

Periocular corticosteroids in diabetic papillopathy

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CLINICAL STUDY

Abstract

Purpose To ascertain the therapeutic effect of periocular corticosteroids in diabetic papillopathy.

Methods Prospectively, five consecutive adult-onset diabetic patients with symptomatic diabetic papillopathy underwent visual fields and fluorescein angiography before and after superonasal subtenon injection of corticosteroids.

Results The median duration of papillopathy was 2.5 weeks by ophthalmoscopy and 3 weeks by fluorescein angiography. The median recovery time of best-spectacle-corrected visual acuity was 2 weeks. Two patients developed sequential diabetic papillopathy, and both reported faster visual recovery and better subjective vision in treated eyes. In these two patients, the final best-spectacle-corrected visual acuity and visual evoked responses were comparable between the two eyes, while automated visual fields were less constricted in treated eyes. Complications included ocular hypertension, mild progression of cataract, and mild ptosis in one patient each.

Conclusions Periocular corticosteroids shortened the duration of diabetic papillopathy from a reported median of 5 months to 3 weeks in the present uncontrolled observational study, partly by their angiostatic and antioedema effects at the level of the anterior optic nerve. Intraocular pressure needs to be monitored in eyes receiving periocular corticosteroids.

Eye (2005) 19, 45–51. doi:10.1038/sj.eye.6701418
Published online 16 April 2004

Keywords: diabetic papillopathy; optic neuropathy; periocular corticosteroids

Introduction

Acute disc swelling with superficial, dilated, radially oriented, fluorescein-incontinent capillaries^{1–5} was initially described in long-standing juvenile diabetic patients, many being asymptomatic, or having simultaneous bilateral disease. Diabetic papillopathy lasted several months, and resolved with mild to moderate visual loss.^{3,6,7} Periocular corticosteroids were used to treat intermediate or posterior uveitis,⁸ optic disc neovascularization from chronic uveitis,⁹ rubeosis iridis,¹⁰ cystoid macular oedema,¹¹ and arteritic ischaemic optic neuropathy.¹² We investigated the effect of periocular corticosteroids on the duration of diabetic papillopathy.

Materials and methods

Six eyes of five consecutive adult-onset diabetic patients attending a referral clinic (AMM) over a 6-month period (August 2002–January 2003) were treated for diabetic papillopathy (one patient was unioocular and four patients had bilateral disease) (Table 1). Eyes were diagnosed with diabetic papillopathy if the disc was swollen with superficial telangiectatic radial vessels, fluorescein angiography did not show delay in either onset or time to completion of prelaminar optic disc filling, a positive history of diabetes mellitus, and a negative history of temporal arteritis and pseudotumour cerebri. Treatment consisted of injecting corticosteroids (5 mg betamethasone dipropionate and 2 mg betamethasone sodium phosphate in 2 ml, Schering-Plough, USA) in the superonasal subtenon space. The Ethics Committee of Khoury Hospital approved the therapy that was administered after informed patient consent. The potential side effects of corticosteroid injections and the investigational nature of the therapy were thoroughly explained.

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Published online: 16 April 2004

The authors have no proprietary interest in any product mentioned in the manuscript.

Table 1 Clinical profile of five patients with diabetic papillopathy

N	Age	Sex	DM (year)	HTN	CAD	Steroid and site	Initial VA	Final VA	Followup	Visual recovery	Resolution of disc oedema	Resolution of disc leakage	Retinopathy	Cup-to-disc	Visual field defect	IOP rise	Macular oedema	Symptomatic
1	68	F	20	Yes	Yes	No OD Yes OS	6/60 6/120	6/6 6/6	33 weeks 26 weeks	8 weeks 2 weeks	NA 2 weeks	NA NA	BDR BDR	0.0 0.0	Yes Yes	NA No	No Yes	Yes Yes
2	50	M	10	No	No	No OD Yes OS	CF 3 m CF 2 m	6/12 6/12	34 weeks 34 weeks	NA 7 weeks	NA 4 weeks	NA 8 weeks#	PPDR PPDR	0.0 0.0	Yes Yes	NA No	No No	Yes Yes
3	47	M	12	Yes	No	No OD Yes OS	6/6	6/6	24 weeks	NA	>20 weeks	>20 weeks	BDR	0.0	Yes	NA Yes	No Yes	No Yes
4	77	F	20	Yes	Yes	Yes OD Yes OS	6/18 CF 1 m	6/6 6/360	24 weeks 24 weeks	2 weeks 2 weeks	1.5 weeks 3 weeks	2.5 weeks 3 weeks	BDR BDR	0.0 0.0	Yes Yes	No No	No Yes	No Yes
5	65	F	18	No	No	Yes OS*	CF 2 m	6/120	17 weeks	4 weeks	2 weeks	2 weeks	BDR	0.0	Yes	No	Yes	Yes

DM = duration of diabetes mellitus; HTN = systemic hypertension; CAD = coronary artery disease; steroid = subtenon corticosteroid injection was given (yes), or was not given (no); Sites included OD (right eye) and OS (left eye); NA = not assessed; VA = visual acuity; CF = finger counting; IOP = intraocular pressure; BDR = background diabetic retinopathy; PPDR = preproliferative diabetic retinopathy. *Patient N.2 had complete resolution of the disc oedema by ophthalmoscopy 4 weeks after therapy, and did not perform fluorescein angiography till 8 weeks after therapy. #Patient N.5 is unilocular.

Case reports

Case 1. This 68-year-old white woman presented with sudden visual loss in the right eye. Systemic history included diabetes mellitus of 20 years, systemic hypertension, coronary artery disease, and prior coronary bypass surgery. Examination of the right eye revealed a best-spectacle-corrected visual acuity of 6/60, diffuse disc oedema and peripapillary retinal venous dilation. After 2 weeks, visual acuity improved to 6/15 with decrease in disc oedema. She developed a similar attack in the left eye 6 weeks after presentation. Best-spectacle-corrected visual acuity in the left eye was 6/120. The left optic disc was elevated and hyperaemic with flat dilated superficial capillaries, peripapillary nerve fibre layer haemorrhages, and mild cystoid macular oedema. The right optic disc was pale. She consented to periocular injection of corticosteroids in the left eye. After 1 week, visual acuity improved to 6/9 with marked decrease in disc oedema. At 2 weeks after injection, visual acuity in the left eye was 6/6 with resolution of disc and macular oedema. The right disc was pale, small in size, and with an effaced cup. The right eye underwent periocular injection of corticosteroids for mild cystoid macular oedema. At 4 weeks after presentation, the visual acuity was 6/6 bilaterally, without an afferent pupillary defect. Visual fields revealed severe constriction bilaterally more pronounced in the right eye, and decreasing after therapy in the left eye (Figure 1). Pattern visual evoked responses had comparable waveforms in both eyes (normal latency and mild attenuation of the amplitudes). Colour vision revealed mild red–green deficiency in the right eye only by H–R–R pseudo-isochromatic plates (American Optical, USA, 2d ed, 1957). There was no change in visual acuity, appearance of disc and macula, and visual fields bilaterally till the last follow-up, 7.5 months after the onset of papillopathy in the left eye.

Case 2. This 50-year-old white man with diabetes mellitus of 10 years presented with sudden visual loss in the right eye. He had an afferent pupillary defect in the right eye. The best-spectacle-corrected visual acuity was counting finger at 3 meters in the right eye and 6/6 in the left eye. Funduscopy revealed marked swelling of the right optic disc, and preproliferative diabetic retinopathy changes bilaterally. He underwent panretinal laser photocoagulation to the right eye. At 2 weeks after laser, the disc oedema decreased, and visual acuity stabilized at the 6/24 level. At 7 months after initial presentation, the patient underwent panretinal laser photocoagulation to the left eye. At 2 months after laser therapy, he developed severe visual loss in the left eye to counting finger 2 m. The left optic disc was diffusely swollen with telangiectatic vessels. He received periocular

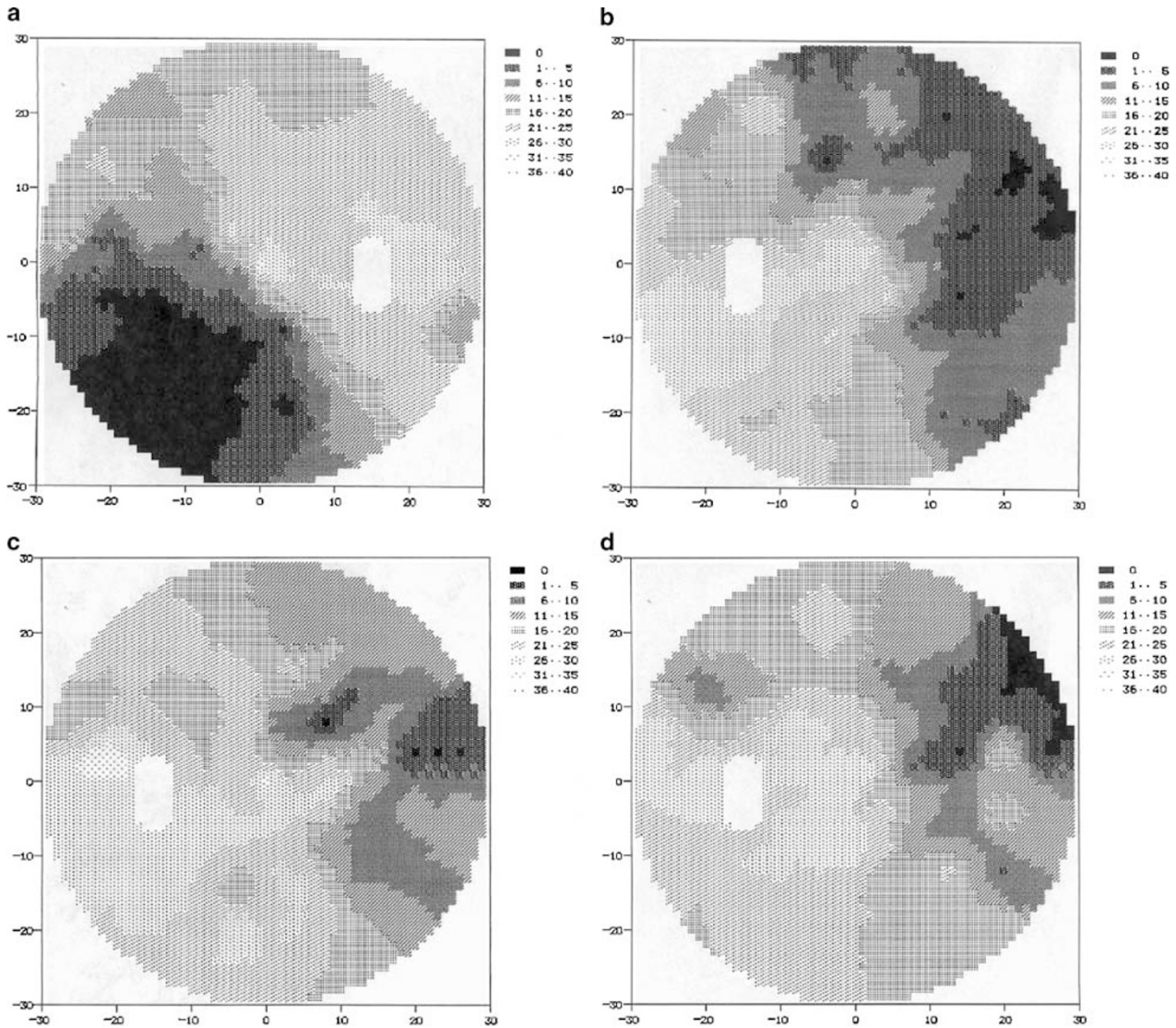


Figure 1 Visual fields of Case 1 in the untreated right eye (a) 9 weeks after the onset of diabetic papillopathy. Visual fields of Case 1 in the treated left eye initially (b), 2 weeks after therapy (c), and 6 months after therapy (d).

corticosteroids in the left eye. The patient reported marked visual improvement 2 weeks after injection. At 4 weeks after injection, best-spectacle-corrected visual acuity in the left eye was 6/60 with resolved disc oedema. Intravenous fluorescein angiography demonstrated an absence of disc leakage in the left eye. Macular oedema was absent bilaterally. Both discs were small in size and had an effaced cup. At 10 weeks after visual loss in the left eye, best-spectacle-corrected visual acuity was 6/12 bilaterally, with a right afferent pupillary defect. Automated visual fields showed severe constriction bilaterally more pronounced in the right eye (Figure 2). Pattern visual evoked responses had comparable waveforms in both eyes (normal latency and mild attenuation of the amplitudes). Both eyes failed to

recognize any colour plate using the H-R-R pseudo-isochromatic plates. The optic nerve appearance, fovea, and visual fields were bilaterally unchanged 22 and 34 weeks after the onset of papillopathy in the left eye.

Case 3. This 47-year-old white man with diabetes mellitus for 12 years noted sudden visual loss in the left eye. Best-spectacle-corrected visual acuity was 6/15 in the left eye with elevation of the optic disc superiorly, background diabetic retinopathy, and a normal-appearing fovea. He had a large inferior arcuate visual field defect in the left eye. Colour vision was positive for medium red-green defect bilaterally by the H-R-R pseudo-isochromatic plates. Profuse disc leakage of fluorescein dye was noted bilaterally. There was a diffuse perivascular dye leakage from dilated capillaries

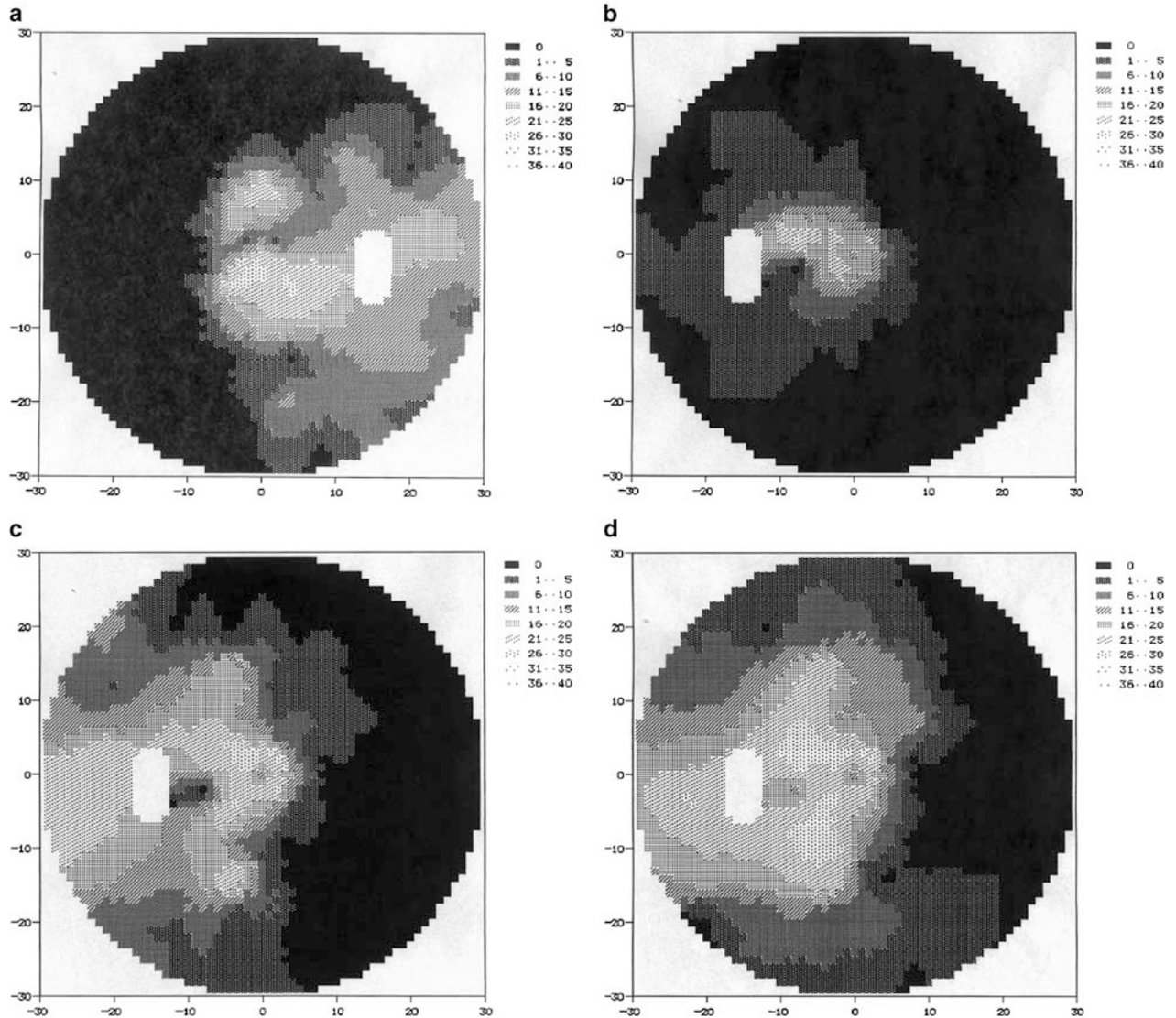


Figure 2 Visual field in the untreated right eye (a) 1 year after the acute onset of diabetic papillopathy in Case 2. Visual fields in the treated left eye initially (b), 2 weeks after therapy (c), and 6 months after therapy (d) in Case 2.

throughout the posterior pole, reminiscent of VEGF retinopathy model.¹³ The patient consented to periocular injection of corticosteroids in the left eye. After 5 days later, best-spectacle-corrected visual acuity improved to 6/9. After 11 days later, best-spectacle-corrected visual acuity was 6/9 with resolution of disc oedema. Visual fields were unchanged. There was marked decrease in disc leakage in the left eye by fluorescein angiography. At 3 weeks after presentation, best-spectacle-corrected visual acuity was 6/6 in the left eye. Intraocular tension rose to 30 mmHg, and was controlled by topical antiglaucoma medication. The status of optic disc and macula in both eyes were unchanged 20 and 24 weeks after the onset of papillopathy. Visual field defects decreased in the left eye 24 weeks after presentation. A 1-mm asymptomatic left ptosis was noted.

Case 4. This 77-year-old white woman with diabetes mellitus of 20 years noted sudden visual loss in the left eye. Best-spectacle-corrected visual acuity was 6/15 in the right eye, and finger counting 1 m in the left eye. The disc was swollen superiorly in both eyes. There was focal superior leakage in the right disc and diffuse severe leakage in the left disc. There was mild cystoid macular oedema in the left eye. Visual fields showed severe contraction of the central field in the left eye and superior arcuate defect in the right eye. The patient underwent bilateral periocular injection of corticosteroids. At 9 days after injection, best-spectacle-corrected visual acuity was 6/9 in the right eye and finger counting 3 m in the left eye. Disc oedema and macular oedema decreased bilaterally. At 15 days after presentation, best-spectacle-corrected visual acuity was 6/9 and finger counting at

4 m. Disk leakage decreased markedly in both eyes on repeat fluorescein angiography (Figure 3). The diffuse visual field defects decreased markedly in both eyes.

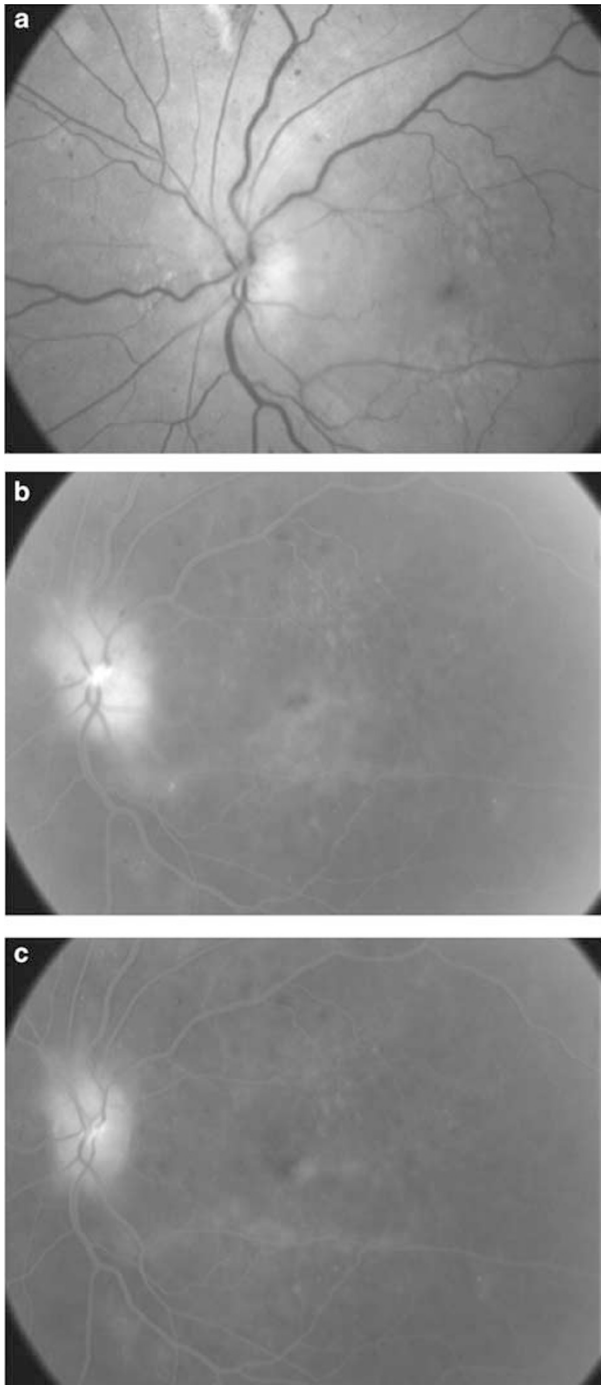


Figure 3 Posterior pole photograph of the left eye (a) in Case 4 (before therapy). During late phases of fluorescein angiography, there is profuse leakage from the abnormal capillaries of the optic disc, resulting in cystoid macular oedema (b) (before therapy). Posterior pole of the left eye in Case 4 during the late phases of fluorescein angiography, 3 weeks after therapy. Both disc and macular leakage of fluorescein have decreased markedly (c).

Posterior pole examination and visual fields were unchanged 10 and 23 weeks after presentation, with best-spectacle-corrected visual acuity of 6/360 in the left eye. Mild cataract progression was noted bilaterally 24 weeks after therapy.

Case 5. This 65-year-old unioocular white woman with diabetes mellitus of 18 years noted sudden visual loss in the left eye. Best-spectacle-corrected visual acuity was finger counting at 2 m in the left eye with diffuse disc oedema, cystoid macular oedema, and background diabetic retinopathy changes. She received periocular injection of corticosteroids. Fluorescein angiography showed early marked disc leakage. She had complete obliteration of central and nasal fields with islands of temporal fields remaining. At 2 weeks after injection, best-spectacle-corrected visual acuity was finger counting at 3 m, with resolution of disc oedema, absence of disc leakage on fluorescein angiography, and improvement in central visual field. Best-spectacle-corrected visual acuity stabilized at 6/120 and visual fields were unchanged 4, 7, 14, and 17 weeks after presentation.

Summary of case reports was tabulated (Table 1). The median duration of papillopathy in treated eyes was 2.5 weeks by 90-D slit-lamp examination, and 3 weeks by fluorescein angiography (Figure 3). Best-spectacle-corrected visual acuity was attained at a median of 2 weeks after therapy. Macular oedema resolved in all treated eyes. Visual field defects decreased in treated eyes after 2 weeks of therapy and stayed stable thereafter (Figures 1 and 2). Ocular hypertension, mild cataract progression, and asymptomatic minimal ptosis occurred, noted in one patient each.

Cases 1 and 2 had sequential papillopathy with the right untreated eye and the left treated eye. Both reported repeatedly 'seeing better' in the treated eye, and both had similar best-spectacle-corrected visual acuity in either eye, comparable pattern visual evoked responses (latency and amplitude) in either eye, but denser scotomas on visual fields in untreated eyes (Figures 1 and 2).

Discussion

Lubow and Makley² initially described diabetic papillopathy in 1971. Visual acuity was moderately reduced and tended to improve spontaneously. Relative pupillary defects and dyschromatopsia were atypical.⁶ Visual field defects included enlarged blind spots, generalized constriction, and arcuate scotomas.^{3,6,7} Disc oedema was often diffuse with hyperoemia. Diabetic papillopathy was considered one form of nonarteritic anterior ischaemic optic neuropathy, with special characteristics: long duration of disc oedema, mild to-moderate initial visual loss, relatively mild-to-

moderate optic nerve dysfunction, and good visual recovery. Unlike nonarteritic ischaemic optic neuropathy,¹⁴ fluorescein angiography in diabetic papillopathy does not show delay in either onset or time to completion of prelaminar optic disk filling. By combining two large series with adult-onset diabetes mellitus (51 eyes of 35 patients^{6,7}), the median duration of papillopathy was 5 months. The aetiology of diabetic papillopathy included a combination of reversible microangiopathy¹⁵ and structural factors (small disc or small cup–disc ratio).⁶

Several patients in the present study had poor initial visual acuity. More than 30% of reported patients with diabetic papillopathy^{3,6,7,16,17} (16 out of 52 patients) had initial visual acuities below or equal to 6/30 as follows: two patients had 6/30, eight patients had 6/60, and six patients had less than 6/60.

The antioedema and angiostatic effects of corticosteroids may explain the resolution of disc oedema in the present cases. Intraocular and periocular corticosteroids reduced the breakdown of blood–retinal barrier¹⁸ partly by downregulating the production of vascular permeability growth factor, also known as vascular endothelial growth factor (VEGF).^{19–22} Periocular corticosteroids reached the posterior segment of the eye experimentally^{19,20,23,24} and clinically.^{21,22} Superonasal injections allowed a high drug concentration around the optic nerve head,²³ while superotemporal injections allowed a high drug concentration around the macular region.²⁵ Early decongestion of small optic nerve head could decrease the damage to peripapillary axons and minimize subsequent optic atrophy. The rapid visual recovery in our uncontrolled observational study could have been spontaneous, unrelated to therapy. Similarly, in the two patients with sequential papillopathy, the patients' impression of better vision in the treated eye could be attributed to a placebo effect.

Macular oedema was a frequent associated finding with diabetic papillopathy, being detected in 70% of eyes.⁶ Macular oedema in diabetic papillopathy resulted from leakage of abnormal disc vessels.¹⁷ By stabilizing the blood–ocular barrier at the disc¹⁷ and macula (Figure 3), periocular corticosteroids resulted in resolution of macular oedema in the present case series.

Complications of periocular corticosteroids included ocular hypertension,²⁶ cataract,²⁷ ptosis,²⁷ inadvertent rupture of the globe,²⁸ systemic toxicity²⁹ and uncontrolled hyperglycaemia. Periocular corticosteroids are not advised in eyes with chronic open-angle glaucoma and in steroid-responsive eyes. In these eyes, periocular (or intravitreal) injection of anti-VEGF EYE001³⁰ or angiostatic steroids (anecortave acetate,³¹ budesonide¹⁹) or bucillamine (antirheumatic drug),²⁰ and hyperbaric therapy³² could be considered in the future.

Besides these modalities, tight blood sugar control, blood pressure regulation, anticoagulation, regular exercise, and good hydration need to be considered in the initial management of diabetic papillopathy.

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