

Optic Disc Drusen

Practical implications and management.



By Tomas M. Grippo, MD; Spencer W. Rogers, MD; and James C. Tsai, MD, MBA

Optic disc drusen (ODD) constitute an important source of vision loss and present unique clinical challenges. They consist of acellular concretions of calcium, amino and nucleic acids, mucopolysaccharides, and sometimes iron. ODD are contained within the optic nerve above the lamina cribrosa and usually below the plane of Bruch membrane. Although sometimes associated with other ocular conditions like angioid streaks, retinitis pigmentosa, and open-angle glaucoma,¹ ODD are usually incidentally found, isolated abnormalities. They are thought to be congenital. ODD have been clinically reported in 0.2% to 0.3% of the eyes of white² and Asian³ patients but are only rarely observed in the eyes of black patients.⁴ Postmortem anatomic studies, however, have found histologic evidence of ODD in up to 2.4% of eyes.⁵ These nerve head concretions can enlarge throughout life, and although they are mostly asymptomatic, ODD may lead to significant visual field loss through acute vascular events and slowly progressive mechanisms.

PATHOPHYSIOLOGY AND NATURAL COURSE

Factors leading to the development of ODD and to subsequent visual pathology are incompletely understood. Tso postulated abnormal axonal metabolism leading to the deposition of calcium crystals in mitochondria, subsequent axonal disruption, and extrusion of mitochondria into the extracellular space, with calcium deposition's occurring continuously throughout the process.⁶ Seitz implicates reduced anterograde and retrograde axoplasmic flow, sometimes in the setting of anomalous optic nerve head outflow routes. Axoplasmic stasis triggers nerve fiber disintegration and subsequent accumulation of calcified cellular components.⁷

Reduced axoplasmic flow may be related to predisposing nerve head anatomy. Several individuals have hypothesized that the abnormality underlying ODD is a small scleral canal containing a crowded optic disc, and they have pointed to this finding in various series of patients with drusen.⁸⁻¹⁰ More recent debatable evidence, however, suggests that a tight canal may not be the key etiologic

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ic feature of most cases of ODD.¹¹ Having conducted family studies on the incidence of ODD and related optic disc anomalies, Antcliff and Spalton concluded that the primary pathology is likely to be an inherited dysplasia of the optic disc and its blood supply.¹² A genetic basis does seem to underlie this aggregate of etiologic factors,^{2,13} but specific genes contributing to ODD have yet to be identified.

ODD are a dynamic phenomenon. They grow slowly throughout the patient's life owing to an ongoing aggregation of calcium and other materials. Additionally, drusen that at a younger age may be described as “buried” (ie, situated near the lamina cribrosa deeply enough that their morphology is obscured by ganglion cell axons, vessels, and glia) can become more visible on fundoscopy later in life, as the overlying tissue layer thins and the drusen become bigger secondary to continuous apposition of material.^{14,15}

DRUSEN-RELATED VISUAL FIELD LOSS

Enlarging calcific bodies in a crowded space that cannot expand exacerbates mechanical stress on the delicate structures contained within the prelaminar scleral canal, occasionally leading to significant visual field loss. The impairment of blood flow through the nerve head in this condition can predispose the patient to acute vascular events, including retinal artery occlusion, retinal vein occlusion, and anterior ischemic optic neuropathy.¹⁶ Chronic ischemia to peripapillary tissues may cause subretinal neovascularization, sometimes bilaterally and at a young age.¹⁷ Symptoms of transient visual obscurations are common, occurring in up to 8.3% of patients with ODD,¹⁸ and they are likely due to brief episodic nerve head ischemia. With compression of vascular structures, drusen plausibly may promote nonarteritic anterior

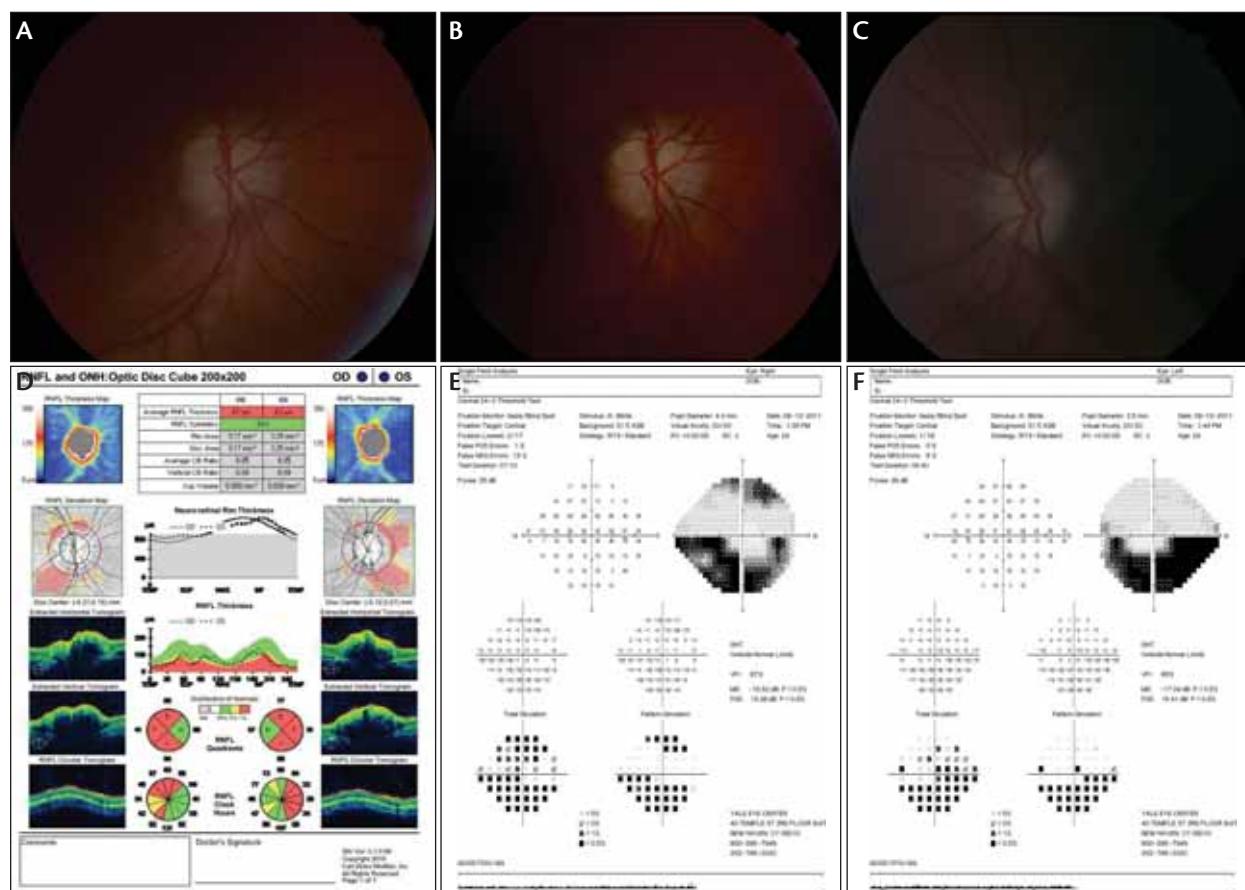


Figure 1. Right eye of a patient with visible ODD. Note the inferior RNFL defect corresponding to the drusen located at clock hour 6 (A). The same eye with different illumination highlighting the drusen (B). Left eye of the same patient with visible drusen (C). OCT of the same patient shows a decreased RNFL OU (D). Achromatic automated perimetry shows severe visual field loss in the patient's right (E) and left (F) eyes.

ischemic optic neuropathy¹⁹ that may present early in life (in the third to fourth decades) and that may even recur in a previously affected eye.²⁰

Slowly progressive visual field loss, which is more common in eyes with ODD, is likely a direct effect of the mechanical forces described earlier, which cause axonal dysfunction followed by gradual axonal degeneration. The frequency of visual field defects in adults with ODD has been reported to range from 24% to 87%,²¹⁻²³ and typically progresses at a rate of around 1.6% per year on Goldmann perimetry.²⁴ Frequently described visual field defects include enlargement of the blind spot, arcuate scotomata, or peripheral defects. Nasal steps and generalized constriction have also been reported,¹ as has rare involvement of central vision.

Attempts have been made to correlate the presence of field loss with the extent and location of drusen. In a retrospective analysis of 103 eyes completed by Grippo et al, those with grade 3 (visible) drusen had significantly more

visual field loss than did those with grade 1 (buried) drusen.²⁵ The location of the field loss, however, has not been correlated with that of observed ODD. This may, in part, be due to deeper, invisible drusen's contributing to axonal damage. Decreased visual acuity, rapidly progressive visual field loss, and the development of acute scotomata are not typical findings and ought to prompt the physician to consider other etiologies regardless of the drusen's clinical appearance.

DRUSEN AND OCULAR HYPERTENSION

Ocular hypertension seems to exacerbate the insidious field loss in ODD. In the previously mentioned series of 103 eyes of 60 patients with ODD, 22 eyes were hypertensive (mean IOP, 27.1 ± 5 mm Hg), and 81 were normotensive (mean IOP, 15.7 ± 2.4 mm Hg). Visual field loss was present in 20 of 22 (90.9%) hypertensive eyes, compared with 54 of 81 (66.7%) normotensive eyes. Higher IOP was statistically associated with a greater prevalence of field

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loss independent of age, sex, and the drusen's visibility.²⁵ Figure 1 provides an example of a 22-year-old man with visual field loss in a setting of ocular hypertension and bilateral ODD.

ELECTROPHYSIOLOGIC AND STRUCTURAL TESTING

Retinal ganglion cell axons in an early phase of mechanical stress may, instead of immediately degenerating, enter into a state of functional impairment evidenced by abnormal latency values on visual-evoked potentials (VEPs). The literature evaluating conventional VEP (cVEP) in patients with ODD is conflicting, however, with abnormally prolonged latency measured in 0% to 41% of ODD-affected eyes.^{14,26,27} Because of its ability to simultaneously evaluate VEP responses from 60 sectors within the central 24° visual field and to detect localized latency delays, the multifocal VEP (mfVEP) has helped to clarify this picture and appears to be a more sensitive indicator of ODD-related axonal dysfunction. In a recent study by Grippo et al,²⁸ the drusen-affected eyes of 10 patients underwent cVEP, mfVEP, and achromatic automated perimetry testing; cVEP was abnormal in 28% of eyes, whereas mfVEP detected prolonged latencies in up to 70%. The investigators concluded that mechanical compression from enlarging drusen might be a viable explanation for axonal damage in these patients and that mfVEP might be a useful method by which to evaluate the effects of potential ODD treatments.

Optical coherence tomography (OCT) likewise has the potential to play an important role in monitoring damage caused by ODD. Roh et al suggested that OCT might provide a reliable objective evaluation of changes in the retinal nerve fiber layer (RNFL) in a condition where clinical interpretation of the optic nerve head is obscured by the anomalous presence of enlarging drusen.²⁹ This capability, the investigators noted, might be useful in patients both with and without coexisting glaucoma. Although it cannot currently differentiate between drusen-related and glaucoma-related RNFL thinning, OCT offers the advantages of ease of adminis-

tration and widespread availability. The technology therefore may be increasingly relied upon to track ODD morbidity. (Figure 1D provides a sample OCT image of the same patient mentioned earlier and shows a reduced RNFL.)

MANAGEMENT AND FUTURE CONSIDERATIONS

Clinicians' maturing comprehension of the mechanisms underlying ODD-related visual morbidity will inform future managerial strategies. The axoplasmic stasis theory has prompted experimental surgical decompression of the scleral canal, but the literature in this area is scant; radial optic neurotomy has been attempted in a few cases, with variable success.³⁰ If gradual field loss in ODD is due to direct mechanical compression of ganglion cell axons, lowering the IOP may, to some extent, alleviate this process and delay axonal dysfunction and death.³¹ Additionally, ocular antihypertensives may improve blood flow to the optic nerve head, potentially reducing the chance of vascular events due to the presence of drusen. The value of these and other prospective treatment modalities, such as neuroprotective agents, has yet to be explored. Physicians can hope that future research will exploit these opportunities for reducing morbidity attributable to this not infrequently encountered condition.

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Glaucoma or optic disc drusen: what is causing the field loss?



By Richard A. Lewis, MD

Spectral domain optical coherence tomography (SD-OCT) has changed the diagnosis and management of glaucoma.¹ Not since thresh-

old visual field testing was automated in the 1980s has a technology so significantly affected day-to-day glaucoma care. Imaging of the disc and retinal nerve fiber layer (RNFL) has become the standard of care. Disc analysis and the early detection of RNFL loss combined with the development of progression analysis programs may provide a higher level of standardization than we have come to depend on for interpreting visual field loss. The clinical acceptance of this technology has been rapid, and it is extraordinarily sensitive for the detection of RNFL damage. Glaucoma-related complications result in deterioration of the RNFL evident on SD-OCT, but it is important to note that not all disc abnormalities detected by SD-OCT arise from this disease.

ABOUT OPTIC DISC DRUSEN

Over the years, optic disc drusen have been referred to by various names, including *pseudopapilledema*, *buried disc drusen*, and *anomalous discs*. Unlike drusen found in the macula, optic disc drusen are globules of mucoproteins that calcify in the optic disc.² They are considered to be the residue of the axonal transport of degenerated retinal ganglion cells. One percent of the population is thought to have optic disc drusen, but that estimate preceded current SD-OCT imaging technology. Prevalence

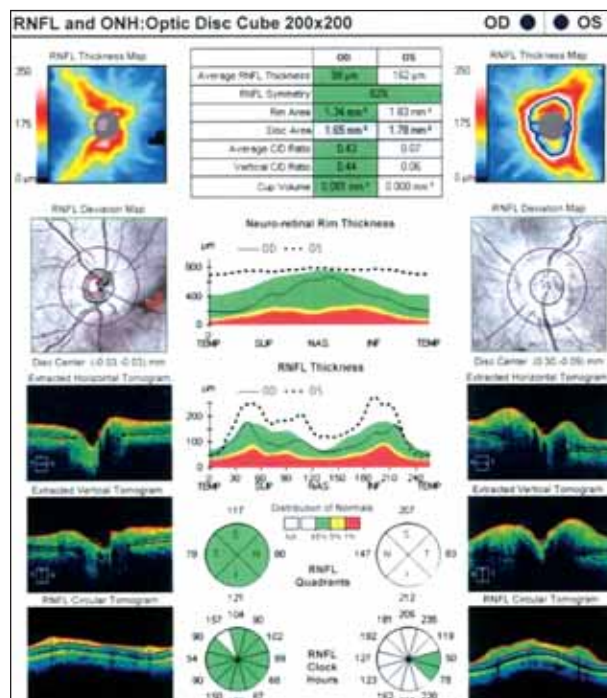


Figure 1. SD-OCT of bilateral disc drusen. Note the minimal cupping, tomographic elevation of the disc margin, and neuroretinal rim thickness that far exceeds the normative data.

data using this modality have not been published.

Clinically, it is not always easy to detect disc drusen with ophthalmoscopy. Most disc drusen remain asymp-

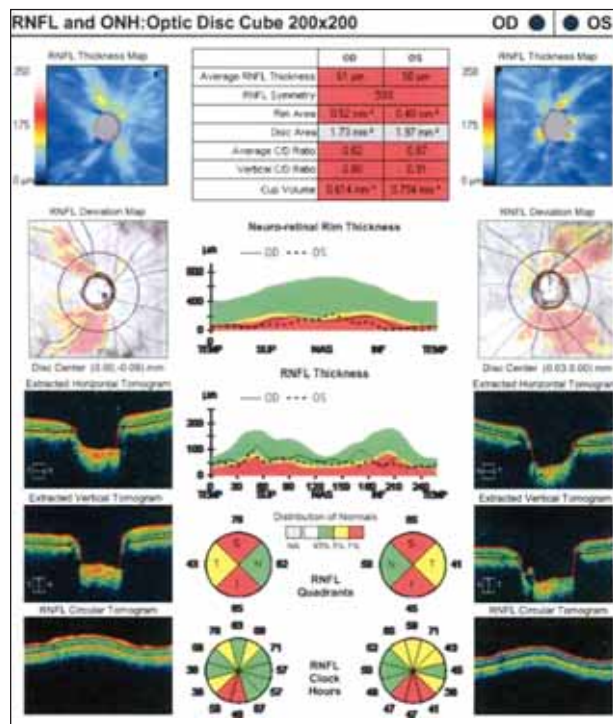


Figure 2. SD-OCT of bilateral glaucomatous cupping. The tomograms indicating deep excavation of the cup and neuroretinal rim thickness demonstrate significant RNFL loss compared with the normative database.

tomatic; about 50% of patients discovered to have the condition by ophthalmoscopy or ultrasound biomicroscopy develop visual field loss. In patients with elevated IOP, it may be difficult to differentiate whether the field loss is due to glaucoma or drusen. In a study by Wilkens and Pomeranz, 73% of optic discs with visible drusen had abnormal visual fields compared with only 36% of optic discs with buried drusen ($P < .05$).³ Researchers have used B-scan ultrasound and/or magnetic resonance imaging of the orbit to confirm disc drusen, but these tests are costly and not widely available.

THE ROLE OF SD-OCT

SD-OCT can distinguish between optic disc drusen from glaucoma and optic nerve head edema. The key to understanding the difference is to examine the extent of RNFL thickness, especially in the nasal area.⁴ Drusen are visualized on SD-OCT as a focal, hyperreflective, subretinal mass with a discrete margin.⁵ Instead of a cup depression characteristic of glaucoma, the extracted disc tomogram in cases of disc drusen reveals elevation, often irregular and discontinuous (Figure 1). Some patients have coexisting glaucoma and disc drusen, and in such cases, both conditions may be contributing to disc dam-

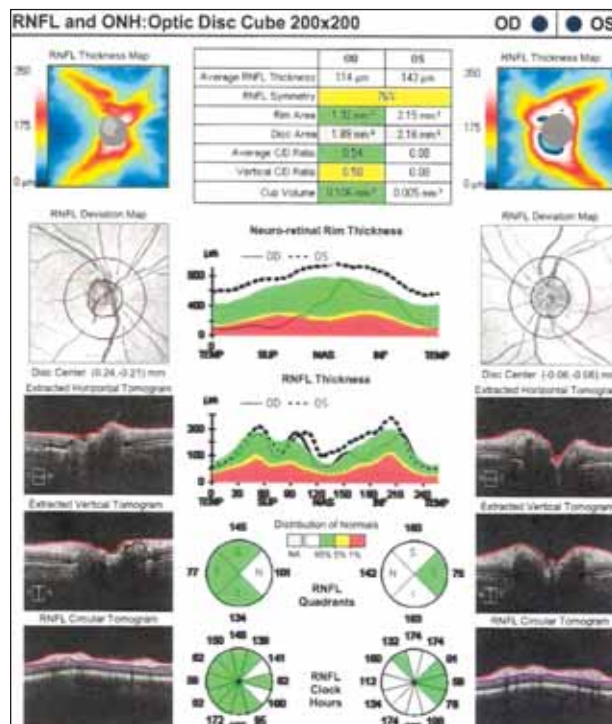


Figure 3. SD-OCT of acute optic neuritis in the patient's left eye. Note the enlarged disc area in the left versus right eye, with minimal cupping and asymmetry of the neuroretinal rim thickness.

age and field loss. SD-OCT, however, is very helpful for the differential diagnosis (Figures 2 and 3).

CONCLUSION

The role of SD-OCT in imaging of the optic disc and retina and the diagnosis of ocular disease continues to broaden. This evolution should provide clinicians with a greater understanding of the anatomy and pathology of the optic disc. SD-OCT will help physicians diagnose glaucoma earlier and improve their ability to differentiate disease states. □

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