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Progression of asymptomatic optic disc swelling to non-arteritic anterior ischaemic optic neuropathy

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ABSTRACT

Background The time of onset of optic disc swelling in non-arteritic anterior ischaemic optic neuropathy (NAION) is not known, and it is commonly assumed to arise simultaneously with vision loss. Our goal is to report the presence and persistence of optic disc swelling without initial vision loss and its subsequent evolution to typical, symptomatic NAION.

Methods Clinical case series of patients with optic disc swelling and normal visual acuity and visual fields at initial presentation who progressed to have vision loss typical of NAION. All subjects underwent automated perimetry, disc photography and optic coherence tomography and/or fluorescein angiography to evaluate optic nerve function and perfusion.

Results Four patients were found to have sectoral or diffuse optic disc swelling without visual acuity or visual field loss; the fellow eye of all four had either current or prior NAION or a 'disc at risk' configuration. Over several weeks of clinical surveillance, each patient experienced sudden onset of visual field and/or visual acuity loss typical for NAION.

Conclusions Current treatment options for NAION once vision loss occurs are limited and may not alter the natural history of the disorder. Subjects with NAION may have disc swelling for 2–10 weeks prior to the occurrence of visual loss, and with the development of new therapeutic agents, treatment at the time of observed disc swelling could prevent vision loss from NAION.

INTRODUCTION

Non-arteritic anterior ischaemic optic neuropathy (NAION) is the most common acquired optic primary optic neuropathy in persons over the age of 50. The primary risk factor for NAION appears to be a small, crowded optic disc. Additional identified risk factors include hypertension, hyperlipidaemia (particularly in younger patients), diabetes mellitus, obstructive sleep apnoea and use of specific medications including erectile dysfunction drugs.[1–5] Patients typically experience sudden, painless loss of visual acuity and/or visual field in the affected eye, and the diagnosis is made clinically based on a characteristic optic disc appearance of hyperaemic swelling, often sectoral and corresponding to the area of visual field loss.[6]

Disc swelling, identical in appearance to the described NAION appearance but without visual loss, has been described as 'impending NAION' or 'impending central retinal vein occlusion'.[7] Spontaneously resolving swelling in diabetic subjects has been termed 'papillopathy'. Observation of swelling with serial examinations and documentation of later vision loss typical of NAION has been described in a cohort of largely diabetic subjects.[8] We present four examples of initial disc swelling without visual loss in subjects without diabetes and its progression over weeks or months to produce typical findings of vision loss in NAION and discuss the potential use of this information in therapeutic decision making.

MATERIALS AND METHODS

Subjects were seen in academic neuro-ophthalmology practices of the authors and represent all patients seen by the authors who presented with asymptomatic and later symptomatic optic disc swelling between January 2011 and December 2015. Records of patients who presented with asymptomatic disc swelling that did not progress to visual acuity and/or visual field loss were not reviewed as part of this analysis, in part because of a lack of standardised diagnostic codes that would have permitted accurate identification of such patients by searching clinical diagnostic or billing records (see Discussion). Institutional Review Board approval was not required for this limited retrospective analysis per institutional rules. All subjects underwent a comprehensive neuro-ophthalmic examination including Snellen visual acuity, colour plate recognition (Ishihara or Hardy-Rand-Rittler), pupillary reactions, extraocular movements, confrontation visual fields, applanation tonometry and slit lamp and fundus examinations. Standard automated perimetry (Carl Zeiss Meditec, Dublin, California, USA) was performed at each examination visit. Colour fundus photographs, fluorescein angiography (FA) and/or optical coherence tomography (OCT) of the optic nerve and macula were obtained at the initial examination and when changes in visual status occurred.

RESULTS

Four subjects were identified who presented with optic disc swelling in the setting of normal visual acuity and automated perimetry. Time to progression from initial presentation to vision loss varied from 2 to 10 weeks. All subjects reported sudden, painless visual loss in the study eye after initial neuro-ophthalmic examination. Optic disc swelling was characterised by clinical examination, FA and/or OCT.

Case 1

A healthy man in his late 60s experienced sudden vision loss in his left eye and presented for evaluation. Visual acuity (VA) was 20/20 right eye (OD) and 20/40 left eye (OS) with a left relative afferent pupillary defect (RAPD). There was mild right optic disc swelling and moderate left optic disc

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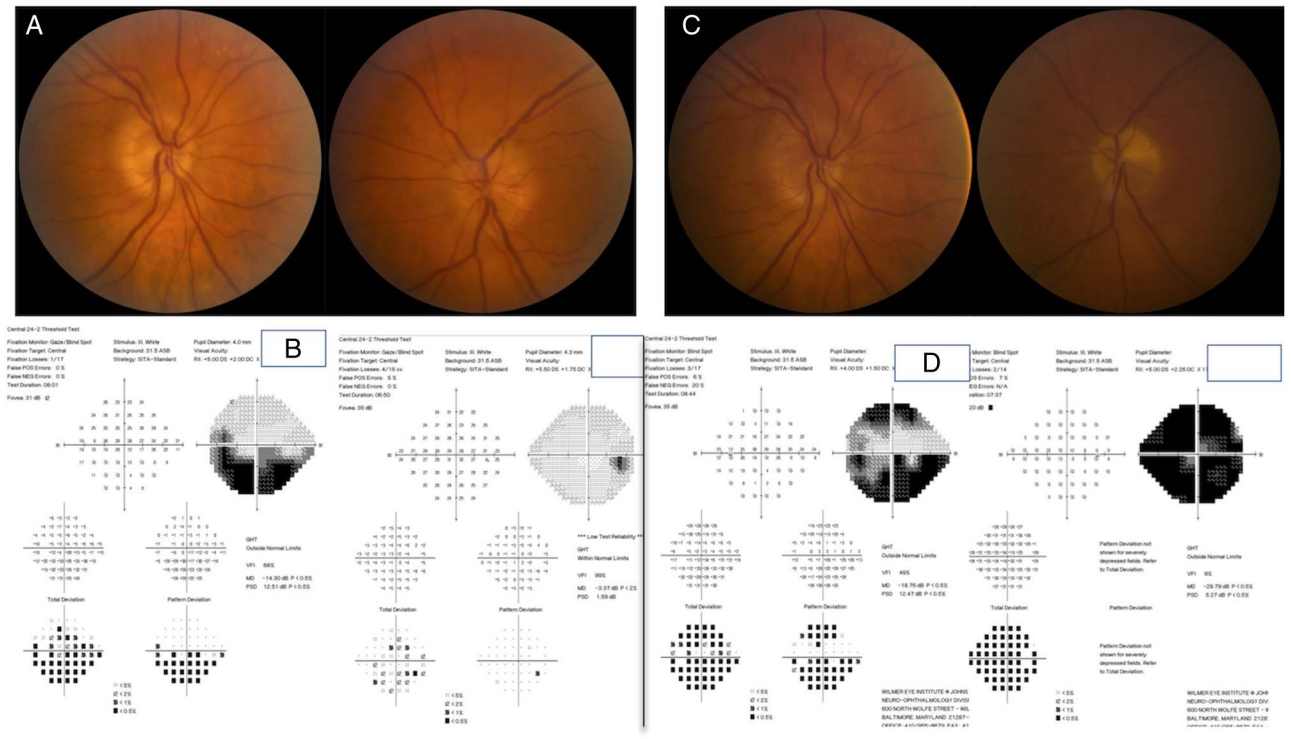

Figure 1 Case 1, optic disc photos and automated perimetry results. (A) Right optic disc shows mild superior disc oedema; left optic disc has more diffuse swelling and peripapillary haemorrhage. (B) Automated perimetry in the right eye is normal; left eye shows an inferior altitudinal defect. (C) Worsening optic disc swelling right eye (OD) with onset of vision loss OD; left optic nerve has superior pallor. (D) Automated perimetry after vision loss OD shows diffuse depression OD and an incomplete superior arcuate defect with inferior altitudinal loss left eye (OS).

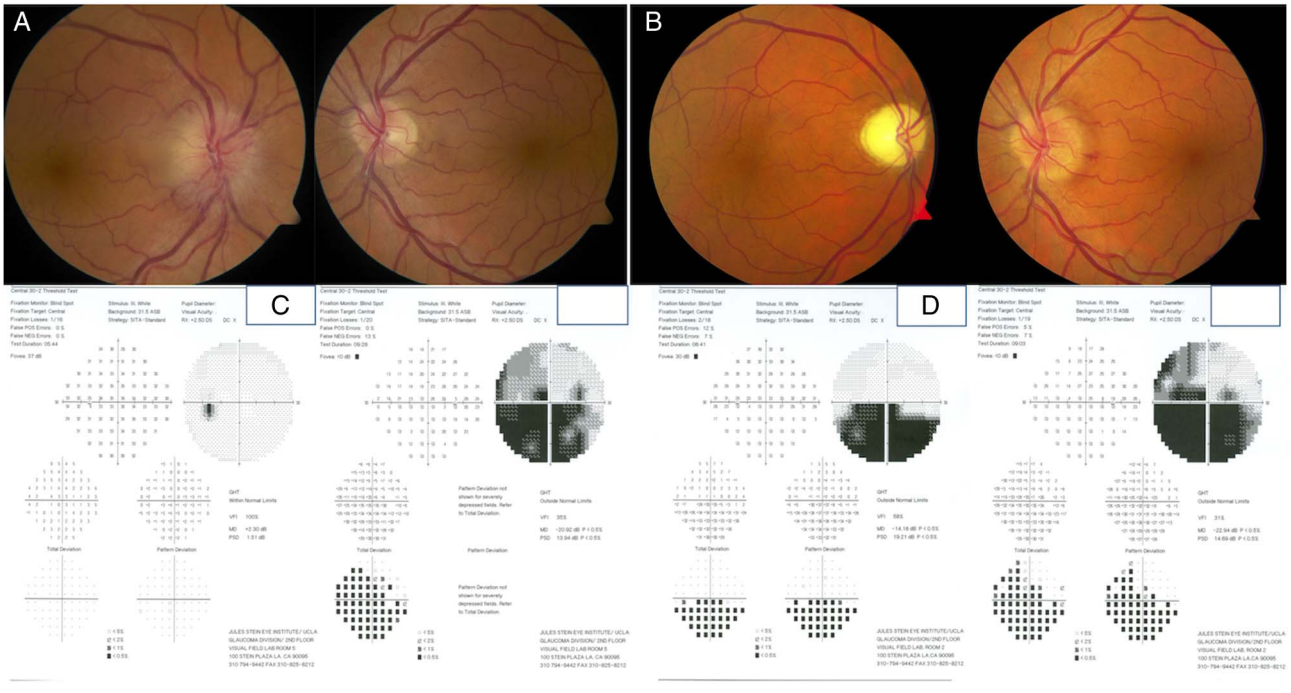

Figure 2 Case 2, optic disc photos and perimetry results. (A) Acute non-arteritic anterior ischaemic optic neuropathy (NAION) right eye (OD) (7 years prior) with normal left optic disc. (B) Optic disc appearance at presentation, with pallor OD and swelling left eye (OS). (C) Inferior and paracentral field loss on perimetry OD, normal results OS. (D) Perimetry 2 weeks later with new inferior altitudinal defect OS and stable findings in the OD. This figure is modified from an article entitled 'The spectrum of optic disc ischemia in patients younger than 50 years (an American Ophthalmological Society thesis)' in the *Trans Am Ophthalmol Soc* 2013;111:93–118 and republished with permission of the American Ophthalmological Society.

swelling with peripapillary haemorrhages (figure 1A). Perimetry showed an inferior altitudinal defect in the OS only (figure 1B). No medical treatment was initiated. Neuroimaging performed prior to his referral was reviewed and showed no pathology of the optic pathways. Two weeks later, a new superior visual field defect in the OS was noted; the OD remained asymptomatic with persistent optic disc swelling. Two months later, the patient noted new vision loss in the OD with VA 20/25, an inferior altitudinal defect OD and superior optic disc swelling with hyperaemia; the left optic disc had superior pallor (figure 1C). The visual field loss and VA OD worsened over the next month despite treatment with intravenous erythropoietin (figure 1D), and then stabilised with onset of optic disc pallor both eyes (OU).

Case 2

This case has been presented in a prior publication.[9] A man in his early 50s with borderline lipids had NAION in the OD 7 years prior to presentation (figure 2A). He presented now after noticing new coloured flashes of light in the OS. VA was 20/60 OD, 20/15 OS with a right RAPD. The right optic disc was pale, and the left optic nerve had hyperaemic swelling with a temporal peripapillary haemorrhage (figure 2B). Perimetry showed a generalised defect, denser inferiorly in the OD and was normal in figure 2C. He was prescribed topical brimonidine three times daily in the OS and oral pentoxifylline 400 mg three times daily. Two weeks later, he reported sudden vision loss OS with VA 20/50 OD, 20/200 OS and a new left RAPD. New inferior altitudinal and paracentral scotomas were present OS with stable findings OD (figure 2D). Optic disc swelling resolved over the next several weeks with onset of superior pallor OD.

Case 3

A woman in her late 60s with hypertension and hyperlipidaemia had photopsias OD for 3 days. VA was 20/20 OU with no RAPD. Automated perimetry was normal in OU (figure 3A). The right optic disc had mild swelling, with a small optic disc noted in the OS (figure 3B). Disc oedema OD was confirmed by FA (figure 3C). Six weeks later, she had sudden central vision loss OD with VA 20/40 OD, a new right RAPD and persistent right optic disc swelling and leakage on FA (figure 3D). A central scotoma was present on perimetry OD (figure 3E). No treatment was initiated. Four months after initial presentation, the right optic disc had temporal pallor and no swelling (figure 3F).

Case 4

A healthy woman in her late 60s had 2 weeks of intermittent photopsias OD. VA was 20/30 in the OD, consistent with cataract, 20/20 in the OS, with no RAPD. Perimetry was normal in OU (figure 4A). The right optic disc was swollen, and FA showed temporal hyperfluorescence and delayed filling of the remaining disc area (figure 4B). One week later, she had sudden loss of inferior visual field OD; examination showed a new RAPD OD and persistent OD disc swelling. Perimetry showed a new inferior incomplete altitudinal defect (figure 4C). No topical or oral medical treatment was given. By 4 weeks after onset of vision loss, the disc swelling had resolved with appearance of pallor and the visual field defect remained stable.

DISCUSSION

One of the defining features of NAION is hyperaemic, often sectoral, optic disc swelling in the affected eye, often with accompanying peripapillary haemorrhages and/or venous

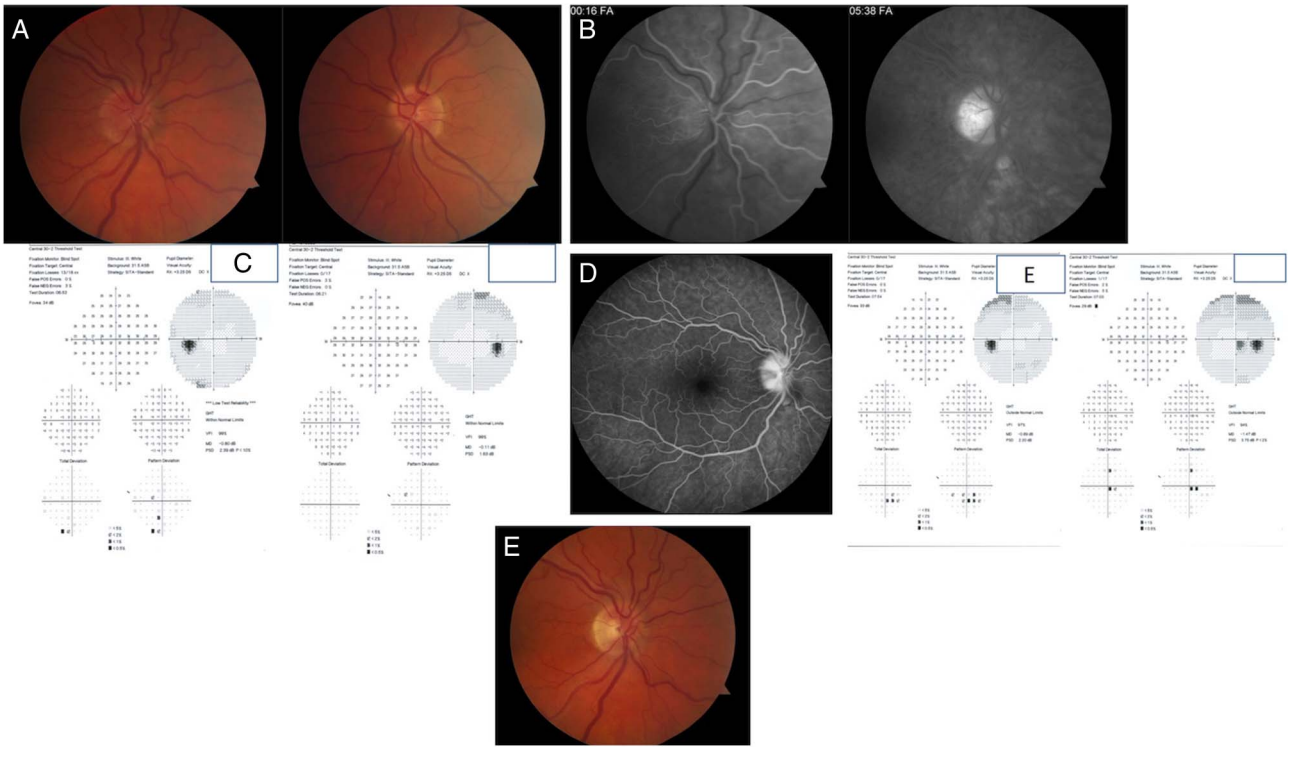

Figure 3 Case 3, photographs and perimetry results. (A) Colour fundus photos showing swollen right optic nerve and small left optic nerve. (B) Fluorescein angiogram (FA) demonstrates early hyperfluorescence and late temporal leakage of the right optic nerve. (C) Normal perimetric results in OU. (D) FA 6 weeks after presentation shows persistent optic disc leakage OD. (E) Perimetry showing new central scotoma OD 6 weeks after initial evaluation. (F) Temporal optic disc pallor on colour photo of the right optic nerve, 4 months after initial presentation.

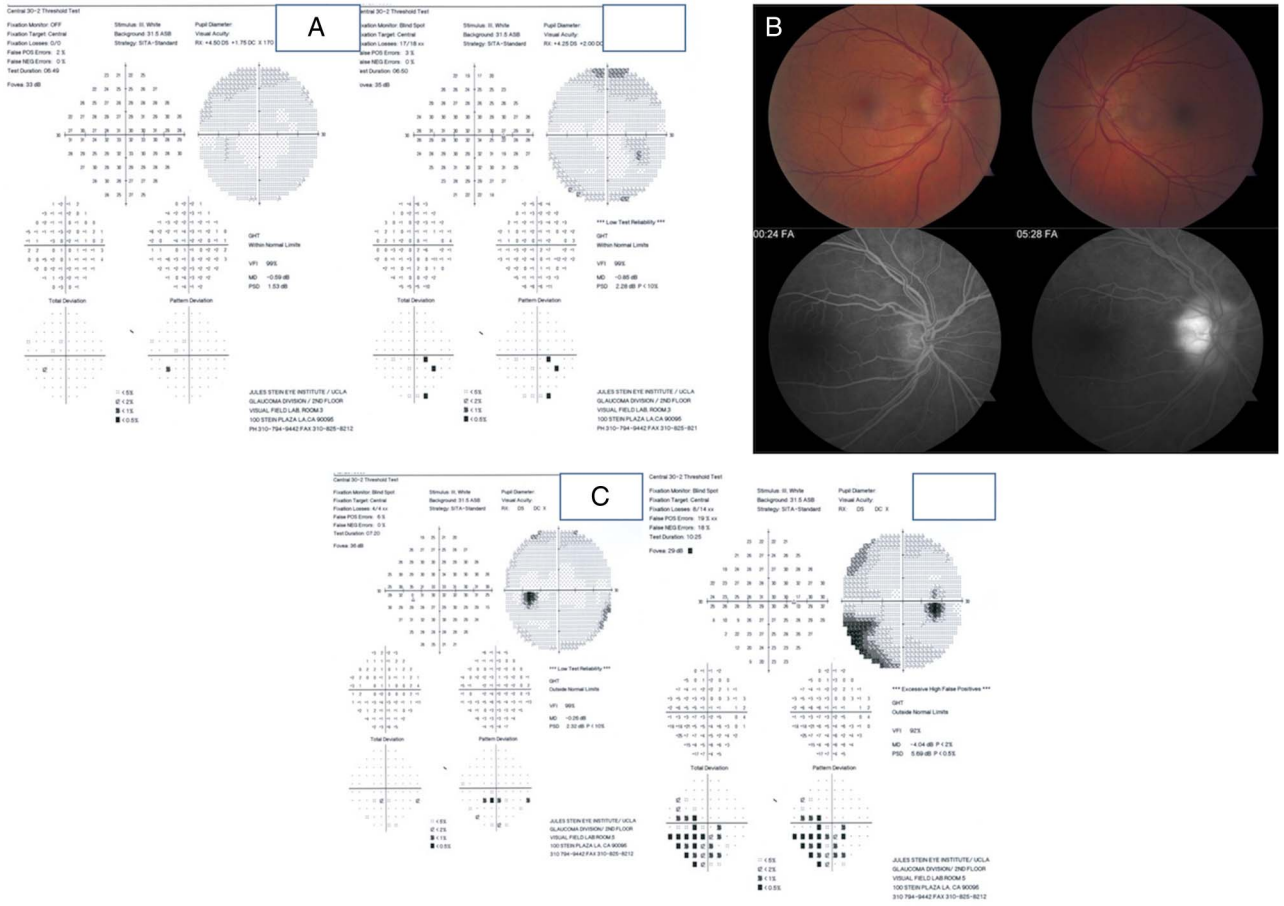

Figure 4 Case 4, photographs and perimetry results. (A) Normal perimetry results at presentation. (B) Colour photos and fluorescein angiogram (FA) showing right optic disc swelling with temporal hyperfluorescence and late leakage. (C) Inferior incomplete altitudinal perimetry defect OD at onset of vision loss, 1 week after initial evaluation of optic disc swelling.

engorgement. When found in association with sudden, painless visual acuity and/or visual field loss, and in patients who fit the typical clinical profile and age, a diagnosis of NAION is given. In these cases, further clinical or radiological workup for other causes of vision loss is rarely pursued by neuro-ophthalmologists, and management often centres on identifying and treating underlying risk factors such as hypertension, hyperlipidaemia, obstructive sleep apnoea and diabetes mellitus.[10] Arteritic anterior ischaemic optic neuropathy from giant cell arteritis (GCA) or other vasculitidies must be considered in the differential diagnosis, although both central and peripheral vision loss tend to be more profound than in typical NAION. The subject in case 1 did undergo temporal artery biopsy because of the extent of visual field loss in the OD when symptoms began, with negative results. In cases 3 and 4, the lack of systemic symptoms, relative preservation of central visual acuity and hyperaemic rather than pallid optic disc swelling were compelling reasons against GCA being the cause of the disc swelling. In case 2, the patient's age and prior NAION in the fellow eye also make GCA unlikely. Although spontaneous improvement of ≥3 lines of Snellen visual acuity occurs in over 40% of patients with NAION, visual field recovery is much less frequent, and it has been suggested that improved VA may reflect patient adaptation and visual search rather than true improvement in optic nerve function.[11]

Medical treatment of acute NAION remains controversial in light of conflicting or absent data regarding the efficacy of numerous agents tried to date including corticosteroids (parenteral and oral), intravitreal anti-vascular endothelial growth factor agents, intravenous erythropoietin, topical brimonidine, oral levodopa/carbidopa and oral pentoxifylline.[10 12–16] Treatment often is initiated, as in cases 1 and 2, when second eye involvement occurs or is judged imminent. In this report, treatment with erythropoietin did not start in case 1 until the second eye experienced vision loss, while in case 2, treatment with brimonidine and pentoxifylline was ineffective in preventing vision loss that occurred 2 weeks after disc swelling was documented. The duration of optic disc swelling without VA or visual field loss was between 2 weeks (case 2) and 10 weeks (case 1), and disc swelling may have been present for an undisclosed amount of time prior to its discovery in these patients. FA, when performed, showed delayed disc filling, consistent with ischaemia.[9] A prior study on asymptomatic disc oedema did not report on disc perfusion, noting only 'abnormal staining' by FA, and no treatment was given.[8]

A limitation of our study is that we are unable in this study to describe the outcome of asymptomatic patients with similar medical comorbidities and disc swelling who never experienced vision loss. The prevalence of asymptomatic optic disc swelling that resolves spontaneously is impossible to determine without prospective screening of an extremely large cohort, perhaps in internal medicine or family practice offices. Such patients would be very unlikely to present to an eye care specialist except by chance, because their lack of symptoms would not lead them to seek an eye evaluation.[7] The high prevalence of diabetes mellitus in previously reported cohorts of patients with

asymptomatic optic disc swelling may point to an ascertainment bias from routine diabetic eye examination rather than a true occurrence rate,[8 17] although NAION itself may occur with greater frequency in patients with diabetes than in non-diabetic patients.[5 18] With or without corticosteroid treatment, the disc swelling may resolve over 9–10 weeks after it is first recognised.[17] In addition, up to 20% of patients with asymptomatic disc swelling and spontaneous resolution may later suffer recurrent disc swelling with vision loss from NAION[17]

Initiating NAION treatment after vision loss has occurred ultimately may not be the most effective strategy, given that irreversible cellular processes such as apoptosis may be activated at the time of acute symptom onset. Future treatment may target patients such as are presented here, in whom a window of opportunity may exist for treatment of disc swelling before vision loss ensues. Further study and surveillance of patients with disc at risk, as well as those patients who suffer unilateral NAION, may afford additional knowledge about the frequency and duration of presymptomatic optic disc swelling in this population and the subsequent progression to full-blown disease with permanent loss of visual acuity and/or visual field.

Contributors PSS: data collection and analysis, drafting manuscript, study supervision, final approval and accountable for all aspects of the work; LKG, LB and ACA: data collection and analysis, critical review of manuscript, final approval and accountable for all aspects of the work.

Competing interests None declared.

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Notes