

NAION: What To Do and When

IN THE SETTING OF NEW VISUAL ACUITY OR VISUAL FIELD LOSS AND A SWOLLEN OPTIC DISC, HOW SHOULD PATIENTS BE EVALUATED AND MANAGED BY THE COMPREHENSIVE OPHTHALMOLOGIST OR GLAUCOMA SPECIALIST?



BY PREM S. SOBRAMANIAN, MD, PhD

Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common non-glaucomatous optic nerve disorder in patients older than 50 years, although any age group may be affected. Patients typically present with sudden painless loss of vision in one eye.¹ Most have both loss of central acuity and a visual field (VF) defect, although VF loss alone may occur. Visual acuity may range from 20/20 to hand motions or worse, and a relative afferent pupillary defect is almost always present in the affected eye if the fellow eye is normal.

VF testing should be performed, and it will commonly demonstrate altitudinal defects in patients with NAION (Figure 1). Fundus examination in the acute phase (within 2 weeks of onset of vision loss) demonstrates hyperemic swelling of the affected optic disc, with possible dilation of capillaries and venules and retinal nerve fiber layer hemorrhages, as shown in Figure 1. Swelling may be diffuse or confined to a sector of the optic disc, and it does not necessarily correspond to the area of VF loss. The contralateral disc is usually normal (see below for exceptions), aside from having a small or crowded appearance (Figure 1).

The pathogenesis of NAION is not fully understood, but it is thought to involve hypoperfusion of the posterior ciliary arterial circulation, which leads to axonal swelling and additional compression of the vasculature in an escalating vicious cycle. This process culminates in axonal dysfunction and eventual cell death from ischemia.²

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for NAION includes arteritic anterior

ischemic optic neuropathy (AAION), which can occur with any type of vasculitis. Giant cell arteritis must be considered in all patients older than 50 years who present with acute vision loss and optic disc swelling. The Table lists signs and symptoms that should increase suspicion for AAION rather than NAION.

It is advisable to measure erythrocyte sedimentation rate and C-reactive protein levels in patients over age 50 years with suspected NAION. If the lab results are abnormal

AT A GLANCE

- ▶ Nonarteritic anterior ischemic optic neuropathy is a common cause of optic neuropathy in patients with demographics that match those of many glaucoma patients.
- ▶ The presence of optic disc pallor should alert the ophthalmologist to a nonglaucomatous process.
- ▶ Although no treatment for NAION is available at this time, prompt referral of patients for treatment of systemic risk factors may protect their remaining vision and overall health.

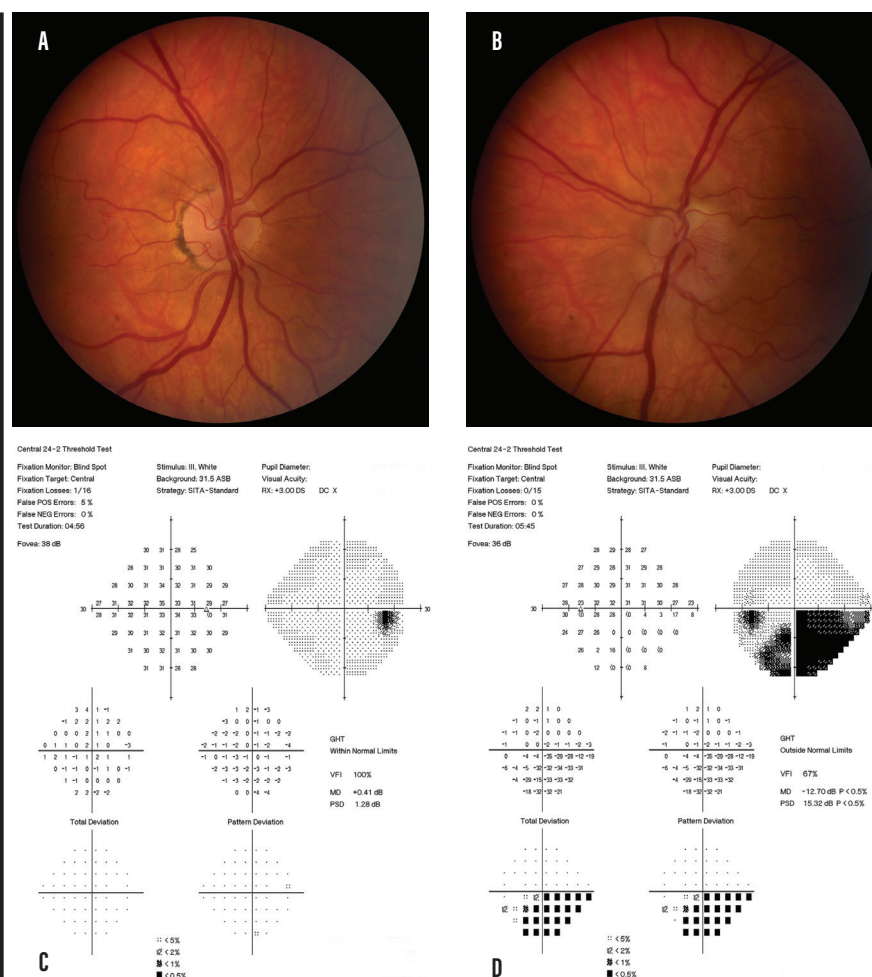


Figure 1. Findings consistent with NAION in a 57-year-old man who presented with sudden, painless vision loss in his left eye. Right optic disc with minimal cupping and no swelling or hemorrhage (A). Left optic disc with hyperemic swelling and dilation of superficial disc capillaries; a few hemorrhages were seen temporally (B). Normal VF in the right eye (C). Incomplete inferior altitudinal VF defect in the left eye (D).

for the patient's age, consultation with his or her primary care provider and/or a neuro-ophthalmologist about the need for empiric steroid therapy and temporal artery biopsy is recommended.

The primary risk factor for NAION is thought to be an anatomically crowded optic disc, the so-called *disc at risk*. Additional systemic risk factors include hypertension, diabetes, ischemic heart disease,³ and hypercholesterolemia,⁴

and patients should be referred to their primary care providers for diagnosis and management of these modifiable risk factors.

More recently, obstructive sleep apnea has been found to be much more common in patients with NAION than in control populations.⁵⁻⁷ Patients with newly diagnosed NAION should be screened and possibly treated for obstructive sleep apnea, as adherence to treatment with continuous positive airway pressure ventilation may reduce⁸ but not eliminate⁹ the risk of subsequent fellow eye involvement. Patients should also be questioned about their use of erectile dysfunction drugs, as a two- to threefold increased risk of NAION has been found with use of phosphodiesterase-5 inhibitors.¹⁰

Other differential diagnoses include optic neuritis, which is usually less sudden in onset and is accompanied by pain; infiltrative optic neuropathy, which is usually painless with a subacute onset, possibly more severe vision loss, and disc swelling with pallor; and central or branch retinal vein occlusion, in which retinal hemorrhages are usually more prominent in relationship to optic disc swelling. Appropriate tests, including fluorescein angiography and possibly neuroimaging, should be considered if there is diagnostic uncertainty; however, NAION remains a clinical diagnosis.

Because the primary risk factor for NAION is a disc at risk with a small or nonexistent cup, and optic disc swelling is seen in the affected eye acutely, most cases of NAION are unlikely to be confused with glaucoma. However, the VF defects in NAION and glaucoma are similar in that they both tend to respect the horizontal meridian and may spare the central VF (Figure 2). Patients may present to the ophthalmologist months or years after VF loss has occurred, and some patients may be unaware of the VF loss if it is mild or does not encroach upon fixation.

TABLE. SYMPTOMS AND FINDINGS THAT HEIGHTEN CONCERN FOR NAION

Systemic symptoms (jaw claudication, weight loss, fevers)
Age greater than 70 years (giant cell arteritis risk rises exponentially with decade of life)
Pale rather than hyperemic disc swelling
Presence of cotton wool spots/nerve fiber layer infarcts
Visual acuity worse than 20/200
Patchy visual field loss (not respecting the horizontal) to suggest choroidal ischemia

OLD NAION VERSUS GLAUCOMA

How can the glaucoma specialist distinguish old NAION from glaucoma? Atrophic cupping may occur weeks or months after NAION, although the cup is shallower in NAION than in glaucoma.¹¹ OCT evaluation of the retinal nerve fiber layer or macular ganglion cell complex may not distinguish remote NAION from glaucoma, as the patterns of loss may be identical (Figure 2).

The presence of optic disc pallor should alert the ophthalmologist to a nonglaucomatous process. As shown in Figure 2, the superior optic disc pallor in the optic nerve that corresponds to the inferior arcuate field defect should prompt further investigation for a cause other than glaucoma. Further, although NAION is the most likely cause of this pattern of visual acuity loss or VF loss, particularly in the setting of a fellow-eye disc at risk, other conditions such as compressive optic neuropathy must be considered if optic disc swelling was not previously observed in the patient. Referral to a neuro-ophthalmologist in such cases should be considered.

POTENTIAL THERAPIES

There is no accepted therapy for acute NAION aside from risk factor modification. Corticosteroids have been studied for their ability to reduce edema and thus potentially improve functional outcomes, and a large retrospective series of patients treated with oral prednisone reported superior visual outcomes compared with untreated patients.¹² However, a recent prospective, randomized, masked, placebo-controlled study of NAION patients enrolled within 1 month of disease onset showed that oral prednisolone started at 80 mg daily for 2 weeks and then tapered was no more effective than placebo.¹³

Similarly, case reports have suggested that bevacizumab (Avastin, Genentech) may lead to rapid resolution of disc edema in acute NAION,¹⁴ but visual outcomes in large case series have been equivalent to natural history.¹⁵ A phase 2/3 double-masked, randomized, drug-versus-sham-treatment clinical trial (NCT02341560) is being conducted by Quark Pharmaceuticals to evaluate the efficacy of an intravitreal injection of QPI-1007, a small

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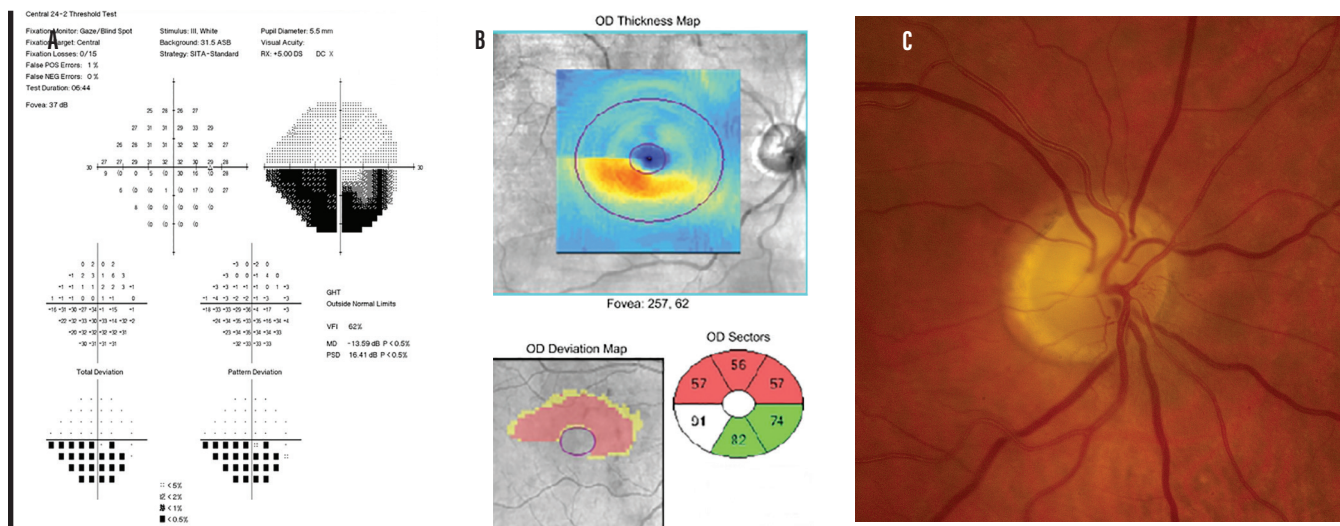


Figure 2. Late findings in NAION. A 75-year-old man was discovered to have VF loss in the right eye. Right eye VF showed an inferior arcuate versus incomplete altitudinal defect that spared fixation; visual acuity was 20/20 (A). Corresponding superior retinal nerve fiber layer and macular ganglion cell complex loss as seen on spectral-domain OCT (B). Superior pallor without significant cupping of the right optic disc (C), consistent with remote or old NAION, not glaucoma.

inhibitory RNA that blocks caspase-2 expression, and thus apoptosis, in the treatment of acute NAION.

CONCLUSION

NAION is a common cause of optic neuropathy in patients with demographics that match those of many glaucoma patients. Acute NAION is rarely confused with glaucoma, but a patient diagnosed with VF loss months or years after an acute event may be referred initially to a glaucoma specialist because of atrophic cupping or subtle pallor that is confused with glaucomatous changes. Although no treatment for NAION is available at this time, prompt referral of patients for treatment of systemic risk factors may protect both their remaining vision and their overall health. ■

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