits. Likewise, a chest CT scan, purified protein derivative (PPD), EKG, echocardiogram, and Doppler of the carotids were obtained, with results within normal limits.

Goldmann's visual field revealed a residual central and temporal islet in the RE and normal findings in the LE (Fig. 4).

During two years of follow-up, the patient remained clinically stable. However, the appearance of new periventricular lesions on subsequent MRIs, combined with the suspicion of initial optic neuritis, has led to the diagnosis of MS and the initiation of treatment with interferon beta-1 by the Neurology Service (Fig. 5).

Discussion

We present a patient with an unusual initial presentation of MS combining a CRAO with a possible optic neuritis in the RE. Such an atypical case may represent one extreme

of the retinal vasculitis spectrum associated with demyelinating disease.

The IU associated with MS is characterized by the presence of pars planitis (occasionally accompanied by anterior uveitis) and the presence of peripheral retinal vasculitis in the form of periphlebitis (venous sheathing) in 6–26% of patients.³

In the majority of patients, these retinal vessel changes are asymptomatic. Regardless, certain studies have shown that the presence of peripheral vascular disease in a patient with isolated sheathing in typical optic neuritis may predict the development of MS in the future, with a relative risk of 11.4%.^{4,5} Other studies have linked the presence of vascular sheathing with the severity of the neurological dysfunction in MS patients.^{3,6}

Nonetheless, despite the fact that in the majority of patients, these retinal vascular changes are asymptomatic, there are numerous publications demonstrating a spectrum that ranges from simple peripheral retinal periphlebitis to the presence of peripheral occlusive retinal vasculitis in 6.5% of patients.^{1,4,7} This condition leads to other complications, such as retinal ischemia, neovascularization, retinal detachment, vitreous hemorrhage,² or neovascular glaucoma.⁸

This patient belongs within the group of patients with occlusive retinal vasculitis associated with demyelinating disease. However, this case is unusual in that the intense retinal vasculitis was associated with CRAO.

The pathogenic mechanism that occurs in retinal vasculitis is that of infiltration of the retinal venules by T-cell lymphocytes, of which 35–90% are CD4+.¹

Recent immunogenetic studies have revealed that the HLA-DR15 allele may encode a predisposition for the development of MS and pars planitis, which demonstrates that the processes share a similar immunopathogenic substrate.^{9,10}

In patients for whom MS and IU are associated, MS tends to be the first disease to present clinically. Thus, in the study by Biousse,³ neurological symptoms occurred nine years prior to the start of uveitis in 57.1% of cases. In addition, only one patient in the study had an initial presentation with simultaneous ocular and neurological symptoms.

Our patient's visual symptoms led to the diagnosis of MS through a cranial MRI, which showed typical demyelinating lesions. However, she had not previously presented with neurological symptoms.

With respect to the differential diagnosis of occlusive retinal vasculitis, in addition to the demyelinating etiology, we must consider sarcoidosis, Behçet's disease, and tuberculosis. Additionally, as in MS, all of these diseases may alter the central nervous system (for example, neuro-Behçet and neuro-sarcoidosis), thus further complicating the differential diagnosis in certain cases.⁸

A study conducted in Tunisia described 18 patients with CRAO secondary to posterior uveitis. The most frequent etiology was toxoplasmosis, followed by rickettsiosis and Behçet's disease. There were no patients with demyelinating disease, and only one patient presented with an idiopathic etiology.¹¹ Similar studies have shown that the presence of CRAO associated with MS is infrequent. Nonetheless, there are publications in which the presence of CRAO and branch retinal artery occlusion (BRAO) is described in optic neuritis patients, with similar frequencies from demyelination versus post-vaccination.^{12–15}

In the study by Kahloun et al., various mechanisms are proposed to explain the occurrence of retinal arterial occlusions



Figure 1. (A) Fundoscopy in which the presence of a slightly hyperemic RE optic disk is prominent, with retinal ischemic pallor in the posterior pole, compatible with acute CRAO and a preserved cilioretinal artery. (B–C) Fluorescein angiography showing delay in the retinal arterial filling and diffuse retinal capillary non-perfusion at the central and temporal macula compatible with CRAO. The retinal circulation in the cilioretinal artery's territory is preserved. The retinal vessels stain in later frames. Dye leakage at the optic disk in the context of uveitis is observed.

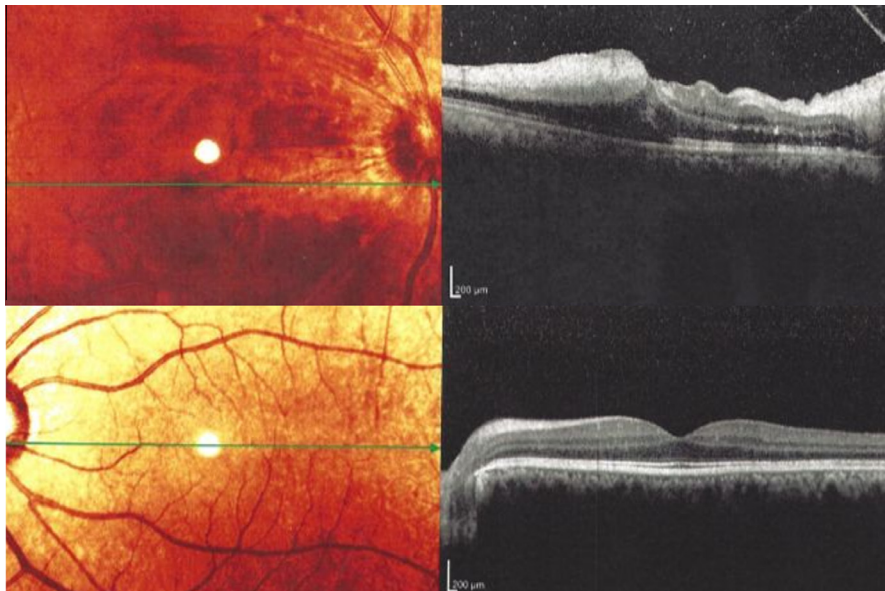


Figure 2. Optical coherence tomography (OCT) shows increased reflectivity of the neurosensory retina at the temporal macula, typical of acute CRAO (top image). The left macular scan is normal (bottom image).

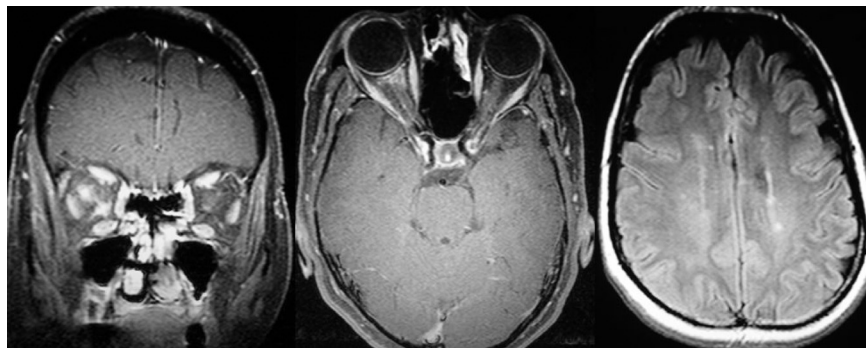


Figure 3. Cranial and orbital MRI showing the presence of typical demyelinating periventricular lesions (some of them with contrast enhancement), along with slight enhancement of the optic nerve after contrast injection (coronal and axial T1 sequence after contrast injection).

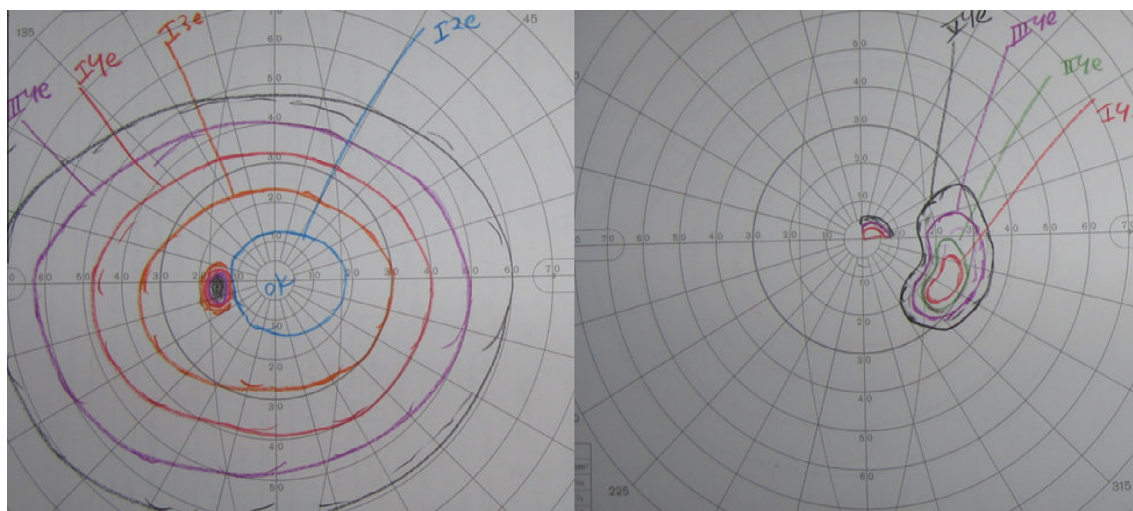


Figure 4. Goldmann's visual field test revealing a residual central and temporal island in the RE and a normal LE.

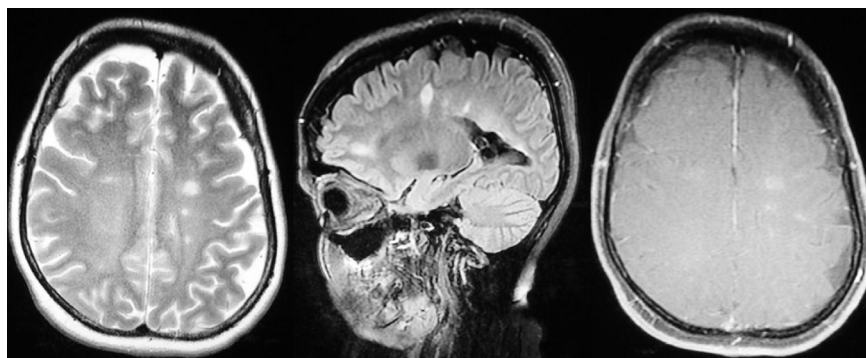


Figure 5. Cranial MRI performed two years later showing the presence of typical demyelinating periventricular and pericallosal lesions (some of them with contrast enhancement) (axial T2, sagittal FLAIR and axial T1 sequence after contrast injection).

in posterior uveitis: direct compression of the arteriole by a retinitis or chorioretinitis focus, arteriolar constriction due to neurotransmitter secretion by mast cells in response to the inflammatory stimulus, and infiltration of the vascular wall by inflammatory cells, causing a secondary arterial thrombosis.¹¹

However, in MS patients with associated optic neuritis and retinal vasculitis, some authors propose a mechanism of vessel compression secondary to optic nerve inflammation. Relevant studies include the investigation by Akarsu et al.,¹⁶

in which the retrobulbar hemodynamics were measured in patients with MS and optic neuritis, demonstrating hemodynamic worsening in the central retinal artery and in the posterior ciliary arteries. These authors propose that patients with optic neuritis might exhibit direct compression of the blood vessels inside the scleral canal. Alternatively, vasospasm might be produced secondary to an increase in plasma endothelin-1, which may act as a potent vasoconstrictor, thereby leading to increased blood flow resistance.

Our patient also presented optic nerve impairment, as enhancement was observed on the MRI after contrast injection. It is questionable whether this finding represented optic neuritis or, rather, edema of the optic nerve secondary to uveitis. Thus, although we believe that the fundamental mechanism of the vascular occlusion was inflammatory, we cannot rule out compression of the central retinal artery as it passed through the optic nerve head.

Conflict of interest

The authors declared that there is no conflict of interest.

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