Drusen of the Optic Disc

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Optic disc drusen are acellular calcific deposits occurring in small, crowded optic discs with abnormal vasculature. Evidence suggests axoplasmic transport alteration and axonal degeneration are involved in disc drusen formation. In affected patients, the number and size of disc drusen are highly variable, and the drusen may be visible near the disc surface or buried within the disc, causing them to appear as pseudopapilledema. B-scan echography is the most sensitive method for detecting disc drusen. Most patients with disc drusen are asymptomatic, but progressive visual field loss and vascular complications, including anterior ischemic optic neuropathy and choroidal neovascularization, may occur. Optic disc drusen have no established effective treatment. Diagnosing disc drusen correctly is important to avoid unnecessary work-up and to avoid overlooking potential serious conditions such as true papilledema. Disc drusen patients with more-than-expected visual field defects or progressive visual loss should have work-up to exclude other causes.

Introduction

Drusen of the optic nerve head are acellular calcific deposits first described histologically by Müller [1] in 1858. The word *drusen* is the plural form of a German word used for incrustations of small crystals or metals in the spaces inside a rock. Optic disc drusen often occur bilaterally in small, crowded optic nerve heads. When optic disc drusen are on the optic disc surface they can easily be visualized as refractile, beige, rounded deposits embedded within the substance of the optic nerve. However, when optic disc drusen are buried within the optic nerve head, the optic disc appearance is variable, ranging from near normal to optic disc edema. Diagnosing optic disc drusen correctly is important to avoid unnecessary work-up and to avoid missing potentially serious conditions. For instance, differentiating pseudo disc edema caused by optic nerve drusen from papilledema caused by increased intracranial pressure is critical. However, having optic nerve drusen does not preclude the development of other disorders such as papilledema.

Pathogenesis

Histologically, optic disc drusen are basophilic, calcified acellular bodies that contain mucopolysaccharides, amino acids, DNA, RNA, and iron [2]. Most disc drusen are located anterior to the lamina cribosa and behind the Bruch's membrane. In rare instances, disc drusen are found posteriorly to the lamina cribosa or anteriorly protruding into the vitreous.

Evidence suggests optic disc drusen are related to the axoplasmic transport alteration and axonal degeneration of optic nerve fibers [3,4]. Optic disc drusen occur in small, crowded optic nerve heads. Congenitally abnormal disc vasculature, such as abnormal branching pattern, presence of relatively large blood vessels connecting the superficial and deep disc circulations, and increased disc capillarity, may contribute to drusen formation by allowing transudation of plasma proteins that in turn serve as a nidus for the deposition of extracellular materials [5]. Abnormal axonal metabolism related to abnormal vasculature and possibly a narrow scleral canal lead to intracellular mitochondrial calcification. Some axons rupture and mitochondria are extruded into the extracellular space. Calcium is deposited heavily in the extracellular mitochondria. Small calcified microbodies are produced and serve as nidi for further calcium deposition, leading to drusen formation. The scleral canal areas in disc drusen eyes as measured by optical coherence tomography (OCT) are not smaller than in control eyes, and narrow scleral canals as an etiologic factor in the pathogenesis of disc drusen requires further investigation [6•].

Clinical Presentation

Most people with optic disc drusen have no symptoms. Symptomatic patients usually present with transient visual obscuration or chronic insidious visual loss from visual field defects. A less frequent symptom is acute visual loss. Most cases of optic disc drusen are found on routine eye examinations.

The prevalence of optic disc drusen in adult autopsy eyes is near 2% [7]. The prevalence of clinically diagnosed optic disc drusen is much lower because small surface drusen and buried drusen are easily missed or not detectable on examination, and diagnostic testing of drusen is typically performed only in those who are suspected of having optic drusen. Given the high prevalence of optic disc drusen in autopsy eyes, only a small portion of people with disc drusen develop visual symptoms. In addition, optic disc drusen are more common in whites than in blacks because optic disc drusen occur in small optic discs and blacks generally have larger discs. Familial cases of optic drusen have been reported and are likely related to the inheritance of small optic discs with abnormal vasculature [8].

Disc drusen develop in childhood and progress throughout adulthood. Visible optic disc drusen in children in the first decade of life are rare. Longitudinal reports have demonstrated the development from small elevated optic discs in the first decade of life with subsequent progression to visible drusen [9]. Optic disc drusen occur more often in female patients than male patients and are bilateral in 65% to 90% of cases [10,11].

Most optic disc drusen cases are not associated with any ocular or systemic conditions. However, several conditions are associated with a higher occurrence of optic disc drusen, including retinitis pigmentosa, pseudoxanthoma elasticum, and angioid streaks [7]. Optic disc drusen associated with retinitis pigmentosa are likely related to retinal ganglion cell axonal degeneration secondarily to the retinal degenerative process. Both angioid streaks and pseudoxanthoma elasticum are rare disorders. Optic disc drusen are reported in 5% to 21% of patients with angioid streaks. Optic disc drusen are more common in pseudoxanthoma elasticum because a majority of affected patients with pseudoxanthoma elasticum have angioid streaks [12,13].

Clinical Findings

Visual acuity is generally preserved in optic disc drusen, although marked impairment occurs in severe cases. Severe visual acuity loss is typically preceded by progressive severe visual field constriction [14].

Visual field defects from nerve fiber loss are the characteristic feature of visual loss from optic disc drusen. Most children and adults with disc drusen have minimal or no visual field defects. However, visual field deficits are commonly detectable in the second decade of life in patients with pseudopapilledema due to optic disc drusen [15]. In adults with clinically diagnosed disc drusen, progression of visual field defects occurs with age but is generally mild [16•]. Compared with eyes with buried drusen, eyes with visible drusen are more likely to have visual field defects [17–19]. Eyes with buried disc drusen usually do not have visual field defects and have normal average retinal nerve fiber layer (RNFL) thickness on OCT, although reduced focal RNFL thickness may occur [20]. Severe visual loss can occur with disc drusen alone or in conjunction with vascular insufficiency, including anterior ischemic optic neuropathy and retinal vascular occlusion [21].

In patients with disc drusen, the number and size of superficial and buried drusen are highly variable. Although superficial disc drusen are visible with direct ophthalmoscopy, a careful stereoscopic examination of the optic disc using the slitlamp biomicroscope and funduscopic lenses will provide a three-dimensional assessment of the number and size of the drusen. Optic disc with drusen are typically small and crowded and often accompanied by irregular vascular pattern. Cilioretinal arteries and retinal choroidal venous collaterals (ie, optociliarry shunts) occur more frequent in disc drusen [22–24]. In discs with visible drusen, the disc may have a lumpy appearance or appear swollen (Fig. 1). The appearance of discs with buried drusen ranges from near normal to pseudopapilledema (Fig. 1). Compared with pseudopapilledema from disc drusen, true papilledema from increased intracranial hypertension tend to have more exudates, hyperemia, hemorrhages, venous congestion, cotton wool spots, and peripapillary circumferential subretinal fluid lines (Patton's lines). However, clinically distinguishing pseudopapilledema from true papilledema can be difficult, making further diagnostic testing necessary.

Diagnostic Testing

Diagnostic testing is critical in detecting and evaluating the severity of disc drusen, particularly in cases in which optic disc drusen are not visible on examination. B-scan echography is the preferred diagnostic method for detecting disc drusen and is more reliable compared with both CT and autofluorescence performed with preinjection photography for fluorescein angiography [25]. The calcified disc drusen appear as rounded shadows with high reflectivity on B-scan echography, and larger drusen are readily detectable. For smaller drusen, the expertise and experience of the echographer become more important.

Although CT helps to exclude diagnosis of an intracranial mass lesion and is superior to ophthalmoscopy in detecting buried disc drusen, it is not as sensitive in detecting disc drusen compared with echography because of its resolution limitation. In addition, variability in axial CT slice positioning of the optic nerve heads reduces the ability of CT to detect small disc drusen.

Optic disc drusen are autofluorescent and glow visibly when viewed through the fundus camera with the fluorescein angiography filters before fluorescein injection. Autofluorescence photography is more sensitive in detecting disc drusen than ophthalmoscopy and can also be used to confirm visible drusen, but it is not as sensitive as echography in detecting drusen. On fluorescein angiography, both discs with papilledema and discs with drusen are hyperfluorescent, although discs with drusen have

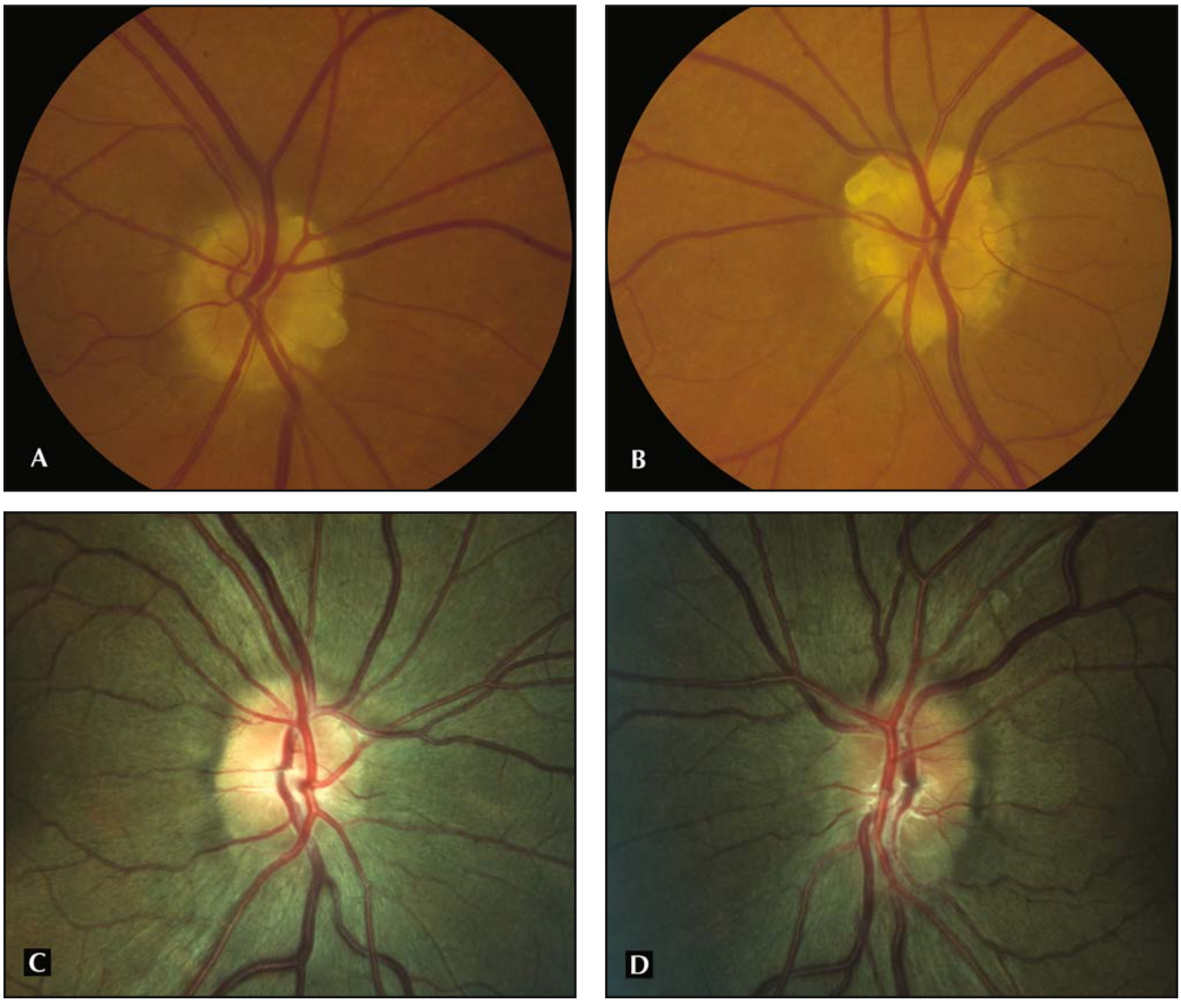

Figure 1. Optic discs with drusen of two asymptomatic patients with normal visual acuity and visual fields. **A** and **B**, Optic disc appearance of the right eye and left eye of a 65-year-old woman; multiple surface optic drusen are present. **C** and **D**, Optic disc appearance of the right eye and left eye of a 46-year-old woman with pseudopapilledema from buried optic disc drusen diagnosed by ultrasound.

uneven hyperfluorescence [26]. However, this distinction is possible only when each stage of the angiogram is carefully studied and should not be used as a reason to not obtain neuroimaging.

OCT is a sensitive and early indicator of RNFL thinning in disc drusen, and RNFL thinning is associated with increased numbers of clinically visible disc drusen [27,28]. In eyes with visible disc drusen, RNFL thinning progression is very slow, similar to the slow progression of visual field defects [29]. RNFL thinning as measured by scanning laser polarimetry also correlates well with functional loss in eyes with disc drusen but is not correlated to the clinical visibility of disc drusen [30]. In addition, measurements of RNFL thickness by OCT may aid in the diagnosis of other concomitant optic neuropathies such as glaucoma, where glaucomatous cupping may not be apparent because of disc drusen [31].

Complications

Vascular complications of optic disc drusen include optic disc and retinal hemorrhage, anterior ischemic optic neuropathy (AION), central retinal artery occlusion (CRAO), central retinal vein occlusion, and peripapillary choroidal neovascularization. Possible mechanisms include compressive effects of disc drusen on blood vessels causing mechanical interruption in vascular integrity, vascular congestion, or ischemia. Optic nerve retinal fiber hemorrhages and deeper hemorrhages on the optic disc and peripapillary region are found in up to 10% of eyes with disc drusen [24,32,33]. The hemorrhages are usually found incidentally and rarely produce symptoms.

Optic discs with drusen are at high risk for AION. AION not related to giant cell arteritis (nonarteritic AION) occurs more frequently in small optic nerve heads. In general, optic discs with drusen are even smaller than

the affected and fellow discs of patients with nonarteritic AION [34]. Compared with patients with nonarteritic AION without disc drusen, patients with optic disc drusen and nonarteritic AION are younger and more likely to report preceding episodes of transient visual obscuration and have a more favorable visual outcome [35]. Prevalence of vascular risk factors (eg, hypertension, diabetes), pattern of visual field loss, and occurrence of a subsequent AION in the fellow eye are similar between patients with nonarteritic AION with and without disc drusen.

Compared with CRAO in general, CRAO associated with disc drusen occurs most often in younger people. In addition, CRAO with disc drusen often occurs in the presence of other factors such as migraines, high altitude, and oral contraceptives [36,37]. Central retinal vein occlusion is also associated with disc drusen and is related to the compressive effect of drusen in reducing venous flow and increasing turbulence [5].

Peripapillary choroidal neovascular membranes associated with optic disc drusen cause subretinal hemorrhages and generally have a good prognosis for visual acuity, although severe visual loss may occur [33,38]. Small nonprogressive neovascular membranes are observed, and laser coagulation should be considered for progressive choroidal neovascular membranes, particularly if the macula is threatened [39,40].

Treatments

No established effective treatment is available for optic disc drusen. Reports of therapy with radial optic neurotomy and optic nerve sheath decompression are controversial and consist of cases that are not supported by definitive studies [41,42]. Surgical removal of large, superficial optic disc drusen is also controversial and can reduce vision [43].

Pitfalls

When optic disc drusen are buried, the optic discs may appear swollen, requiring B-scan echography to make the diagnosis. If ocular echography is not readily available, CT may be helpful but it has lower sensitivity and may miss small drusen. In many cases of buried optic disc drusen, it is difficult to distinguish pseudopapilledema from true papilledema based on funduscopic examination. Even in cases of visible superficial optic drusen, the patient may also have superimposed true papilledema because of conditions such as intracranial mass or idiopathic intracranial hypertension. In addition, the small optic discs with drusen may mask glaucomatous cupping, and crowded optic discs may be more susceptible to glaucomatous damage compared with larger discs [44].

Conclusions

Optic disc drusen are caused by axonal degeneration, but the condition generally carries a favorable prognosis. Disc drusen is an important cause of optic disc abnormalities including pseudopapilledema. Although no established treatment is available, correctly diagnosing optic disc drusen provides prognosis and avoids unnecessary work-up. Disc drusen patients with visual field defects out of proportion to the amount of drusen or those with relatively more rapid progressive visual loss than expected from drusen should have proper work-up to exclude other causes.

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Disclosures

No potential conflicts of interest relevant to this article were reported.

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