ORIGINAL ARTICLE

Increased Prevalence of Optic Disc Drusen after Papilloedema from Idiopathic Intracranial Hypertension: On the Possible Formation of Optic Disc Drusen

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ABSTRACT

This is a 25-year observational retrospective review of 372 consecutive participants with optic disc drusen or resolved papilloedema from idiopathic intracranial hypertension. The prevalence of optic disc drusen at 19% among eyes with resolved papilloedema was approximately 10 times higher and significantly increased ($p < 0.001$) as compared with the occurrence in the general population. Eyes with both resolved papilloedema and optic disc drusen had similar visual acuity and visual field outcome as compared with resolved papilloedema alone. Eyes with exposed drusen had significantly worse visual acuity and visual field outcome ($p < 0.001$) than buried drusen. The high prevalence of optic disc drusen after papilloedema has resolved suggests a non-coincidental relationship. Optic disc drusen formation can be a sequela of papilloedema.

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Introduction

Optic disc drusen (ODD) are abnormal accumulations of calcified mitochondrial deposits in the optic nerve head.^{1–4} ODD are often identified on routine clinical examination, without a history of known optic nerve disorder. Postmortem and in vivo studies have documented histologically that drusen are composed of calcium and phosphorous crystals ($\text{Ca}_3(\text{PO}_4)_2$).^{1,2,5} ODD are often considered congenital, and several mechanisms have been proposed explaining their formation. An accepted theory is that a small scleral canal may cause axonal distress due to the physical limitations of a large number of optic nerve axons travelling through a small space.^{6,7} This crowding effect may limit the axonal transport capacity of axons, leading to axon degeneration and ODD formation. This is evidenced by the association of ODD with small scleral canals⁶ and the hereditary pattern of optic disc drusen.^{7–9}

A second theory of drusen formation is that ODD arise due to abnormal vasculature of the optic disc causing axonal ischaemia, distress, and

impaired axonal metabolism, resulting in drusen formation. This is evidenced by the association of drusen with abnormal optic disc vasculature visualised on examination, and reduced blood flow in the central retinal artery as measured by colour Doppler imaging.^{7,10}

The mechanism of drusen formation from axonal distress has been postulated to be related to calcium metabolism.^{2,11} Tso proposed that altered axonal metabolism leads to calcium deposition in mitochondria. The mitochondria are then extruded from the degenerating nerve fibres and are exposed to high concentrations of extracellular calcium, creating a nidus that may progress to drusen formation.² ODD may then increase in size over time from presumed progressive accumulation of axoplasm.⁷

We propose to expand the theory of ODD formation and include papilloedema as a possible cause of acquired drusen. Axonal distress appears to be a key mechanism of both aforementioned hypotheses of drusen formation. Axonal distress

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can be caused by many other conditions that cause a reduction in axonal transport, thus altering axonal calcium metabolism. An anecdotal association between ODD and optic nerve tumours has been reported, and postulated to arise from tumour compression of optic nerve axons.¹² Papilloedema, specifically optic disc oedema from increased intracranial pressure, is known to cause axoplasmic stasis due to mechanical obstruction of axons, ischaemia, or both and so could promote ODD formation.^{13–15}

The alternative relationship is also possible: ODD may contribute to the likelihood or severity of papilloedema by crowding the optic disc. Optic discs with drusen have a higher incidence of vascular complications such as retinal artery occlusions, peripapillary haemorrhages, and anterior ischaemic optic neuropathy.^{16–21} A proposed theory explaining this connection is that ODD may crowd the axonal fibres and compress the surrounding vasculature.¹⁸ If axonal fibres are compressed from optic disc drusen, then in the setting of high intracranial pressure (ICP), crowded discs may predispose fibres to axonal swelling, lowering the threshold for optic disc oedema (papilloedema).

In this study, we investigated the possibility that there may be an association between papilloedema and ODD by measuring the prevalence of ODD in eyes with resolved papilloedema from idiopathic intracranial hypertension (IIH). We selected IIH because its effect on vision occurs principally due to papilloedema, and it is often reversible by non-surgical methods such as 5–10% weight loss.²² If there is a non-coincidental association, then the prevalence of ODD would be higher than the expected 0.3–2.4% rate found in the general population.^{7,23}

A secondary aim of this study was to characterise the visual outcomes of eyes with both drusen and resolved papilloedema. ODD by themselves are associated with visual field deficits in 70% of affected individuals.^{10,24,25} ODD tend to evolve over time from being buried to becoming exposed in the setting of optic atrophy and reduction of the retinal nerve fibre layer (RNFL) thickness.²⁵ Worse visual field deficits are associated with exposed drusen as compared with buried drusen.^{24,25} Vision loss from IIH, most commonly an enlarged blind spot, occurs in 50–90% of patients, and approximately 10–25% may have permanent

vision loss.^{26–28} It is unknown if the visual acuity and visual field outcomes of eyes harbouring both conditions, ODD and papilloedema, are different from eyes with either condition alone. If visual outcomes data are significantly worse in eyes with both ODD and papilloedema as compared with papilloedema alone, these findings could suggest a need for a more aggressive management of patients with combined ODD and papilloedema.

Methods

Patient data were reviewed from the neuro-ophthalmology practices of one of the authors (L.N.J.) over a period of 25 years (1990–2015) from the University of Missouri Columbia/Mason Eye Institute (Columbia, Missouri, USA) and Brown University/Lifespan/Rhode Island Hospital (Providence, Rhode Island, USA). Institutional review board approval was obtained from each institution to perform the study, the research was Health Insurance Portability and Accountability Act (HIPAA) compliant, and it adhered to the tenets of the Declaration of Helsinki. Patients' charts were reviewed if they were over 18 years old and diagnosed with papilloedema "Frisen grade ≥ 1 " from IIH or if they had ODD from 1990 to 2015.²² Papilloedema was diagnosed using one or more of the following methods: ophthalmoscopy, optical coherence tomography (OCT), or fundus photography (Figure 1). IIH was diagnosed based on the patient's medical history, magnetic resonance imaging (MRI), and/or computed tomography (CT) demonstrating normal or small ventricles, empty sella, posterior eye globe flattening, and no other aetiologies for elevated ICP, and lumbar puncture demonstrating increased ICP of over 250 mm H₂O. Our interest for this study was not with the acute phase of papilloedema (Figure 1A and B); rather, we were interested in cases in which the papilloedema had resolved (Figure 1C). Consequently, charts were excluded if papilloedema had not resolved during the patients' entire period of follow-up visits. Resolved papilloedema was defined as having no evidence of papilloedema using ophthalmoscopy, OCT, or fundus photography. Cases with resolved papilloedema from IIH had resolution of clinical symptoms (diplopia, transient visual obscuration, and tinnitus), documented resolution of disc oedema, and almost all had spontaneous venous pulsation indicating return of

Figure 1. (A) Time-domain optical coherence tomography (OCT) demonstrating acute papilloedema and optic disc drusen (ODD). The images represent normal optic nerve (A), ODD with moderate (B) and marked (C) elevation, and optic disc oedema/papilloedema with mild (D), moderate (E), and marked (F) elevation, based on the papilloedema grading scale of Johnson et al.²² The “lumpy-bumpy” internal contour of the optic nerve head in ODD (B) and recumbent “lazy V” pattern of the subretinal hyporeflective space (SHYPS) in papilloedema (D) are evident. Reprinted courtesy of Johnson et al.³ (B) Spectral-domain optical coherence tomography (OCT) and fundus photography demonstrating acute papilloedema for Patient A and optic disc drusen (ODD) for Patient B. The recumbent “lazy V” pattern of the subretinal hyporeflective space (SHYPS) in acute papilloedema for Patient A and the classic “lumpy-bumpy” mass of ODD for Patient B are present. (C) Fundus photograph and optical coherence tomography (OCT) in a patient with combined resolved papilloedema and buried optic disc drusen.

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normal intracranial pressure. There was no interval required between papilloedema resolution and study inclusion, nor for the length of follow-up time.

Patients were excluded if they had other ocular diseases that could account for vision loss such as non-arteritic anterior ischaemic optic neuropathy (NAION), optic neuritis, severe cataracts, glaucoma, or maculopathy. Only one eye per patient was included. If both eyes met the inclusion criteria, the eye with the worse visual field deficit was included. Some patients with resolved papilloedema had ODD in one or both eyes. For patients who had both ODD with resolved papilloedema in one eye and only resolved papilloedema in the fellow eye, we selected the eye with the combined ODD with resolved papilloedema for inclusion.

The diagnosis of ODD was made in the setting of either visible optic disc drusen on ophthalmoscopy or

the presence of ODD identified on imaging studies, including OCT demonstrating a “lumpy-bumpy” optic nerve head from the drusen with abrupt taper of the subretinal hyporeflective space (SHYPS) (Figure 1), fundus photograph and autofluorescence on pre-injection fluorescein angiogram, B-scan ultrasound calcification, or CT scan calcification.³ Eyes identified as having ODD on OCT had classic findings of drusen as shown in Figure 1. Supplementary findings included normal intracranial pressure on lumbar puncture and persistence of disc elevation on follow-up examinations. Pseudodrusen are white refractile bodies in the setting of papilloedema that resolve when papilloedema subsides. Because our study enrolled patients with resolved papilloedema, pseudodrusen would not have been present.²⁸ Distinction between exposed drusen and buried drusen was made by clinical

examination, with exposed drusen having calcification on the disc surface or peripapillary optic disc. Exposed drusen and buried drusen were analysed separately on subgroup analysis because it is expected that exposed drusen would contribute more significantly to visual field deficits and may mask any effect buried drusen have on the visual field. Visual outcomes data were recorded from the last clinic visit (i.e., most distant clinic visit from the initial diagnosis of IIH) in which the papilloedema had completely resolved as defined in the inclusion criteria. If there was no clinic visit in which the papilloedema had completely resolved, the chart was excluded.

Data collected included age at first presentation, gender, Snellen visual acuity, mean deviation (MD) of the visual fields via Humphrey automated perimeter (Humphrey Instruments, San Leandro, CA, USA) program 24-2 SITA Fast, and time from first presentation to last follow-up visit. Visual acuities were converted to logMAR visual acuity for statistical computation. If patients had an unreliable visual field, either due to elevated false-positive (greater than 20%) or false-negative (greater than 30%) errors, then records were searched for an earlier visual field that was performed after documentation of resolved papilloedema. If this was not found, then the patient was excluded.

There were three main categories of participants: (1) optic disc drusen alone without prior history of papilloedema (ODD); (2) resolved papilloedema alone (rPAP); and (3) combined optic disc drusen with resolved papilloedema (cODD-rPAP). We further characterised five subsets of participants based on the presence of buried or exposed optic disc drusen: (a) buried optic disc drusen without prior history of papilloedema (BD); (b) exposed optic disc drusen without prior history of papilloedema (ED); (c) resolved papilloedema alone (rPAP); (d) combined resolved papilloedema with buried drusen (rPAP-BD); and (e) combined resolved papilloedema with exposed drusen (rPAP-ED).

Statistical analysis was performed using SAS version 9 (SAS Institute, Cary, NC, USA). Descriptive statistics were used to characterise the participant groups; the chi-square test was used to compare the groups on categorical variables such as gender. Generalised linear models were used to test if patients with no, buried, or exposed drusen and/or resolved papilloedema exhibited differences in visual acuity

and visual fields. For the aforementioned five subsets of participants, the Snellen visual acuity was modelled as a binomial proportion of approximately equal logarithmic steps between 20/15 and 20/200. This was chosen to appropriately constrain the distribution between physiologically appropriate end points and model the resultant change in shape of distribution as the upper and lower bounds are approached. The visual field mean deviation dB was modelled as a Gaussian distribution, approximating analysis of variance (ANOVA). Alpha was maintained at 0.05 across follow-up pairwise comparisons between subsets using the Holm test. Inferences were based on these adjusted *p* values, whereas confidence intervals were unadjusted.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

Results

A total of 418 consecutive participants met the inclusion criteria of having ODD, rPAP, or both (cODD-rPAP). Twenty-one participants were excluded because they did not have resolution of papilloedema by the last follow-up visit, and 25 patients were excluded because they had another pathology affecting their vision, such as NAION, proliferative diabetic retinopathy, or clinically significant cataracts, leaving a total of 372 (88%) patients enrolled in the study. There were 170 consecutive participants with ODD alone (107 bilateral, 63 unilateral), 159 consecutive participants with rPAP alone (148 bilateral, 11 unilateral), and 43 consecutive participants with cODD-rPAP (32 bilateral, 11 unilateral). Only 1 eye per participant was included in the analysis (based on the eye with the worse visual field deficit if both eyes met the inclusion criteria, or the eye with both ODD and resolved papilloedema if the fellow eye only had resolved papilloedema); hence, 170 eyes had ODD alone, 159 eyes had rPAP alone, and 43 eyes had cODD-rPAP.

Among eyes with ODD, 81 (48%) of 170 eyes had buried drusen (BD) and 89 (52%) had exposed drusen (ED). Of the 43 eyes with both drusen and

resolved papilloedema (cODD-rPAP), 23 (53%) eyes had buried drusen (rPAP-BD) and 20 (47%) had exposed drusen (rPAP-ED). OCT imaging was obtained for 31 (72%) of the 43 eyes with cODD-rPAP. These 31 eyes were composed of 19 (82%) of the 23 eyes with rPAP-BD and 13 (56%) of the 20 eyes with rPAP-ED. All eyes identified as having ODD on OCT had classic findings of drusen as demonstrated in [Figure 1](#). Of the 43 cODD-rPAP participants, 23 (53%) underwent lumbar puncture at our institution with documented intracranial pressure over 250 mm H₂O. The remaining 20 (47%) participants had documented elevated intracranial pressure elsewhere.

The overall prevalence of optic disc drusen for eyes with resolved papilloedema, that is, prevalence among the 159 eyes with rPAP and 43 eyes with cODD-rPAP, was 21.3% (43 of 202 eyes). Because in our study design the eye with combined ODD and resolved papilloedema (cODD-rPAP) was selected when a participant had rPAP in one eye and cODD-rPAP in the fellow eye, this could falsely elevate the rate of ODD in the setting of resolved papilloedema. Consequently, to avoid a false elevation of the frequency of ODD in the setting of resolved papilloedema, we analysed the prevalence of ODD using both eyes of participants who had resolved papilloedema. We found the prevalence of ODD was 19% in eyes with prior papilloedema (75 of 392 eyes). When compared with Friedman et al.'s autopsy study [23], which had one of the highest rates of disc drusen in the general population at 2.0% (15 of 737 eyes), the proportion of eyes with ODD and prior IIH (cODD-rPAP) in our study at 19% was significantly greater than expected ($p < 0.001$). The prevalence of ODD among individuals with papilloedema from IIH was almost 10 times greater than the prevalence of ODD in the general population. In the study, 31 (72%) of the 43 eyes with cODD-rPAP

had classic findings of ODD on OCT as shown in [Figure 1](#), confirming the diagnosis of optic disc drusen. If the prevalence of cODD-rPAP was limited to patients with OCT only to reduce the likelihood of misclassification of ODD, then the prevalence of cODD-rPAP among participants with a prior history of papilloedema would be 15.3% (31 of 202 eyes), still significantly higher than the general population.

[Table 1](#) provides a summary of the participants' demographics. One-way ANOVA compared all three groups, and if $p < 0.05$, then post hoc t tests (two-tailed t test of unequal variance) were performed. Participants with ODD were significantly older ($p < 0.001$) at 39.9 years as compared with participants with rPAP alone or cODD-rPAP at 34 and 32 years, respectively. The proportion of female participants was higher for rPAP than ODD (95% vs. 73%; $p < 0.001$). The mean duration of follow-up was longer for participants with rPAP and cODD-rPAP at 21 and 20 months, respectively, as compared with ODD follow-up at 9 months ($p < 0.001$). However, there were no significant differences in the mean age, gender, and duration of follow-up between participants with rPAP and those with cODD-rPAP.

[Figure 2](#) is a scatterplot of a binomial transformation of the logMAR visual acuities with equivalent Snellen transformations listed on the y -axis. Testing of visual acuity among the five subsets of participants identified significantly worse ($p = 0.025$) mean logMAR visual acuity for eyes with combined resolved papilloedema with exposed drusen (rPAP-ED) (0.14 logMAR; approximately 20/30 Snellen) as compared with eyes with buried optic disc drusen alone (BD) (0.029 logMAR; approximately 20/20 Snellen). No other visual acuity comparisons among the five subsets of participants were significantly different.

[Figure 3](#) displays the means and 95% confidence intervals of the visual field MDs across all five

Table 1. Demographics of among patients meeting inclusion criteria for ODD, rPAP, and cODD-rPAP.

Characteristic	ODD only	rPAP only	cODD-rPAP	p value (F value)	Post hoc t test (rPAP vs. cODD-rPAP)
Number of eyes	170	159	43		
Age, mean (SD)	38.9 (17.7)	32 (10.2)	34 (10.7)	$p < 0.001$ (10.04)	$p = 0.28$
Female, number (%)	124 (73)	151 (95)	41 (95)	$p < 0.001$	$p = 0.92$
Male, number (%)	46 (27)	8 (5)	2 (5)	$p < 0.001$	$p = 0.92$
Duration of follow-up, months, mean (SD)	8.7 (23.3)	21.1 (37.9)	20.7 (26.7)	$p < 0.001$ (7.4)	$p = 0.93$

Note. ODD = optic disc drusen; rPAP = resolved papilloedema; cODD-rPAP = combined optic disc drusen and resolved papilloedema.

Figure 2. Scatterplot depicting the visual acuities of eyes with exposed optic disc drusen (ED), buried optic disc drusen (BD), resolved papilloedema (rPAP), resolved papilloedema and buried drusen (rPAP-BD), and resolved papilloedema and exposed drusen (rPAP-ED). The logMAR visual acuity was transformed and plotted on a scale from 0 to 1. The means and 95% confidence intervals are shown. The equivalent Snellen visual acuities are labeled on the right y-axis. The mean logMAR visual acuity for eyes with rPAP-ED at 0.14 logMAR was significantly worse than eyes with buried optic disc drusen alone (BD) at 0.029 logMAR ($p = 0.025$). No other visual acuity comparisons among the five subsets of participants were significantly different.

Figure 3. The 95% confidence intervals and means of the visual field mean deviation (MD) are displayed for eyes with exposed optic disc drusen (ED), buried optic disc drusen (BD), resolved papilloedema (rPAP), resolved papilloedema and buried drusen (rPAP-BD), and resolved papilloedema and exposed drusen (rPAP-ED). The mean visual field MD at -9.88 dB for ED was significantly worse than for eyes with buried drusen (-3.35 dB, $p < 0.001$), rPAP (-4.8 dB, $p < 0.001$), rPAP-BD (-4.26 dB, $p = 0.005$), and rPAP-ED (-6.02 dB, $p = 0.018$). Eyes with rPAP-ED at -6.02 dB had significantly worse visual field MD than eyes with BD at -3.35 dB ($p = 0.047$).

subsets of participants. Eyes with exposed drusen alone (ED) at -9.88 dB had significantly worse MD than eyes with buried drusen (-3.35 dB, $p < 0.001$), rPAP (-4.8 dB, $p < 0.001$), rPAP-BD (-4.26 dB, $p = 0.005$), and rPAP-ED (-6.02 dB, $p =$

0.018). Eyes with resolved papilloedema combined with exposed drusen (rPAP-ED) at -6.02 dB had significantly worse visual field MD than eyes with buried drusen (BD) at -3.35 dB ($p = 0.047$). We found no interaction effect on linear regression

analysis between ODD and papilloedema for visual acuity and visual field MD.

Discussion

Our study is the first and largest study to our knowledge that describes the visual outcome of adults with both ODD and resolved papilloedema. It also is the first study evaluating the prevalence of ODD for adults with resolved papilloedema. We documented the prevalence of ODD in participants with resolved papilloedema from IIH to be significantly higher at 19% compared with the expected rate of 0.3–2.4% in the general population.^{7,23} This high rate of ODD in the setting of resolved papilloedema was surprising and could potentially have occurred if we had misclassified patients as having acute IIH and papilloedema when only ODD was present. However, this postulate is untenable, as it would not account for the documented elevated intracranial pressure on lumbar puncture, resolution of symptoms related to IIH, and most important the resolution of the previously identified papilloedema. Another possible source of misclassification is patients who truly had papilloedema that had resolved could have an abnormal-looking optic disc that we misclassified as ODD. However, if the prevalence of ODD after papilloedema was limited to the 31 eyes with ODD on OCT as demonstrated in Figure 1 to reduce potential misclassification of ODD, then the prevalence of ODD in resolved papilloedema at 15.3% was still significantly higher than observed in the general population.

The high rate of ODD could reflect a skewed referral pattern to our neuro-ophthalmology practices such that we were primarily referred patients with IIH who had combined ODD with papilloedema because the management of these patients was more challenging. This appears unlikely, as we are unaware of any previously published data documenting differences in outcomes between patients with papilloedema alone versus patients with combined ODD and papilloedema that would prompt a skewed referral pattern to a neuro-ophthalmologist.

The high rate of ODD in the setting of resolved papilloedema was unexpected, as classically we have been taught that papilloedema and ODD are separate and unrelated entities. Additionally, these two entities can be discerned and differentiated at high rates by neuro-ophthalmologists and

other clinicians skilled at examining the fundus as compared with other medical specialties.²⁹ Nonetheless, it was only after we had analysed the data of patients with resolved papilloedema that we recognised the joint occurrence of papilloedema and ODD, fulfilling the oft-quoted Merrill Sosman axiom, “*You see only what you look for; you recognize only what you know.*”

The coexistence of ODD and IIH may be purely random and represent independent observations, or their coexistence could suggest an interaction between ODD and IIH. The high rate of ODD in IIH with resolved papilloedema at almost 10 times higher than expected in the general population suggests that the coexistence of ODD and IIH is not random. Interestingly, a 2016 report from Gospe et al.³⁰ identified 48% (13 of 27) of their pediatric IIH cases having evidence of buried ODD on OCT after papilloedema had resolved. It is uncertain if the development of ODD is more likely to occur when papilloedema from IIH develops in the prepubescent period as compared with an older age of IIH onset.

Either having IIH with resolved papilloedema increases the likelihood of ODD occurrence, or the converse, the presence of ODD increases the likelihood of IIH occurrence. The cause-and-effect relationship cannot be determined from this study, as temporal onset cannot be established because none of the patients with cODD-rPAP were evaluated before the development of IIH and papilloedema.

A biologically plausible mechanism for papilloedema leading to acquired ODD formation may be that papilloedema decreases optic nerve axonal transport. Calcium metabolism is then altered, leading to accumulation of calcium in the mitochondria, and the mitochondria are then extruded to create a nidus for optic disc drusen. It has been established through animal studies that papilloedema can cause axonal flow stasis,^{13,14} and increased ICP results in disorganised nerve fibre structure, swollen axons, and axonal atrophy.³¹ It may be that the severity and duration of papilloedema both affect ODD formation on a continuum: Too much axonal flow disruption may result in optic nerve atrophy and/or drusen formation, and too little axonal flow disruption may not affect calcium metabolism.

On the contrary, a plausible biological mechanism for an increased risk of papilloedema in eyes with drusen may be that drusen reduce the available space for optic nerve axon swelling, lowering the threshold for papilloedema in the setting of increased ICP. However, to our knowledge, the presence of ODD has not been shown to be a risk factor for instigating the development of IIH (which is more often triggered by weight gain, hormonal imbalance, or pharmacotherapy) or inciting the development of papilloedema from non-IIH causes. Further studies are needed for elucidation of the mechanism at the physiologic and molecular levels.

It is also possible that the higher prevalence of ODD can be explained by misdiagnosing residual pseudodrusen from optic disc drusen. Pseudodrusen are accumulations of extruded axoplasm due to chronic papilloedema and by definition are absent with resolved papilloedema.^{31–35} Pseudodrusen, although non-calcified, are similar to drusen, and both may be associated with obstructed axonal transport and accumulations of axoplasm.⁷ It is possible that pseudodrusen and ODD represent a spectrum of optic nerve disorder resulting from axoplasmic flow stasis. It also is possible that the definition of pseudodrusen needs to be revised and that pseudodrusen may result in real optic nerve head drusen.

The age and gender of our participants with ODD without a prior history of papilloedema were significantly different from participants with combined ODD with resolved papilloedema from IIH. It is known that ODD can arise from conditions other than IIH, and our data likely reflect that difference in population. However, among participants with IIH with and without ODD, there were no significant differences with respect to age and gender. The similarities in age and gender for participants with resolved papilloedema without ODD and those with ODD could suggest a non-coincidental relationship between papilloedema presence and ODD development. More data on the duration of papilloedema, severity of the papilloedema, and size of the optic disc would be helpful in answering why papilloedema may sometimes be associated with ODD.

Our study identified visual field loss and visual acuity to be significantly worse among eyes with exposed drusen (ED) without a history of papilloedema as compared with eyes of all other groups, including buried drusen (BD), rPAP-BD,

and rPAP-ED. Likewise, eyes with resolved papilloedema combined with exposed drusen (rPAP-ED) had significantly worse visual field as compared with eyes with BD without a history of papilloedema. These findings are similar to other previously published studies that identified that visual field is often affected when exposed ODD are present.^{7,10,24,25} However, it is against our expected hypothesis that eyes with ED without a history of papilloedema had 3.86 dB worse Humphrey visual field (HVF) mean MD compared with rPAP-ED (−9.88 vs. −6.02 dB), as we originally thought the combination of both conditions (cODD-rPAP) might lead to a worse visual outcome than either condition alone.

There was no statistically significant difference in HVF mean MD between eyes with BD without a history of papilloedema and rPAP-BD. Eyes with rPAP-ED had reduced HVF mean MD by 1.76 dB compared with eyes with rPAP-BD (−6.02 vs. −4.26 dB), although this did not reach the level of statistical significance ($p > 0.05$), possibly due to a low number of patients in each group (rPAP-ED, $n = 20$; rPAP-BD, $n = 23$). A reasonable conclusion from the findings in our study and the published literature is that the most significant factor for visual outcome is the presence of exposed drusen.

In some cases, exposed drusen may begin as buried drusen and gradually become exposed over time as optic nerve fibres atrophy, as measured by thinning of retinal nerve fibre layer.²⁵ DeWitt and colleagues have documented a positive correlation between the degree of optic atrophy and the degree of visual field loss, such that increasing severity of optic atrophy is associated with more prominent and worse visual field loss.³⁶ In contrast, there was no correlation between the severity of optic atrophy and the severity of visual acuity loss. Consequently, because exposed ODD are more often accompanied with optic atrophy, more profound visual field loss would be predicted.^{25,36} There is, however, no evidence to support a hypothesis that optic nerves with drusen, either exposed or buried, are at more risk for further atrophy when papilloedema is present. This may indicate that the presence of drusen does not affect the ability of the optic nerve axons to recover once papilloedema subsides, nor is the presence of drusen a marker of more severe, irreversible papilloedema.

There are limitations of our study, including its retrospective design and the inability to determine

if ODD were present before the occurrence of papilloedema. Our smallest conditional group was 20 (eyes with exposed drusen and papilloedema), which could limit the statistical power to detect a difference. The sample of participants could bias the sample towards those with more severe visual defects or visual acuities, although both the visual field defects and visual acuities of eyes with drusen and papilloedema were consistent with reported literature. The potential association between papilloedema and the secondary development of ODD is a new area that requires further investigation.

Conclusions

The higher than expected prevalence of ODD with resolved papilloedema suggests a non-coincidental relationship, and that papilloedema may contribute to the development of ODD. The simultaneous occurrence of ODD and resolved papilloedema is not associated with worse visual outcome.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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