

BEWARE THE IMPOSTOR

Differentiating glaucoma from anterior ischemic optic neuropathy.

BY SIDDARTH RATHI, MD, MBA, AND DAVID S. GREENFIELD, MD

CASE PRESENTATION



A 77-year-old woman was referred for an evaluation of vision loss in her right eye. She had a history of medically controlled noninsulin-dependent diabetes mellitus and hypertension. In the right eye, BCVA measured 20/80,

untreated IOP was 20 mm Hg and central corneal thickness was 545 μm . The optic disc was pale with minimal cupping and no focal neural rim tissue loss (Figure 1). There was an inferior and centralized visual field (VF) depression (Figure 2), and spectral domain optical coherence tomography showed diffuse retinal nerve fiber layer (RNFL) atrophy (Figure 3). Orbital and cranial magnetic resonance imaging was negative for compressive lesions.

The diagnosis was nonarteritic ischemic optic neuropathy (NAION) in the right eye.



Figure 1. Rim pallor in excess of cupping. Note the absence of focal thinning or notching of the neural rim.

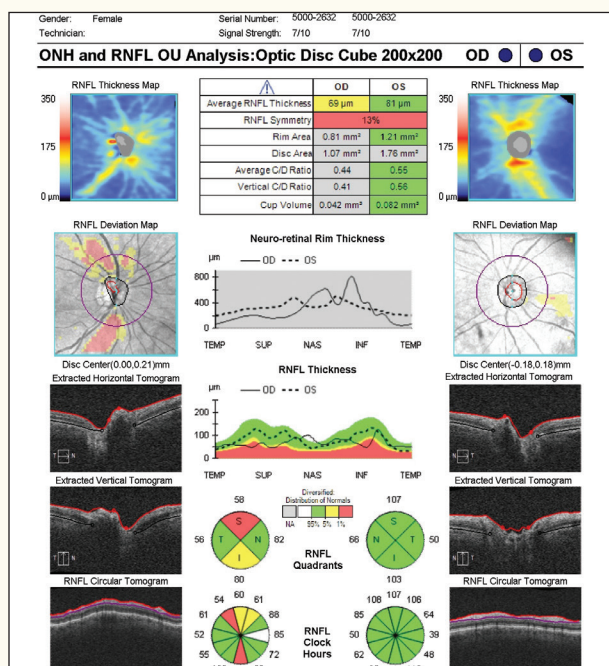


Figure 2. Spectral domain optical coherence tomography shows diffuse atrophy of the peripapillary RNFL of the right eye.

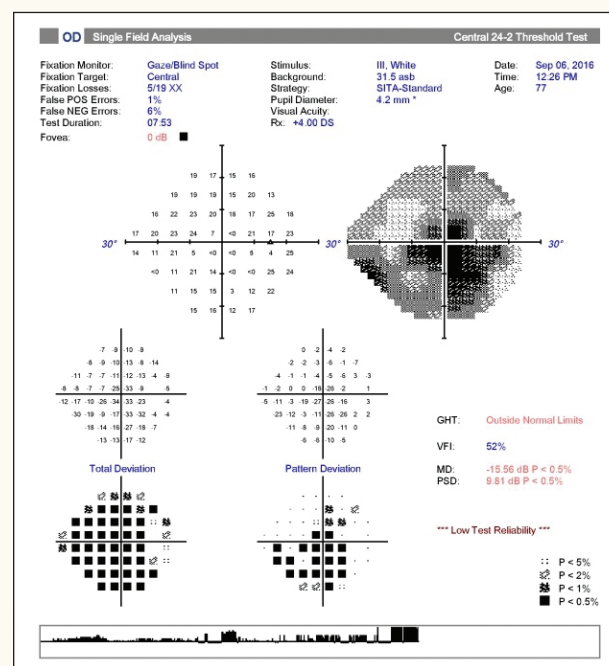


Figure 3. Standard automated visual field testing demonstrates an inferior depression with centralized involvement.

TABLE. ANCILLARY TESTS IN THE DIAGNOSTIC EVALUATION OF NORMAL-TENSION GLAUCOMA

Test	Symptoms	Ocular Signs
Brain/orbital MRI	Unexplained vision loss	Optic disc pallor or edema, 20/40 acuity or worse, vertically aligned visual field defect, proptosis
Carotid Doppler	Transient visual obscuration (amaurosis fugax)	Retinal emboli, iris or retinal neovascularization, midperipheral intraretinal hemorrhage
ESR, C-reactive protein	Temporal headache, jaw claudication, scalp tenderness, weight loss, muscle pain	Optic disc pallor or edema, retinal artery occlusion, reduced temporal artery pulse with tenderness or induration
CBC	History of anemia or recent blood loss	Optic disc pallor, retinal hemorrhage
VDRL, FTA-ABS	History of syphilis, reduced vision	Optic disc pallor or edema, uveitis or chorioretinitis, vasculitis, interstitial keratitis

Reprinted with permission of Slack Incorporated from Greenfield DS.¹

Abbreviations: MRI, magnetic resonance imaging; ESR, erythrocyte sedimentation rate; CBC, complete blood count; VDRL, Venereal Disease Research Laboratory; FTA-ABS, fluorescent treponemal antibody absorbed.

THE CUPPED DISC

Nonglaucomatous disorders may produce optic disc cupping and VF disturbances that resemble the clinical profile of open-angle glaucoma associated with normal IOP (normal-tension glaucoma [NTG]). It is important that clinicians recognize these impostors, which include dominant optic atrophy, optic nerve infarction, trauma, methanol toxicity, demyelinating optic neuritis, syphilis, and optic nerve compression.

Although Trobe and colleagues reported that neuroretinal rim pallor was 94% specific in predicting nonglaucomatous cupping and that focal or diffuse neuroretinal rim obliteration was 87% specific in predicting glaucomatous cupping,² clinically differentiating these disorders from glaucoma is subjective and challenging. Thus, ancillary tests have been proposed in the diagnostic evaluation of NTG (Table). Most of these tests are unnecessary in eyes with typical glaucomatous features.

Compressive visual pathway lesions simulating NTG are uncommon.³ Ahmed and colleagues found intracranial masses in only 6% of NTG patients.⁴ The likelihood of identifying intracranial lesions increases in patients younger than age 50 and in those with a visual acuity below 20/40, optic nerve rim pallor, or vertically aligned VF defects.³

ANTERIOR ISCHEMIC OPTIC NEUROPATHY VERSUS GLAUCOMA

Anterior ischemic optic neuropathy (AION) is the most common acute optic neuropathy among individuals over

the age of 50.⁵ The condition is characterized by sudden vision loss, disc swelling, and VF defects.⁶ Arteritic AION (AAION) represents a vasculitic⁵ occlusion of the posterior ciliary arteries.⁶ NAION is typically idiopathic and presumably results from vascular dysregulation and impaired microcirculation of the optic nerve head.^{5,7} Many patients have coexisting systemic vascular disease.

After the resolution of disc edema, AION can be difficult to differentiate from NTG. Both conditions are associated with normal IOP and produce nerve fiber bundle VF defects, RNFL atrophy, and atrophic disc cupping. Although optic nerve cupping after NAION is uncommon, approximately 50% of eyes with AAION develop optic disc cupping.⁸ Danesh-Meyer and colleagues compared optic disc topography in eyes with AION, NAION, and glaucoma.⁶ After controlling for the degree of VF loss, they found that glaucomatous eyes had larger, deeper cups and less rim volume. Other distinguishing features of AAION include a history of jaw claudication, scalp tenderness, weight loss, headache, and fatigue. Fellow eyes with NAION often have a crowded “cupless” disc or disc at risk. (See *Clinical Pearls*.)

MANAGEMENT

Patients with suspected AAION warrant systemic corticosteroid initiation, prompt laboratory evaluation, and a temporal artery biopsy to confirm granulomatous vasculitis. There are no proven treatments for NAION, but management of vascular risk factors should be addressed.

CLINICAL PEARLS

- Vascular risk factors contribute to the pathogenesis of glaucoma and anterior ischemic optic neuropathy (AION). They include systemic hypertension and hypotension, vasospasm, and reduced ocular perfusion pressure.
- Unlike in glaucoma, AION patients typically report sudden vision loss, frequently upon awakening.
- Neural rim pallor in excess of cupping is consistent with AION.
- The optic nerve head (ONH) in eyes with nonarteritic ischemic optic neuropathy is crowded and “cupless,” producing a disc at risk. A common sequela of arteritic AION is ONH cupping and pallor.
- Glaucoma diagnosis should be predicated on the clinical detection of neural rim narrowing, retinal nerve fiber layer (RNFL) atrophy, and posterior deformation of the ONH (cupping). Remaining neural rim tissue color is pink, not pale.
- A history of optic disc hemorrhage in the absence of optic disc edema is consistent with glaucoma.
- Patients with AION often have reduced central vision and dyschromatopsia (abnormal color vision).
- The pattern of visual field loss may not distinguish glaucomatous damage from AION, because both may produce altitudinal scotoma, central or paracentral scotoma, and diffuse visual field depression.
- The pattern of RNFL atrophy on optical coherence tomography may not distinguish glaucomatous damage from AION, because both conditions may produce either diffuse or localized RNFL atrophy.

As reported in the Collaborative Normal-Tension Glaucoma Study (CNTGS), therapy should achieve a 30% IOP reduction in glaucomatous eyes.⁹ The Low-Pressure Glaucoma Treatment Study (LoGTS) demonstrated reduced VF progression in eyes treated with brimonidine 0.2% compared to timolol 0.5% despite equivalent IOP lowering in both cohorts.¹⁰

NTG eyes with confirmed VF progression despite a low treated IOP may benefit from filtration surgery to achieve single-digit IOP targets. Glaucoma drainage devices typically do not produce sufficiently low IOP levels. Schultz and colleagues demonstrated that single-digit pressures may be safely achieved in 80% of eyes after trabeculectomy,¹¹ which had a beneficial effect on slowing or preventing further VF progression.¹² In patients with high myopia or in very elderly patients on anticoagulation therapy, trabeculectomy should be avoided, given the high risk of postoperative hypotony and associated complications. ■



AT A GLANCE

- Nonglaucomatous disorders may produce optic disc cupping and visual field disturbances that resemble the clinical profile of normal-tension glaucoma. It is important that clinicians recognize these impostors.
- Anterior ischemic optic neuropathy is the most common acute optic neuropathy among individuals over the age of 50. The condition is characterized by sudden vision loss, disc swelling, and visual field defects.
- After the resolution of disc edema, anterior ischemic optic neuropathy can be difficult to differentiate from normal-tension glaucoma.

Supported in part by an unrestricted grant from Research to Prevent Blindness in New York.

1. Greenfield, DS. In which patients with glaucoma should I perform neuroimaging, cardiovascular evaluation, and/or laboratory testing? In: Gedde S, ed. *Curbside Consultation in Glaucoma: 49 Clinical Questions*. Thorofare, NJ: Slack; 2015:71-74.
2. Trobe JD, Glaser JS, Cassady J, et al. Nonglaucomatous excavation of the optic disc. *Arch Ophthalmol*. 1980;98(6):1046-1050.
3. Greenfield DS, Siatkowski RM, Glaser JS, et al. The cupped disc. Who needs neuroimaging? *Ophthalmology*. 1998;105(10):1866-1874.
4. Ahmed II, Feldman F, Kucharczyk W, Trope GE. Neuroradiologic screening in normal-pressure glaucoma: study results and literature review. *J Glaucoma*. 2002;11(4):279-286.
5. The patient with decreased vision: classification and management. In: Foroozan R, Bhatti T, Falardeau J, et al. *Basic and Clinical Science Course: Neuro-ophthalmology*. San Francisco, CA: American Academy of Ophthalmology; 2013.
6. Danesh-Meyer HV, Boland MV, Savino PJ, et al. Optic disc morphology in open-angle glaucoma compared with anterior ischemic optic neuropathies. *Invest Ophthalmol Vis Sci*. 2010;51(4):2003-2010.
7. Hayreh SS. Anterior ischaemic optic neuropathy. Differentiation of arteritic from non-arteritic type and its management. *Eye (Lond)*. 1990;4(1):25-41.
8. Quigley H, Anderson DR. Cupping of the optic disc in ischemic optic neuropathy. *Trans Sect Ophthalmol Am Acad Ophthalmol Otolaryngol*. 1977;83(5):755-762.
9. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. Collaborative Normal-Tension Glaucoma Study Group. *Am J Ophthalmol*. 1998;126(4):487-497.
10. Krupin T, Liebmann JM, Greenfield DS, et al; Low-Pressure Glaucoma Treatment Study Group. A randomized trial of brimonidine versus timolol in preserving visual function: results from the Low-Pressure Glaucoma Treatment Study. *Am J Ophthalmol*. 2011;151(4):671-681.
11. Schultz SK, Iverson SM, Shi W, Greenfield DS. Safety and efficacy of achieving single-digit intraocular pressure targets with filtration surgery in eyes with progressive normal-tension glaucoma. *J Glaucoma*. 2016;25(2):217-222.
12. Iverson SM, Schultz SK, Shi W, et al. Effectiveness of single-digit IOP targets on decreasing global and localized visual field progression after filtration surgery in eyes with progressive normal-tension glaucoma. *J Glaucoma*. 2016;25(5):408-414.

David S. Greenfield, MD

- professor of ophthalmology, Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Palm Beach Gardens, Florida
- (561) 515-1500; dgreenfield@med.miami.edu

Siddharth Rath, MD, MBA

- glaucoma fellow, Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Palm Beach Gardens, Florida