RATIONALIZING THE RED: WHEN RNFL ATROPHY IS NOT GLAUCOMA

Having as much information as possible is essential for proper diagnosis and treatment.

BY KATHERINE RACHON, OD, FAAO, DIPL ABO

Most patients we examine are screened for glaucoma in some way, whether by asking them about their family history, checking their IOP, getting an undilated view of their optic nerve, or a doing a full comprehensive examination with an OCT. We check these things for good reason: Roughly 80 million people worldwide have glaucoma, and 3 million of those people live in the United States. It is estimated that that number is only half of the actual amount of people living with glaucoma.[1,2]

In most cases, glaucoma is a straightforward diagnosis. The patient's IOP is elevated, and they have an increased cup-to-disc ratio and a family history that prompts testing and a treatment plan. However, when the atrophy on the OCT of the nerve doesn't quite seem to fit with a glaucomatous optic neuropathy, a deeper look is needed. The two cases below are examples of situations in which the patient's diagnosis wasn't cut and dry and required further examination.

CASE NO. 1: AN ANOMALOUS NERVE

Initial Presentation

A 45-year-old White male presented to our clinic for a glaucoma evaluation due to elevated IOP and atrophy seen on the optic nerve OCT. He had no relevant medical history and was not taking any topical ocular medications. He did note a positive family history of glaucoma with his paternal grandmother. His VA was 20/20 OD with a refraction of -1.50 + 0.75 x 026 and 20/20 OS with a refraction of -1.50 +1.25 x 114. The patient's IOP was measured with Goldman applanation tonometry at 30 mm Hg OD and 26 mm Hg OS. We continued the glaucoma evaluation with a pachymetry measurement, which was 588 µm OU. An optic nerve OCT was obtained, which showed borderline superior retinal nerve fiber layer (RNFL) atrophy OD and diffuse atrophy OS (Figure 1). The patient had expected gonioscopy findings of scleral spur with 2+ pigment 360° OU. Undilated optic nerve of the right eye showed a cup-to-disc ratio of 0.75; the left eye was 0.10 (Figure 2). Neither nerve had a disc hemorrhage

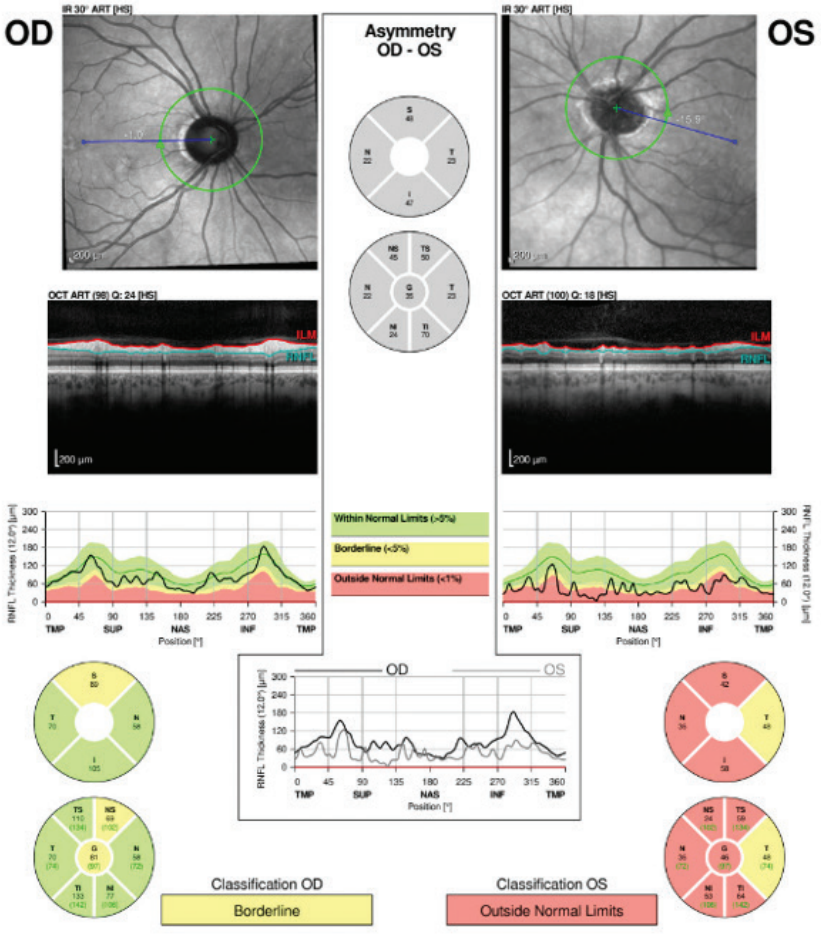


Figure 1. A Humphrey/Zeiss Cirrus OCT (Carl Zeiss Meditec) of the optic nerve shows borderline superior RNFL atrophy OD and diffuse atrophy OS.

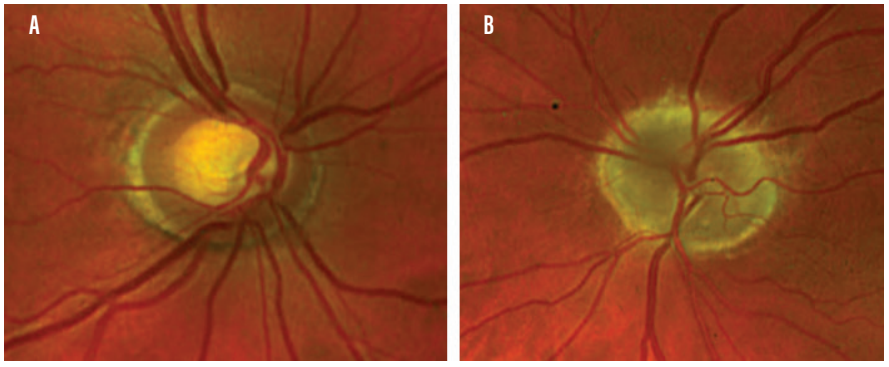


Figure 2. Optos fundus photography (Optos) photo of the right (A) and left (B) optic nerves highlights the difference in nerve appearance and cup-to-disc ratio.

or edema, but the left nerve was slightly larger in size, had a pale, waxy appearance, and had lumpy elevations consistent with optic disc drusen. Upon further questioning, the patient had been diagnosed with optic disc drusen previously but never had elevated IOP.

Treatment Initiated

Due to the cup-to-disc ratio of the right eye and the elevated IOP, it was recommended that the patient begin topical therapy. He was prescribed bimatoprost ophthalmic solution 0.01% (Lumigan, AbbVie) OU every night at bedtime and was seen 4 weeks later for an IOP check and to obtain a visual field. Upon return, his IOP had lowered to 18 mm Hg OD and 17 mm Hg OS. The visual field showed a full field OD and superior and inferior arcuate defects OS (Figure 3). According to the American Academy of Ophthalmology, field defects in both hemifields is classified as severe glaucoma and would warrant a further IOP reduction beyond the 8 mm Hg the patient had in the left eye.[3] However, with a cup-to-disc ratio of 0.10, are the RNFL atrophy and visual field defects *really* caused by glaucoma?

A Word on Optic Disc Drusen

Optic disc drusen are cellular concretions comprised of calcium, amino acids, mucopolysaccharides, and sometimes iron. They are located below the plane of Bruch membrane but above the lamina cribrosa and become more apparent throughout life. Disc drusen can mimic glaucoma by causing RNFL atrophy on the OCT and visual field defects in 24% to 87% of cases.[4]

Unilateral optic disc drusen, as in this patient, represents only 30% of cases; 70% of optic drusen are bilateral.[5,6] I am hesitant to label an optic neuropathy as glaucoma if the cup-to-disc ratio is not enlarged; however, I recommend treating for ocular hypertension if there is further risk of damage to the nerve fiber layer. Although there is no treatment for visual field defects due to optic disc drusen, some studies have investigated the use of topical hypotensive medications in cases of ocular hypertension.[7,8] By lowering IOP, there may be a delay in axonal dysfunction if field loss is caused by direct mechanical compression of the ganglion cell axons. I like to use B-scan

AT A GLANCE

- Glaucoma is typically a straightforward diagnosis, but when the atrophy of the nerve on OCT doesn't quite seem to fit with a glaucomatous optic neuropathy, a deeper look is required.
- Optic disc drusen can mimic glaucoma by causing retinal nerve fiber layer (RNFL) atrophy on the OCT and visual field defects in 24% to 87% of cases. They are also associated with nonarteritic ischemic optic neuropathy, vein and artery occlusions, and choroidal neovascular membranes, making diagnosis and monitoring challenging.
- When RNFL thinning is present on the OCT, comparing the amount of cupping with the damage is helpful in determining whether glaucoma is the cause, as more cupping is more indicative of glaucoma.
- The view of the nerve itself is the most important key in determining whether an optic neuropathy is glaucomatous. If the neuroretinal rim is not thin or asymmetric, other etiologies must be considered.

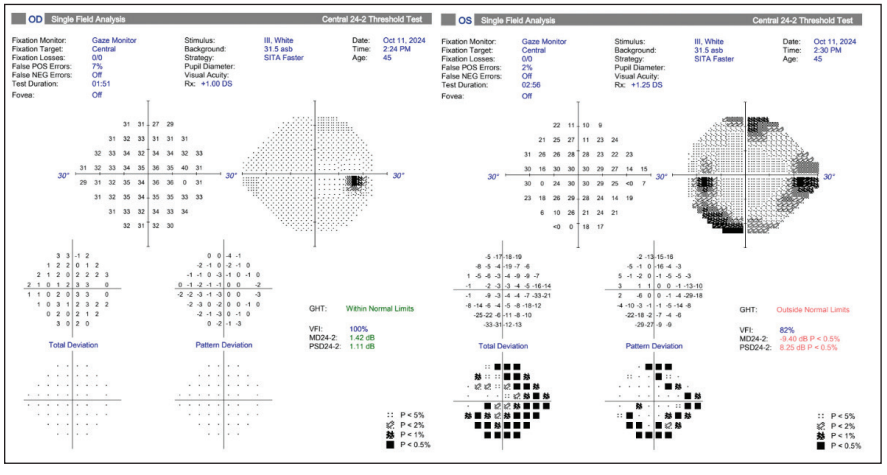


Figure 3. A Humphrey 24-2 visual field shows a full field OD and superior and inferior arcuates OS.

ultrasonography to look for hyperreflective bodies at the optic nerve when evaluating for optic disc drusen.

Additional testing, such as fluorescein angiography and a CT scan of the orbits, can be helpful in confirming the presence or absence of disc drusen. Although not a true fundus autofluorescence, we were able to better highlight his disc drusen (Figure 4). Optic disc drusen are also associated with nonarteritic ischemic optic neuropathy, vein and artery occlusions, and choroidal neovascular membranes, which can also make diagnosis and monitoring more challenging.[9]

CASE NO. 2: PALLOR > CUPPING

A 68-year-old Black male was referred to our clinic for a glaucoma evaluation due to cup-to-disc asymmetry and a positive family history of glaucoma (father). The patient presented with a BCVA of 20/20 OU. His IOP was 18 mm Hg OD and 16 mm Hg OS. Pachymetry was thin in both eyes at 495 µm OD and 501 µm OS. A 2+ relative afferent pupillary defect was noted OS, and an undilated view of the optic nerve showed a cup-to-disc ratio of 0.5 OD and 0.35 OS with superior-temporal optic nerve pallor (Figure 5). An OCT of the nerve was taken that showed no RNFL atrophy OD and superior-temporal atrophy OS (Figure 6). His visual field was full OD but demonstrated an inferior arcuate OS that corresponded with the RNFL

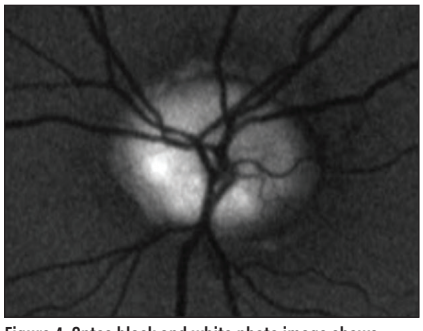


Figure 4. Optos black and white photo image shows hyperfluorescence around the lobular disc drusen in the patient's left optic nerve.

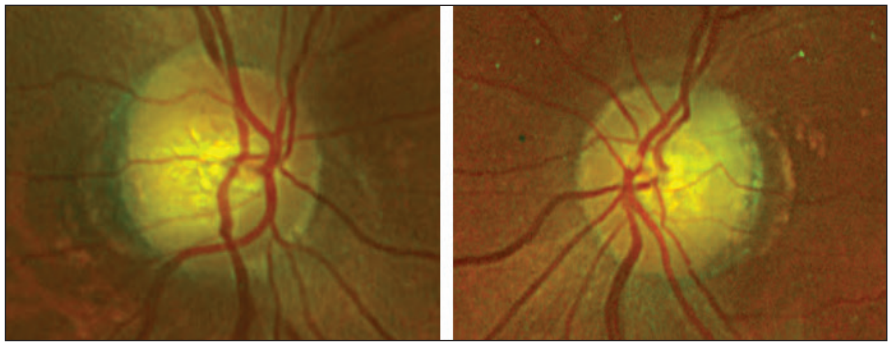
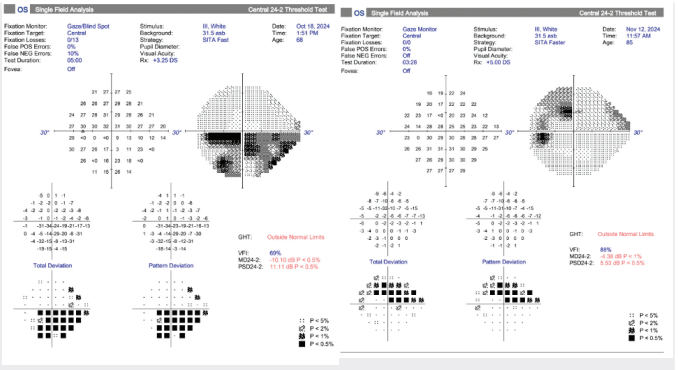


Figure 5. Fundus photos of both optic nerves shows asymmetric cup-to-disc ratios and superior temporal optic nerve pallor OS.

TABLE. Glaucomatous Versus Non-Glaucomatous Visual Field Loss

	BRAO	POAG
Cup-to-Disc Ratios	OD: 0.5; OS: 0.35	OD: 0.8; OS: 0.8
APD	(+) OS	(-)
Baseline IOP	OD: 18 mm Hg; OS: 16 mm Hg	OD: 25 mm Hg; OS: 25 mm Hg
Visual Field		

Abbreviations: APD, afferent pupillary defect; BRAO, branch retinal artery occlusion; POAG, primary open-angle glaucoma

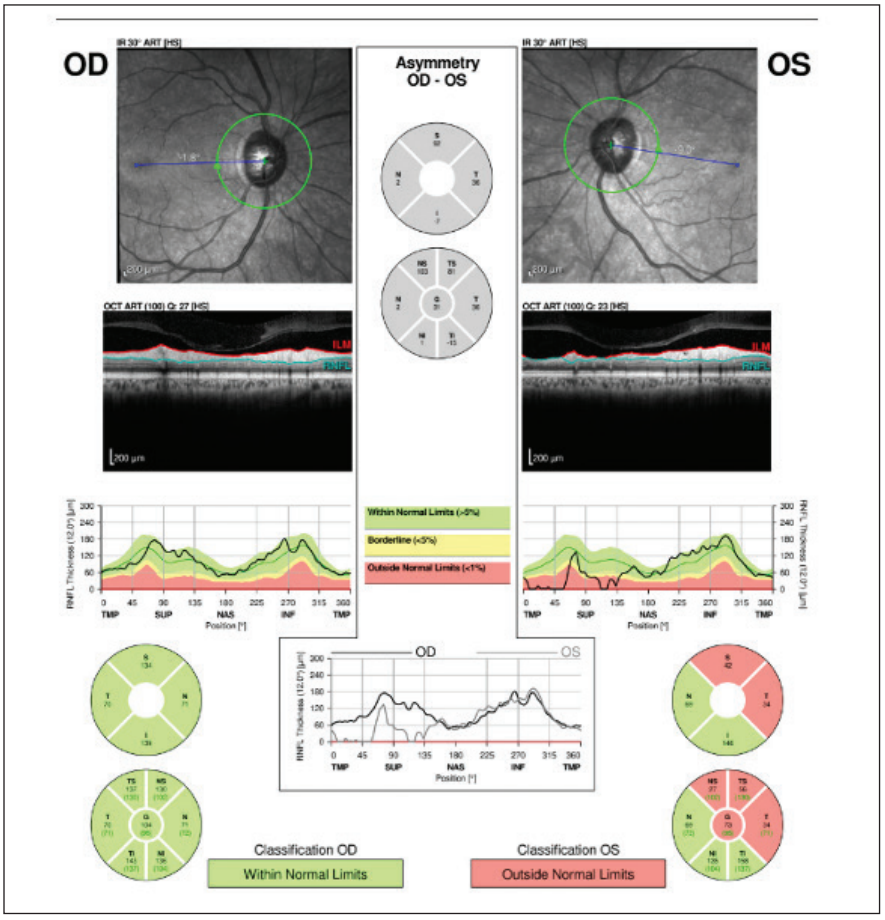


Figure 6. A Humphrey Cirrus OCT of the optic nerve shows superior temporal RNFL atrophy OS.

atrophy (Figure 7).

Although the patient was a glaucoma suspect due to asymmetric cup-to-disc ratios, thin pachymetry, and family history of glaucoma, it did not explain his visual field defect—especially because the eye with the smaller cup-to-disc ratio was the affected eye. His left eye also had an obvious afferent pupillary defect. Pupillary defects are not necessarily rare in patients with glaucoma, especially if the glaucoma is asymmetric, but the prevalence is only 25%.[10]

Optic nerve pallor has several etiologies itself; however, glaucomatous optic nerves usually do not have optic nerve pallor, even at severe stages. I always order fundus photography for patients with glaucoma and those with non-glaucomatous optic neuropathies to monitor for changes. I find it particularly helpful in severely photophobic and uncooperative patients. In this patient's case, reviewing the macular OCT revealed the answer to his RNFL atrophy: Superior outer retinal atrophy was consistent with a previous branch retinal artery occlusion (Figure 8).

Macular OCTs have been helpful in determining the cause of secondary optic atrophy cases where the acute phase was not seen in office. A comparison with a patient with severe

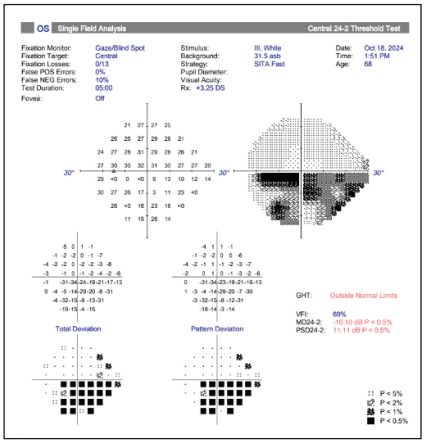


Figure 7. A Humphrey 24-2 visual field OS shows an inferior arcuate defect.

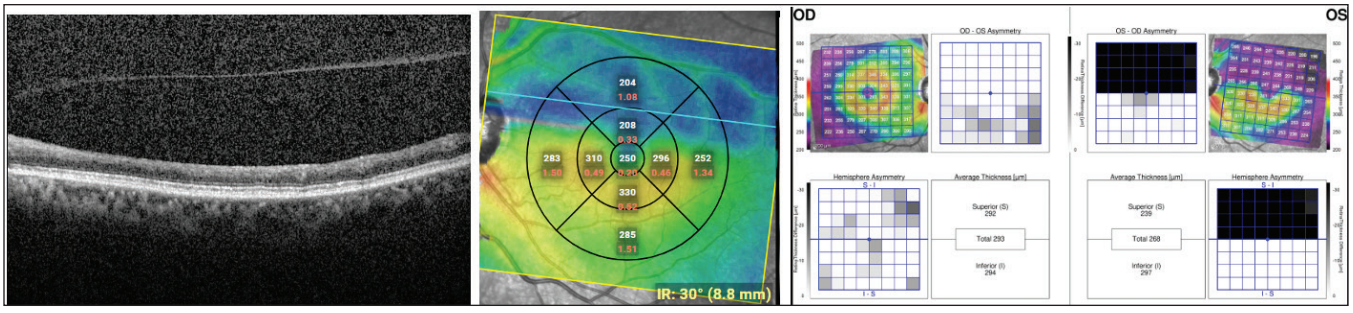


Figure 8. A Humphrey Cirrus OCT of the patient's macula shows diffuse superior outer retinal atrophy OS.

glaucoma shows how similar the cases can be without a close look at the optic nerve (Table). Both patients have arcuate visual field defects, but from very different etiologies. Getting a good view of the optic nerve and obtaining an OCT of the macula were key in differentiating between glaucomatous and non-glaucomatous field loss.

When RNFL thinning is present on the OCT, comparing the amount of cupping with the damage is helpful in determining whether glaucoma is the cause, as more cupping is more indicative of glaucoma.

NEW LEARNINGS

Several factors need to be considered when evaluating for glaucoma and optic neuropathies, so getting all the pieces of the puzzle is crucial to diagnosis and treatment. Besides the OCT of the nerve and visual field defects, evaluating pupil function, color vision, and a thorough history are all important in the patient's initial workup. The most important key in determining whether an optic neuropathy is glaucomatous is the view of the nerve itself; if the neuroretinal rim is not thin or asymmetric, other etiologies must be considered. It is our job as optometrists to be alert for these special cases and consider the differentials of glaucoma. ■

1. Friedman DS, Wolfs RC, O'Colmain BJ, et al; Eye Diseases Prevalence Research Group. Prevalence of open-angle glaucoma among adults in the United States. *Arch Ophthalmol*. 2004;122(4):532-538.
2. Glaucoma: facts & figures. BrightFocus Foundation. Accessed December 7, 2024. www.brightfocus.org/glaucoma/article/glaucoma-facts-figures
3. Gedde SJ, Vinod K, Wright MM, et al. Primary Open-Angle Glaucoma Preferred Practice Pattern. *Ophthalmology*. 2021;128(1): P71-P150.
4. Roh S, Noecker RJ, Schuman JS, Hedges TR 3rd, Weiter JJ, Mattox C. Effect of optic nerve head drusen on nerve fiber layer thickness. *Ophthalmology*. 1998;105(5):878-885
5. Amador-Patarroyo MJ, Pérez-Rueda MA, Tellez CH. Congenital anomalies of the optic nerve. *Saudi J Ophthalmol*. 2015;29(1):32-38.
6. Auw-Haedrich C, Staubach F, Witschel H. Optic disk drusen. *Surv Ophthalmol*. 2002;47(6):515-532.
7. Kohli D, Chen JJ, Bhatti MT, Moore-Weiss JM, Roddy GW. Optic disc drusen in patients with ocular hypertension: a case series and review of the literature. *J Neuroophthalmol*. 2022;42(4):470-475.
8. Malmqvist L, Wegener M, Sander BA, Hamann S. Peripapillary retinal nerve fiber layer thickness corresponds to drusen location and extent of visual field defects in superficial and buried optic disc drusen. *J Neuroophthalmol*. 2016;36(1):41-45.
9. Palmer E, Gale J, Crowston JG, Wells AP. Optic nerve head drusen: an update. *Neuroophthalmology*. 2018;42(6):367-384.
10. Schiefer U, Dietzsch J, Dietz K, et al. Associating the magnitude of relative afferent pupillary defect (RAPD) with visual field indices in glaucoma patients. *Br J Ophthalmol*. 2012;96(5):629-633.

KATHERINE RACHON, OD, FAAO, DIPL ABO
- Optometrist and Residency Director, Virginia Eye Consultants, Norfolk, Virginia
- rachonkm@gmail.com
- Financial disclosure: None