HOW TO RECOGNIZE GLAUCOMA FROM ITS COMMON MASQUERADERS

Helpful pearls for making the distinction.

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Glaucoma is a progressive optic neuropathy characterized by the degeneration of retinal ganglion cells and their axons, resulting in retinal nerve fiber layer loss and corresponding visual field defects. The condition is complex and has varying presentations and rates of progression. Proper treatment of glaucoma requires an accurate diagnosis, which can be challenging when patients present with clinical findings that are similar to those associated with glaucoma but are actually manifestations of a different condition.

It is important for clinicians to rule out these masquerading conditions in order to provide appropriate treatment. This article discusses common causes of glaucoma misdiagnosis and key characteristics that can help differentiate glaucoma from its masqueraders.

OCULAR HYPERTENSION

The Ocular Hypertension Treatment Study defines ocular hypertension (OHT) as an IOP between 24 mm Hg and 32 mm Hg in one eye and between 21 mm Hg and 32 mm Hg in the other eye, in the absence of any visual field defects or optic nerve involvement.[1] It is estimated that 4% to 7% of individuals over the age of 40 years in the United States have OHT.[1]

Although elevated IOP is a significant risk factor for the development of glaucoma, not every patient with OHT develops glaucoma, making this finding a common masquerader of open-angle glaucoma (OAG). The results from the Ocular Hypertension Study demonstrate that early medical treatment of patients with OHT reduces the 5-year incidence of primary OAG (POAG) by 60%; however, this benefit is greatest among high-risk patients.[1] High-risk characteristics for conversion to POAG include older age, higher IOP, central corneal thickness, larger vertical cup-to-disc ratio, and higher pattern standard deviation on the visual field.[2] Reviewing these characteristics in patients with OHT can help differentiate high-risk individuals from low-risk individuals.

Patients who fall into the low-risk category can be monitored without treatment using serial visual field and OCT testing, whereas patients in the high-risk category would benefit from early treatment for POAG. In addition to identifying high-risk characteristics, assessment of structural and functional parameters is important for determining whether POAG has already developed and/or if it is progressing.

TABLE. Common OAG Masqueraders That Can Present With Optic Nerve Cupping

CONDITION	CAUSES
Compressive optic neuropathy	• Tumors along the optic nerve or within the orbit (eg, pituitary adenoma, meningioma) • Orbital disease (eg, thyroid eye disease) • Vascular lesions (eg, aneurysm, fistula)
Noncompressive optic neuropathy	• Hereditary disease (eg, Leber hereditary optic neuropathy, dominant optic atrophy, morning glory syndrome) • Trauma • Ischemic disease (eg, NAION) • Demyelinating disease (eg, multiple sclerosis)
Other	• Retinal vascular occlusions (eg, branch retinal artery occlusion) • Myopic discs

Abbreviations: NAION, nonarteritic anterior ischemic optic neuropathy; OAG, open-angle glaucoma

OPTIC NERVE CHARACTERISTICS

Cupping

Cupping of the optic nerve head is a hallmark feature of glaucoma; however, up to 20% of patients who present with cupping but who do not have glaucoma are misdiagnosed and treated for the condition.[3-5] Other ocular diseases, or manifestations of ocular diseases, can result in pathologic cupping that may masquerade as glaucoma (Table).

Careful history and evaluation can provide valuable information to distinguish between glaucomatous and nonglaucomatous disease. The color of the rim is one of the most important factors to evaluate in patients with cupping.

Pallor

Pallor extending beyond the cup into the rim of the nerve is indicative of a nonglaucomatous etiology and is reported to be approximately 90% specific for nonglaucomatous optic atrophy.[5] Even in advanced glaucoma, where there is an extremely thin rim due to cupping, the neuroretinal rim remains a healthy color until the end stage of the disease.

Rim Thinning

Another important feature to be aware of in differentiating glaucoma masqueraders is the location and the amount of rim thinning. Traditionally, vertical elongation and notching of the neuroretinal rim favor a glaucoma diagnosis. This loss tends to be focal in nature and specifically affects the superior and inferior quadrants, giving the characteristic vertically excavated appearance. Although rim thinning has only been reported to be 47% specific for glaucoma, obliteration of the rim has an 87% specificity for the disease.[5] Eyes with nonglaucomatous disease are characterized by diffuse rim loss that will rarely present as complete loss.[5,6] Other features commonly seen in glaucomatous eyes include the presence of disc hemorrhages and beta zone peripapillary atrophy.

RETINAL VASCULAR DISEASE

Retinal diseases, such as vascular occlusions, can result in changes in the appearance of the optic nerve head and masquerade as OAG. Arterial occlusions, particularly old branch arterial occlusions, can complicate the clinician's ability to make an appropriate diagnosis because the retinal tissue will appear normal after resolution of the event. These patients may present with pallor and cupping of the optic

AT A GLANCE

- Elevated IOP is not only a risk factor for the development of glaucoma, but also a masquerader of open-angle glaucoma.
- The location and amount of rim thinning is another important feature to be aware of in differentiating glaucoma masqueraders (typically, vertical elongation and notching of the neuroretinal rim indicate glaucoma).
- The presence of disc pallor and a history of sudden, painless vision loss should alert the clinician to a nonglaucomatous etiology.

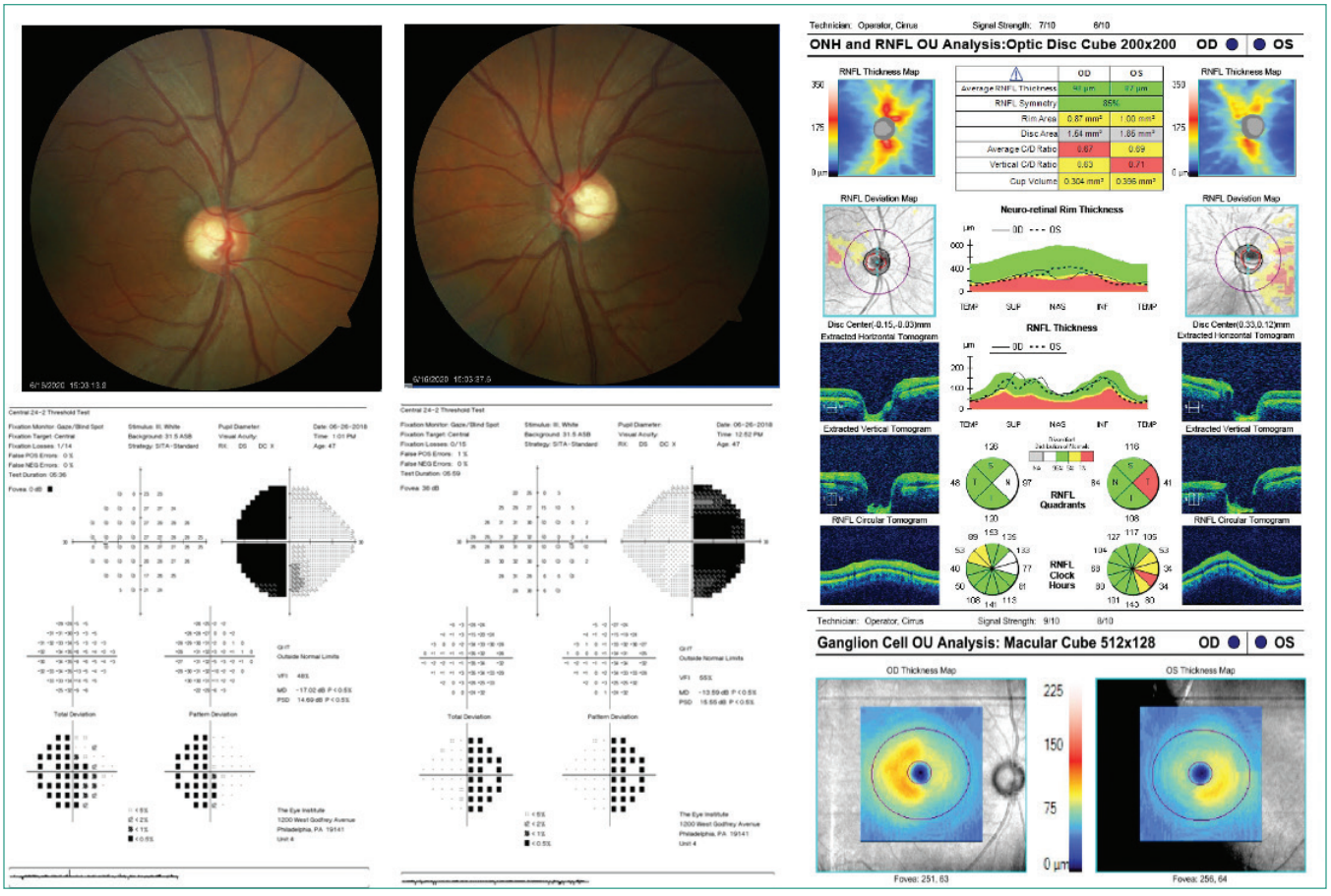

Figure. Optic nerve photos with asymmetric cupping and temporal pallor masquerade as glaucoma (A). Visual field with hemifield defects (B). Retinal nerve fiber layer scan with temporal thinning (C). Ganglion cell complex defects respecting the vertical meridian indicate a nonglaucomatous etiology (D).

nerve years after the initial event, with a corresponding visual field defect that mimics glaucoma.

In fact, approximately 24% of patients present with a superior defect and 29% present with an inferior nasal defect.[7] OCT imaging of the retinal tissue is helpful in making the appropriate diagnosis and will demonstrate thinning of the inner retinal layers, which is not usually seen in glaucoma. In cases of vein occlusions, an additional finding can include collateral vessels, which may help identify the nonglaucomatous etiology.

OPTIC NEUROPATHIES

Anterior ischemic optic neuropathy may be either arteritic (AAION) or nonarteritic (NAION) and can present with findings that mimic glaucoma. Specifically, pallor with cupping of the optic nerve occurs more frequently in patients with AAION (92%) than in patients with NAION (2%).[8,9] A corresponding visual field defect is often present with ischemic optic neuropathy and, although there can be variable visual field defects, a relatively inferior altitudinal defect with absolute inferior nasal defect is the most common pattern specific to NAION.[10] The presence of disc pallor and a history of sudden, painless vision loss should alert the clinician to a nonglaucomatous etiology.

Compressive optic neuropathy may result in glaucomatous-appearing optic nerve cupping (Figure). This can be seen in cases of pituitary adenomas, meningiomas, and other lesions along the optic nerve and within the orbit. Some differentiating features between compressive optic neuropathy and glaucoma include the presence of optic nerve pallor, reduced visual acuity, reduced color vision, and atrophy of the temporal portion of the optic nerve, which can be seen on OCT.[8]

RULING OUT GLAUCOMA

Identifying nonglaucomatous cupping is challenging, but certain distinguishing characteristics should be considered when evaluating suspect patients. Age is a primary risk factor for the development of glaucoma, therefore patients younger than 50 years of age who present should raise suspicion for a nonglaucomatous etiology.[8,11] Another important characteristic is the patient's level of visual acuity and their color vision. These tend to be preserved in the early stages of the disease because glaucoma typically spares the papillomacular bundle until

(continued on page 50)

(continued from page 46)
later stages. Poor visual acuity has been reported to have 77% specificity and is a hallmark for most nonglaucomatous optic neuropathies.[6,11] Glaucoma is well known to be an asymptomatic disease. There should be a high level of suspicion of a nonglaucomatous etiology when a patient presents with sudden or progressive vision changes or with a history of systemic symptoms.[8] Because not all retinal ganglion cells are affected equally in early glaucoma, color vision also tends to be preserved until late in the disease process. In contrast, ischemic, compressive, and other nonglaucomaotus optic neuropathies typically do not preserve color vision.[8]

With glaucoma, optic nerve changes should correspond to visual field defects, characteristically seen as nasal steps and arcuate scotomas. When the amount of visual field loss is out of proportion to optic disc cupping, or when visual fields respect the vertical midline, a nonglaucomatous etiology should be suspected.[8]

WATCH FOR THE SIGNS

Differentiating glaucoma from masqueraders can be difficult, but it is not impossible. Although nonglaucomatous cupping can be seen in a variety of disorders, obtaining a detailed history, performing a thorough ocular examination that includes color vision testing, and paying close attention to the color of the optic nerve can aid in making the appropriate diagnosis.

Color fundus photos can be helpful when evaluating for subtle optic nerve characteristics. Use of imaging modalities, including visual fields and OCT, can also help to distinguish cases that are nonglaucomatous in nature. Although retinal nerve fiber layer thinning is a common finding in both glaucoma and other optic neuropathies, the superior-temporal and inferior-temporal regions of the optic nerve head are more likely to be affected in glaucoma. Eye care providers should understand how to differentiate glaucoma from its masqueraders, so that the correct diagnosis is made and appropriate treatment is initiated. ■

1. Kass MA. The Ocular Hypertension Treatment Study. *Arch Ophthalmol*. 2002;120(6):701.
2. Gordon MO, Kass MA. What we have learned from the Ocular Hypertension Treatment Study. *Am J Ophthalmol*. 2018;189:xxiv-xxvii.
3. Trobe JD, Glaser JS, Cassady JC. Optic atrophy. Differential diagnosis by fundus obversation alone. *Arch Ophthalmol*. 1980;98(6):1040-1045.
4. Dias DT, Ushida M, Battistella R, Dorairaj S, Prata TS. Neuroophthalmological conditions mimicking glaucomatous optic neuropathy: analysis of the most common causes of misdiagnosis. *BMC Ophthalmol*. 2017;17(1):2.
5. Piette SD, Sergott RC. Pathological optic-disc cupping. *Curr Opin Ophthalmol*. 2006;17(1):1-6.
6. Zhang YX, Huang HB, Wei SH. Clinical characteristics of nonglaucomatous optic disc cupping. *Experimental and Therapeutic Medicine*. 2014;7(4):995-999.
7. Hayreh SS, Podhajsky PA, Zimmerman MB. Branch retinal artery occlusion: natural history of visual outcome. *Ophthalmology*. 2009;116(6):188-194.e1-4.
8. Waisberg E, Micieli JA. Neuro-ophthalmological optic nerve cupping: an overview. *Eye Brain*. 2021;13:255-268.
9. Danesh-Meyer HV, Savino PJ, Sergott RC. The prevalence of cupping in end-stage arteritic and nonarteritic anterior ischemic optic neuropathy. *Ophthalmology*. 2001;108(3):593-598.
10. Hayreh SS, Zimmerman B. Visual field abnormalities in nonarteritic anterior ischemic optic neuropathy: their pattern and prevalence at initial examination. *Arch Ophthalmol*. 2005;123(11):1554-1562.
11. Greenfield DS. Glaucomatous versus nonglaucomatous optic disc cupping: clinical differentiation. *Semin Ophthalmol*. 1999;14(2):95-108.

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