Rapidly Progressing Visual Loss Associated with Optic Nerve Head Drusen: Is there a Role for Lowering Intraocular Pressure?

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Abstract

Background: Optic nerve head drusen are acellular hyaline deposits located anterior to the lamina cribrosa, frequently associated with visual field defects. Sometimes rapid worsening of vision may occur due to complications such as acute vascular events, choroidal neovascularization, or serous maculopathy.

Case presentation: Although there are no proven treatments for Optic nerve head drusen associated field loss, we present the case of a patient with Optic nerve head drusen and bilateral rapid progression of visual field loss that has stabilized on intraocular pressure lowering medication. This suggests a role for IOP-mediated retinal ganglion cell loss in this individual. The mechanism of progressive Optic nerve head drusen associated field loss is poorly understood, however experimental glaucoma models and human in vivo imaging studies have shown that structural differences within the optic nerve head are likely to contribute to individual susceptibility to IOP-mediated damage.

Conclusion: We propose that eyes with Optic nerve head drusen may be less able to dampen IOP mediated stress, contributing to loss of retinal ganglion cells in some patients.

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Introduction

Optic nerve head drusen (ONHD) are acellular hyaline deposits of calcium, amino and nucleic acids, and mucopolysaccharides, found in the prelaminar portion of the optic nerve head believed to arise from altered retinal ganglion cell (RGC) axoplasmic flow. First described by Liebreich in 1868, ONHD have been reported to affect 0.4% to 20.4% of individuals. ONHD may be difficult to detect in young patients, or confused with papilledema, as they tend to be buried beneath the surface of the optic disc, close to the lamina cribrosa. Over time ONHD tend to enlarge and become located closer to the surface of the ONH, which acquires an irregular lumpy appearance. While these changes typically occur slowly, in some patients ONHD can enlarge rapidly.

Although ONHD are normally asymptomatic and detected incidentally, they are associated with visual field defects in up to 24% to 87% of affected adults. The mechanism of ONHD-related visual field loss is poorly understood, however drusen typically enlarge slowly throughout life and this is often associated with slow progression of visual field loss. Superficial ONHD are also more commonly associated with visual field defects than those located more deeply. Despite the lack of quantitative longitudinal imaging studies, it is therefore seems likely that progressive field loss in patients with ONHD is due to progressive drusen enlargement.

Occasionally ONHD may be associated with rapid worsening of vision, with reported complications including choroidal neovascularization, serous maculopathy or acute vascular events such as central retinal arterial or venous occlusion or non-arteritic ischemic optic neuropathy. In the absence of these complications, there are no proven treatments for visual loss associated with ONHD.

It is hypothesized that ONHD-related visual field loss may occur as a result of mechanical stress on RGC axons within the prelaminar scleral canal resulting in retrograde axonal degradation and RGC death. The mechanism of ONHD-related visual loss may therefore share some characteristics with glaucoma, in which RGC death is also believed to be due to interruption of retrograde axoplasmic flow. This raises the possibility that treatments to lower intraocular pressure (IOP) might have a role in slowing visual field loss in patients with progressive ONHD-related field loss.

We present the case of a patient with bilateral ONHD with rapidly progressing visual field loss, who has had slowing of disease progression with topical IOP-lowering medication. The patient had extensive investigations to rule of out possible co-existing conditions that might have contributed to visual loss.

Case Presentation

Case History

A 60-year-old female was referred in September 2012 after she complained of slowly worsening vision in the right over the previous year. She had attended her community optometrist who had noted bilateral optic disc swelling. The patient was a low hypermetrope but had experienced no other previous ophthalmic problems. She did however have a history of treated type 2 diabetes mellitus, hypertension and mild asthma. She had not required any systemic steroids for her asthma and there was no significant family history of eye disease.

At presentation, her best-corrected visual acuity was 6/6 in either eye, colour vision was normal and she had normal pupil reactions. IOP was 14mmHg in each eye on applanation tonometry and her central corneal thickness measured 491um and 498um in right and left eyes respectively. Anterior segment examination was unremarkable and she had open drainage angles on gonioscopy. Dilated fundus examination showed...
bilateral ONHD (Figure 1), which were confirmed by fundus autofluorescence and B scan ultrasonography (Figures 2 and 3). The optic discs were not abnormally excavated and no localised retinal nerve fibre layer (RNFL) defects were visible, however there was some inferior beta zone peripapillary atrophy in both eyes. Standard automated perimetry (SAP), which was of good reliability, showed significant decreased sensitivity in both eyes but more advanced in the right eye (Figure 4A) with a mean deviation (MD) of -15.57 dB in the right eye and -3.13 dB in the left. Due to the disc swelling and marked visual field defects she underwent MRI imaging of her brain and visual pathways, which was normal. The visual field defects were thought to be due to the ONHD and as there is no proven treatment for this condition, the patient was counselled regarding the possibility that the field defects may progress. Follow up was arranged for confirmatory visual field testing in 3 months. At the return visit her visual field was slightly worse, with MD of -18.41 dB and -9.59 dB in the right and left eye respectively (Figure 4B). The patient was observed to have good fixation and concentration throughout visual field testing. Her IOP remained 14 mmHg in both eyes. Due to her thin corneas, and the possibility that ONHD might be masking glaucomatous changes to the ONH, at this visit she was commenced on a prostaglandin analogue eye drop to both eyes. Treatment resulted in a reduction in IOP to 10 mmHg in the right eye (29% reduction from baseline) and 11mmHg in the left (21% reduction from baseline).

Over the next 6 months she felt the deterioration in vision in right eye had stabilised but complained that the vision in her left eye was gradually worsening. Visual acuity remained good but visual field testing confirmed a deterioration showing there had been a marked decline in the left eye visual field with MD deterioration from -9.59 to -24.01 (Figures 4C and 4D). Blood tests were taken for common Leber’s hereditary optic neuropathy mutations, which were negative. Vitamin B12 and folate levels were within normal range. Fundus fluorescein angiography (FFA) was also performed, looking for possible associated anterior ischaemic optic neuropathy (AION), but no evidence of late leakage was found. OCT examination of the RNFL was also performed and showed significant thinning in both eyes (Figure 5). Average RNFL thickness was only 57 um in the right eye but measured 87 um in the left, although the inferotemporal sector was outside normal limits in the left eye. Enhanced depth imaging (EDI) OCT was also performed to better ascertain the location and extent of the ONHD (Figure 6). Electro-diagnostic tests showed reduced amplitudes and prolonged latency on
Figure 2. Fundus autofluorescence

Figure 3. B-scan ultrasound
Figure 4. Visual fields

A

Date: 03-09-2012

MD -3.13  P < 1%

Date: 04-12-2012

MD -15.57  P < 0.5%

B

Date: 08-10-2013

MD -9.59  P < 0.5%

Date: 08-10-2013

MD -18.41  P < 0.5%

C

Date: 07-08-2014

MD -17.53  P < 0.5%

Date: 07-08-2014

MD -22.50  P < 0.5%

D

Date: 23-10-2014

MD -24.01  P < 0.5%

Date: 23-10-2014

MD -24.22  P < 0.5%

E

MD -23.05  P < 0.5%

MD -23.75  P < 0.5%
Figure 5. SD-OCT of RNFL

Figure 6. EDI-OCT
the visual evoked potential (VEP) for both eyes, with a normal electroretinogram. The reduced amplitude and prolonged latency on the VEP was suggestive of a non-demyelinating optic neuropathy.

Given the further progression in visual field, the decision was taken to escalate IOP-lowering treatment and the patient was commenced on a topical carbonic anhydrase inhibitor, beta-blocker and an alpha-2-agonist, in addition to the prostaglandin analogue. This resulted in a further decrease in IOP, to 9 mmHg in each eye (36% reduction from baseline). The patient tolerated the treatment well and decided to continue with this treatment and after 1 year, feels her vision has remained stable, which was confirmed with repeat perimetry (MD right eye -23.75 and -23.05 left eye).

Discussion

Despite rapid visual field loss over the preceding 12 months, the patient described in this case showed subjective and objective stabilization following instigation of IOP lowering medication. It is important to acknowledge that this is a single case and other patients may not respond similarly, however the cases raises the possibility that IOP-lowering may have a role in some patients with ONHD.

The mechanism of visual field loss in ONHD is poorly understood, however, it has been postulated that enlarging drusen may damage RGC axons directly through mechanical insult, or indirectly by compressing ONH vasculature leading to ischemia12. Therefore the suggested mechanism of visual loss in ONHD is not dissimilar from that believed to occur in the pathogenesis of glaucoma14. Progressive visual field loss is not infrequent15 with Mustonen and colleagues reporting visual field progression in 22% of patients with ONHD16. The rate of ONHD-related visual field loss is usually slow17, however our patient experienced a fast rate with a change in MD from -3.13 to -17.3 in the left eye and from -15.57 to – 22.50 in the right eye in just over 12 months.

Most previous cases of rapid visual loss in ONHD have been associated with an acute vascular event or choroidal neovascularization. We performed FFA to investigate for secondary causes of visual loss and to look for disc leakage, however FFA was normal. Reduced amplitude and prolonged latency on the VEP, with a normal electroretinogram, suggested visual loss was due to an optic neuropathy. This is in agreement with previous studies, which have shown patients with ONHD to have prolonged latency on VEPs18-20, a finding consistent with a mechanical compressive mechanism of axonal damage. The prolonged latency and reduced amplitude in our patient was likely due to the marked extent of the nerve damage21. Although our patient had marked ONHD, as evident from the EDI-OCT, B scan ultrasonography and autofluorescence, it is not possible to be certain that ONHD was the sole cause of visual deterioration. It is conceivable that she also had coexisting normal tension glaucoma, however the rapid deterioration in visual field would not be characteristic of this condition. Given the difficulty of diagnosing glaucoma in patients with ONHD, and the possible increased risk of IOP-mediated RGC injury in an already compromised eye, we opted to treat our patient with topical IOP lowering medication7,22.

Discerning whether visual field loss is due to glaucoma or ONHD is challenging in eyes with confirmed ONHD, as drusen distort normal ONH anatomy, making detection of glaucomatous structural changes problematic. Furthermore, the pattern of visual field loss is not likely to be helpful in differentiating glaucomatous and ONHD-related visual losses, as the anatomical location of the pathology is similar. Although ONHD can lead to blind spot enlargement, which is not characteristic of glaucoma, drusen can also commonly result in glaucomatous-type defects such as nerve fibre bundle defects16,23.
Improvements in technologies such as EDI-OCT and Swept Source OCT might enable better identification of glaucomatous changes in eyes with ONHD as they allow imaging of deep ocular structures. The ability of EDI-OCT to image structures 500-800 um deeper than conventional OCT allows the posterior limit of the drusen to be imaged. Several studies have recently shown that using EDI-OCT or Swept Source OCT it is possible to visualise the extent of ONHD and to examine the thickness of neighbouring neural tissue. Our patient had marked RNFL loss on SD-OCT, particularly in the right eye. The RNFL thickness was outside normal limits, however, normative databases should be interpreted with caution in eyes with ONHD particularly as the risk of segmentation errors is likely to be higher due to abnormal anatomy. Although glaucomatous RNFL thinning characteristically involves the inferior-temporal and superior-temporal circumpapillary RNFL, the pattern of RNFL loss may not help differentiate whether this is related to ONHD or glaucoma as the location of RNFL defects associated with ONHD is likely to vary depending on location of the ONHD.

There is little previous literature regarding the coexistence of glaucoma and ONHD, however, Samples and colleagues reported a small cases series of 5 patients. The authors concluded that keeping the IOP as low as possible was advisable due to the difficulty of monitoring optic nerve changes. Mamikonian and colleagues examined 35 eyes of 21 patients with ONHD, of which 8 eyes also had glaucoma. Patients with glaucoma were found to have significantly reduced ocular blood flow compared to controls, suggesting ocular blood flow might be useful in differentiating these conditions. However, some eyes with ONHD also have impaired blood flow as evident from the increased risk of ocular vascular events. In an additional manuscript, Roh and colleagues presented 2 cases of combined ONHD and glaucoma where both patients had significant RNFL thinning on time domain-OCT. One of the patients had glaucoma in both eyes but ONHD only in one eye. RNFL thinning was more pronounced in the eye with ONHD, which was suggested to be a result of a possible synergistic effect of both conditions in damaging the RNFL.

An interesting consideration is whether ONHD might increase the likelihood of glaucoma. It has been proposed that structural differences within the ONH could contribute to individual susceptibility to IOP-mediated damage in glaucoma. Eyes with a particular combination of ONH anatomy, mechanical strength or blood supply may be more susceptible to damage at normal levels of IOP, whereas others may be less vulnerable. Recent studies have shown that IOP elevation results in displacement of the lamina cribrosa and expansion of the scleral canal. Eyes that are less able to dampen IOP changes are likely to be higher risk of RGC loss due to mechanical pressure on RGC axons passing through the lamina pores. It is likely that eyes with ONHD may be less able to dampen IOP changes, potentially exposing RGCs to greater mechanical strain, perhaps at levels of IOP that are normally physiological. Other authors have recognised the importance of biomechanical factors in ONHD-related visual loss and it has been proposed that patients with ONHD and congenitally small scleral canals might be at higher risk of visual loss due to lack of space for enlarging drusen.

Conclusion

In conclusion, rapid visual loss is uncommon in patients with ONHD but may due to an acute vascular event, choroidal neovascular membrane or non-arteritic ischemic optic neuropathy. Our patient had none of the above, but nonetheless had rapid loss of visual field over 12 months following initial presentation. Although we could not conclusively establish a diagnosis of glaucoma, objective and subjective measures of vision have stabilised since she was commenced on IOP-lowering...
topical medication. Structural differences within the ONH are likely to contribute to individual susceptibility to IOP-mediated damage and we propose that ONH with ONHD may be less able to dampen IOP stress and strain contributing to loss of RGCs in these patients. IOP-lowering should be considered as a treatment option if other causes of visual loss have been excluded.

**Contest**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

**List of Abreviation**

AION: Anterior ischaemic optic neuropathy  
EDI: Enhanced depth imaging  
FFA: Fundus fluorescein angiography  
IOP: Intraocular pressure  
MD: Mean deviation  
ONHD: Optic nerve head drusen  
RGC: Retinal ganglion cell  …
RNFL: Retinal nerve fibre layer  
SAP: Standard automated perimetry  
VEP: Visual evoked potential

**Competing Interest**

The authors declare that they have no competing interests.

**Authors Contributions**

KE: Data collection, reviewing the literature, preparing the illustrations and figures and drafting the manuscript  
AT: Revising the manuscript critically for important intellectual content and giving final approval of the version to be published

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**References:**


8. R. Du Seo and S. H. Park, “Case of rapidly progressing buried optic nerve head drusen,” (eng),


