

Grand Rounds

A 45-year-old man with unilateral optic disc edema and vision loss

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History

A 45-year-old man was referred to Beth Israel Deaconess Medical Center for evaluation of decreased vision in his left eye of 1 month's duration. He denied pain with eye movement and diplopia. His past medical history included photorefractive keratectomy in both eyes 2 years prior, rosacea, depression, and obesity. He had been seeing his eye doctor frequently for meibomianitis and dry eye syndrome.

Examination

On examination, visual acuity was 20/20 in the right eye and 20/50 in the left eye, with a relative afferent pupillary defect in the left eye. Extraocular motility was full. The patient identified 8/8 Ishihara color plates in the right eye and 0/8 color plates in the left eye. The anterior segment examination was unremarkable in both eyes. On dilated fundus examination, there was trace vitreous cell and diffuse disc edema in the left eye, with dilation of the peripapillary vessels; there was a partial macular star in the left eye. The right eye appeared normal (Figure 1).

Ancillary Testing

Humphrey 30-2 SITA-Fast automated visual field testing demonstrated scattered nonspecific loss in the right eye and generalized dense depression in the left eye, with a mean deviation of -4.50 dB in the right eye and -21.77 dB in the left eye (Figure 2). The following laboratory studies were drawn and results were unremarkable: complete blood count with differential, *Bartonella hensalae* IgG and IgM antibodies, Lyme disease IgG and IgM antibodies, *Toxoplasma gondii* IgG and IgM

antibodies, fluorescent treponemal antibody absorption (FTA-ABS), rapid plasma reagin (RPR), neuromyelitis optica IgG antibody (Aquaporin 4 protein antibody), angiotension converting enzyme (ACE) level, anti-neutrophil cytoplasmic antibody (ANCA), IgG subclasses, and serum protein electrophoresis.

Magnetic resonance imaging (MRI) of the brain with and without contrast was obtained and revealed tram track enhancement of the left optic nerve sheath, with no white matter lesions or other abnormalities (Figure 3).

Additional studies were performed, including a lumbar puncture, which revealed normal cerebrospinal fluid constituents, negative cytology, and insufficient cells to perform flow cytometry. Whole-body PET computed tomography was also negative for signs of sarcoidosis or malignancy.

Treatment

Steroid treatment was initially deferred because of concern for an infectious etiology. Eleven days after presentation, the patient's visual acuity had declined to 20/400 in the left eye, and the infectious work-up was negative. At that time, the patient was started on prednisone 80 mg daily.

Thirty-three days following the initiation of steroids visual acuity improved to 20/30 in the left eye. MRI of the orbit with and without contrast performed at that time showed near resolution of the enhancement (Figure 4); 53 days following the initiation of steroids showed the disc edema and macular star in the left eye had resolved (Figure 5).

Published March 29, 2019.

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doi:10.5693/djo.03.2019.02.002

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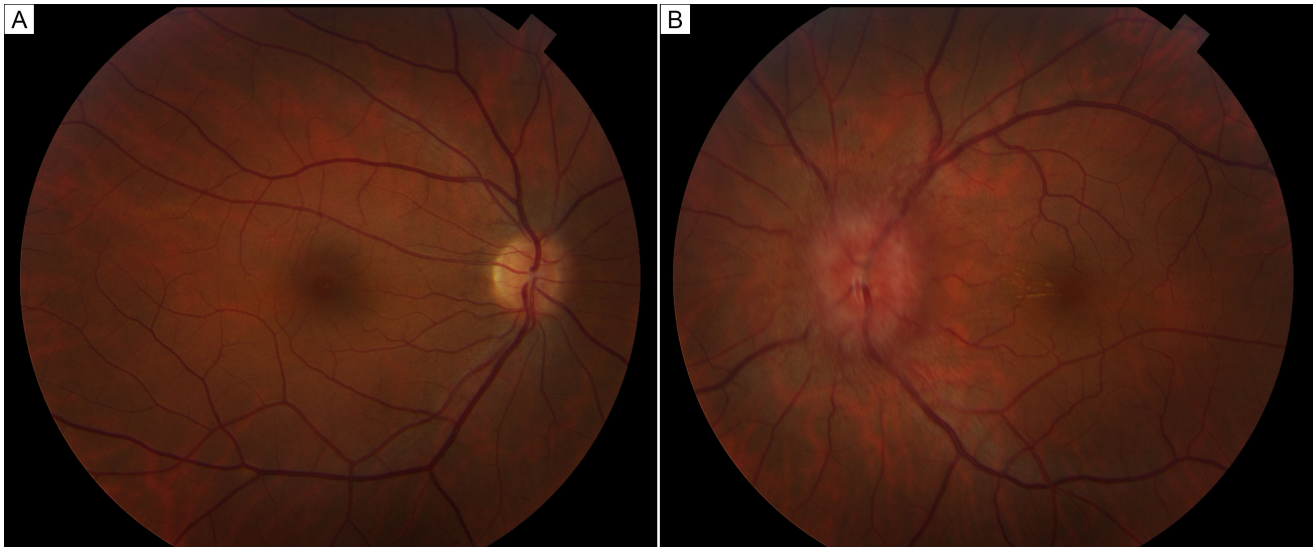


Figure 1. Initial fundus photographs demonstrating a normal posterior pole in the right eye and diffuse disc edema, dilation of the peripapillary vessels, and macular star in the left eye.

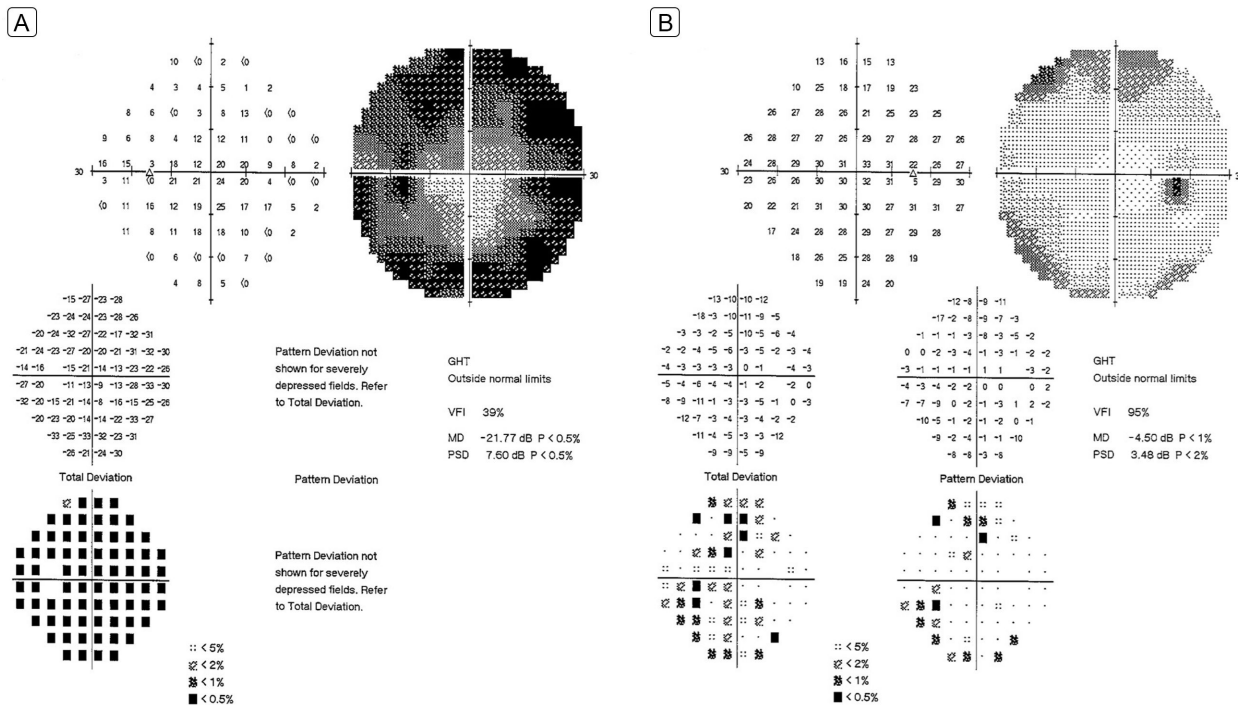


Figure 2. Initial Humphrey 30-2 SITA-fast automated visual field testing with scattered nonspecific loss in the right eye (B) and generalized depression with relative central sparing in the left eye (A).

With taper of prednisone to 10 mg over the next 3 months, the patient’s visual acuity in the left eye declined to 20/40, requiring an increase in the steroid dose.

The patient was placed on monthly pulse intravenous cyclophosphamide for 3 months followed by oral daily azathioprine. Despite this immunomodulatory therapy, the patient was unable to be weaned from steroid ther-

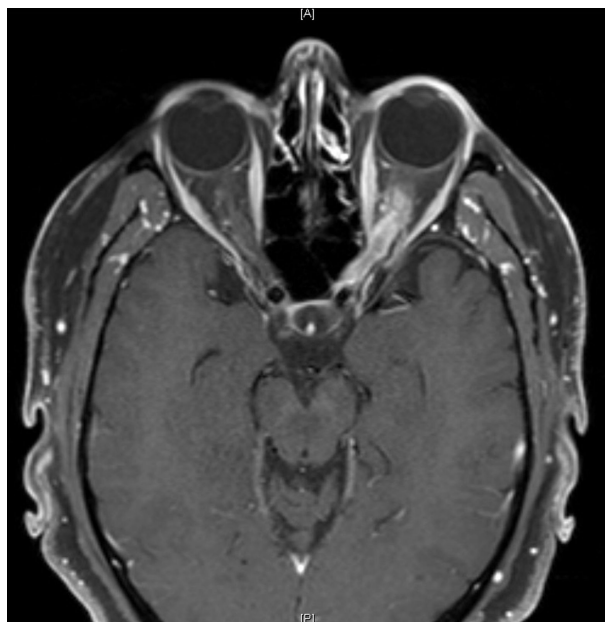


Figure 3. T1-weighted, post-contrast axial magnetic resonance imaging (MRI) of the brain demonstrating tram track enhancement of the left optic nerve sheath complex.



Figure 4. T1-weighted, post-contrast axial MRI of the orbit showing interval improvement in enhancement of the left optic nerve sheath complex.

apy over the 2 years following initial presentation. At prednisone doses below 10 mg, he reported decreased vision in the left eye and demonstrated left optic nerve



Figure 5. Fundus photograph of the left eye showing resolution in disc edema and macular star, with residual exudates in the nasal macula.

sheath enhancement on MRI. His condition remained exquisitely sensitive to steroids, with an increase in prednisone consistently effective in resolving his symptoms and MRI findings. The patient was switched to adalimumab, which facilitated discontinuation of corticosteroids. At his most recent visit, 6 months following initiation of adalimumab, the patient's visual acuity was stable (20/25 in each eye), and the examination showed temporal pallor of the left optic nerve. Humphrey 30-2 SITA-Fast automated visual field showed a corresponding nasal defect in the visual field of the left eye (Figure 6).

Differential Diagnosis

The initial presentation of a relative afferent pupillary defect, unilateral disc edema, and stellate macular exudates is suggestive of neuroretinitis. Causes of neuroretinitis include cat-scratch disease, toxoplasmosis, typhus, Lyme disease, syphilis, diffuse unilateral subacute neuroretinitis (DUSN), sarcoidosis, and inflammatory bowel disease. It can also be idiopathic.¹ The ocular symptoms are frequently preceded by a viruslike prodrome. The disc edema typically precedes the stellate maculopathy by 1 week. The macular star begins to fade by 4 weeks and is usually completely resolved by one year. Neuroretinitis is well known, but optic disc inflammation and associated retinal exudates may also be seen in other conditions, such as papilledema or hypertensive retinopathy.²⁻⁵

In this case, the initial findings prompted laboratory work-up for typical autoimmune or infectious causes of

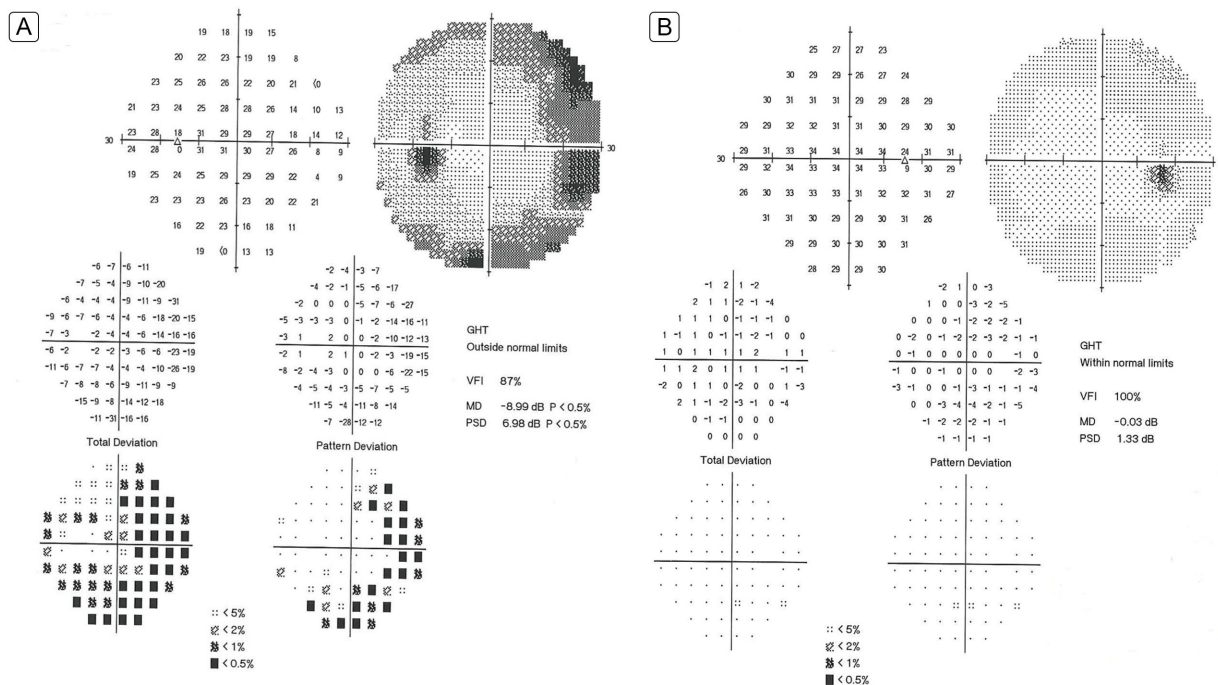


Figure 6. Final Humphrey 30-2 SITA-fast automated visual field testing with nasal defect in the left eye.

neuroretinitis, which was negative. An MRI of the brain was obtained to evaluate for a compressive lesion or evidence of infectious or autoimmune disease of the brain or orbit. The MRI study demonstrated tram track enhancement of the left optic nerve sheath. This finding shifted the differential diagnosis from neuroretinitis to optic perineuritis or optic nerve sheath meningioma. The subsequent clinical and radiological improvement with steroids was diagnostic of optic perineuritis rather than optic nerve sheath meningioma.

Optic perineuritis is characterized by inflammation of the optic nerve sheath and may be idiopathic or secondary to systemic disease, including Behçet disease, Crohn’s disease, granulomatosis with polyangiitis, giant cell arteritis, sarcoidosis, tuberculosis, syphilis, and metastasis.^{6–13} The patient’s extensive studies as outlined above did not reveal an etiology.

Diagnosis and Discussion

The patient was a 45-year-old man with gradual, painless decrease in vision in the left eye presenting with unilateral optic disc edema, partial macular star, and tram track enhancement of the left optic nerve sheath on MRI. He was diagnosed with idiopathic optic perineuritis and was treated successfully with corticosteroids and later adalimumab.

Two reports in the literature have presented similar cases of idiopathic optic perineuritis with unilateral disc edema and a macular star.^{14,15} Zhang et al¹⁴ reported a case involving enucleation because of pain and a concern for an optic nerve sheath meningioma; pathology demonstrated idiopathic optic perineuritis. Wals et al¹⁵ described a patient with a macular star, disc edema, and optic perineuritis who improved without treatment to baseline vision in 11 months; they presented the case as simultaneous optic perineuritis and neuroretinitis. In the case described here, the partial macular star is incomplete and indicates secondary subretinal fluid and exudation from the primary inflammation of the optic disc and optic sheath. For the present case, the diagnosis of optic perineuritis with associated optic disc and macular edema is more appropriate than simultaneous optic perineuritis and neuroretinitis.

This case highlights the importance of differentiating between optic neuritis and optic perineuritis, which is relevant clinically because of the similarity of presentation and difference in treatment (Table 1). Optic perineuritis and optic neuritis may be confused because patients with both diseases present with painful, monocular vision loss and disc edema. However, vision loss in optic perineuritis progresses over weeks, whereas in optic neuritis vision typically declines over the course of

Table 1. Differentiating optic neuritis and optic perineuritis. See ref. 6.

	Optic neuritis	Optic perineuritis
Presentation	Acute decrease in vision over days	Subacute decrease in vision over weeks
Age of onset	Usually young adults	Broader range
MRI findings	Enhancement of ON	Circumferential enhancement of ON sheath
Association with MS	Risk factor for developing MS	No association with MS

MRI, magnetic resonance imaging; *MS*, multiple sclerosis; *ON*, optic nerve.

a few days. Long-term optic neuritis is associated with a 50% 15-year risk of developing multiple sclerosis (MS), while there is no known relationship between optic perineuritis and MS.^{7,16} Finally, MRI is crucial to differentiate the diseases. MRI primarily shows enhancement of the optic nerve itself in optic neuritis and in the nerve sheath in optic perineuritis.⁷

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