5 Tsanaktsidis G, Anarwal SA, Maloof AJ, Chandra J, Mitchell P. Postoperative *Morganella morganii* endophthalmitis associated with subclinical urinary tract infection. *J Cataract Refract Surg* 2003; **29**: 1011–1013.

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Sir,

Tadalafil-associated anterior ischaemic optic neuropathy

Tadalafil (Cialis) is a potent phosphodiesterase-type-5-inhibitor, which has been shown to be effective in the treatment of erectile dysfunction in men. It shares its mechanism of action with sildenafil (Viagra). In concurrence with recent reports of nonarteritic anterior ischaemic optic neuropathy (NAION) associated with the use of sildenafil, we describe a previously undocumented occurrence of NAION following the use of the more recently licensed and longer acting drug tadalafil, in the absence of any known systemic or local risk factors.

Case report

A healthy, nonsmoking 59-year-old man with no known vasculopathic risk factors was prescribed tadalafil for the treatment of erectile dysfunction following a radical prostatectomy for adenocarcinoma of the prostate. Within 7 days of ingesting 20 mg of tadalafil, he began to experience a generalised headache and blurring of vision associated with 'blue areas' and flashing lights in the visual field of the left eye. It is unknown whether or not an erection occurred or if he participated in sexual intercourse.

Ophthalmology examination 3 weeks later revealed snellen visual acuity of 6/6 and 6/9 in the right and left eye, respectively, with decreased left colour vision on Ishihara testing. There was a left relative afferent pupillary defect. Static perimetry revealed a global reduction in the left eye (Figure 1). Dilated fundoscopy showed a swollen left optic disc with an otherwise normal retina, consistent with ischaemic optic neuropathy (Figure 2). The right eye had a healthy retina and optic nerve head (ONH), with normal cup–disc ratio. The remainder of the ophthalmic examination was unremarkable. There were no symptoms or signs of temporal arteritis and an ESR was 7 mm. Fundus fluorescein angiography confirmed the diagnosis of left anterior ischaemic optic neuropathy (Figure 3). Blood pressure (BP) measured 122/70 mmHg, and in view of the absence of any vascular risk factors, further investigations such as 24-h BP monitoring were not performed.

Ophthalmic examination 4 months after presentation revealed pallor of the left ONH with persistent global reduction of sensitivity of the left visual field.

Comment

Six of the seven recent reports of sildenafil-associated anterior ischaemic optic neuropathy (AION) have occurred in patients with anatomically vulnerable optic discs with or without vasculopathic risk factors. [1–3] Our patient had no underlying risk factors for AION, and is the first documented report of such a case associated with the use of tadalafil.

Penile erection during sexual stimulation involves the local release of nitric oxide (NO) in the corpus cavernosum, which stimulates the synthesis of cyclic guanosine monophosphate (cGMP), thus producing relaxation of smooth muscle in the corpus cavernosum and penile arteries, therefore increasing penile blood flow. Tadalafil enhances the effect of NO by inhibiting phosphodiesterase type 5 (PDE 5), which is responsible for the degradation of cGMP in the corpus cavernosum. The subsequent increased levels of cGMP results in enhanced erectile function. Both tadalafil and sildenafil exert their effects by this mechanism; however, the former has a significantly longer duration of action, effective for up to 36 h.[4] When compared to sildenafil, tadalafil also exhibits a 70-fold greater selectivity for PDE5 than for PDE6 (responsible for retinal phototransduction), possibly accounting for its documented lower incidence of transient changes in perception of colour.[5,6]

NAION is known to occur typically in patients with small vessel occlusive cerebrovascular disease, including hypertension, diabetes mellitus, raised cholesterol or

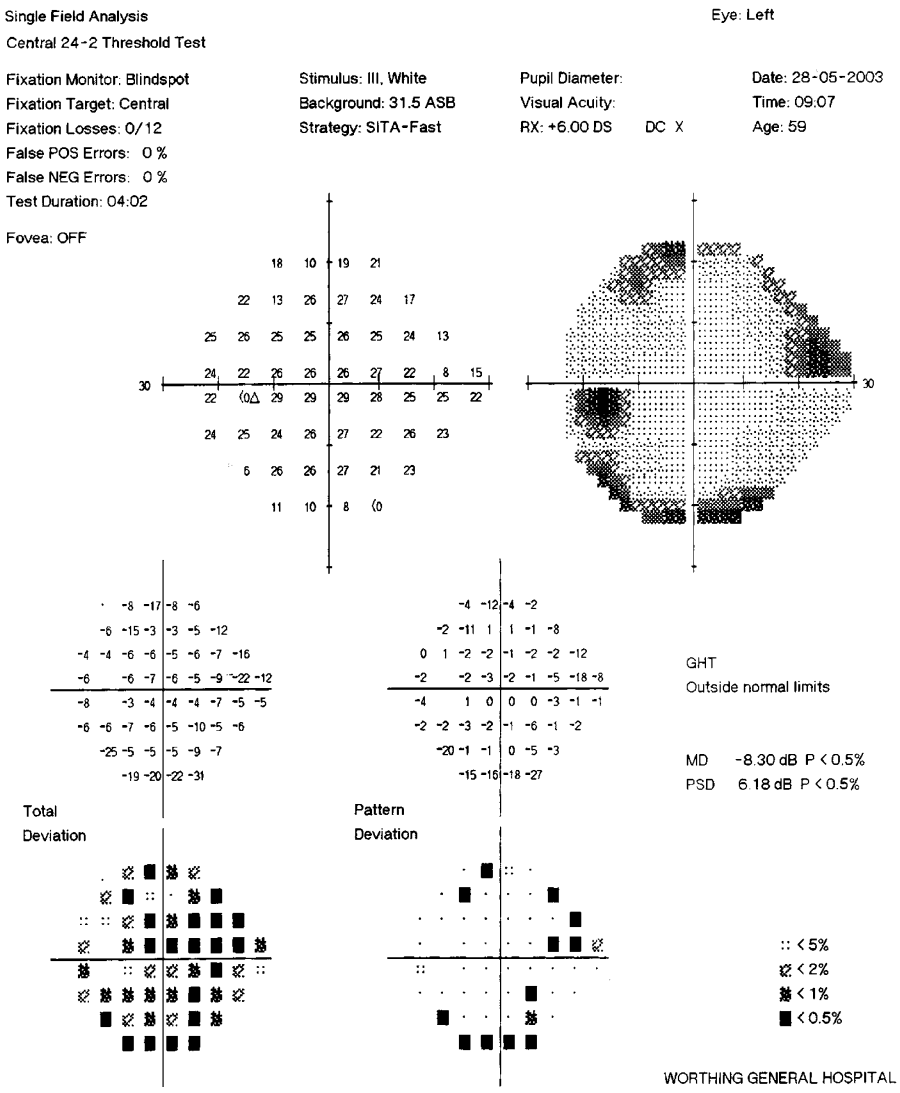

Figure 1 24-2 Humphrey visual field perimetry of the left eye showing global field reduction.

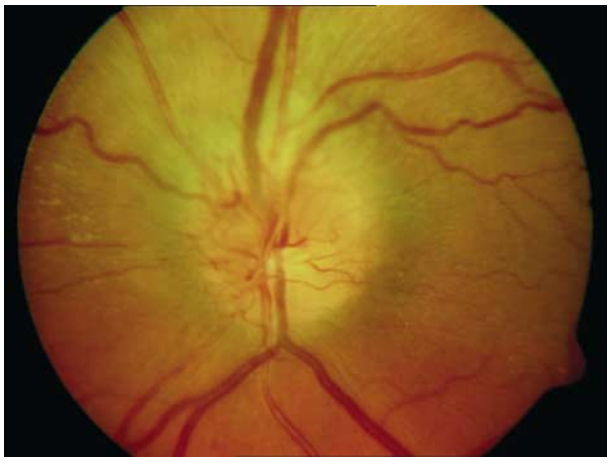

Figure 2 Left AION showing oedematous left optic disc with multiple splinter haemorrhages.

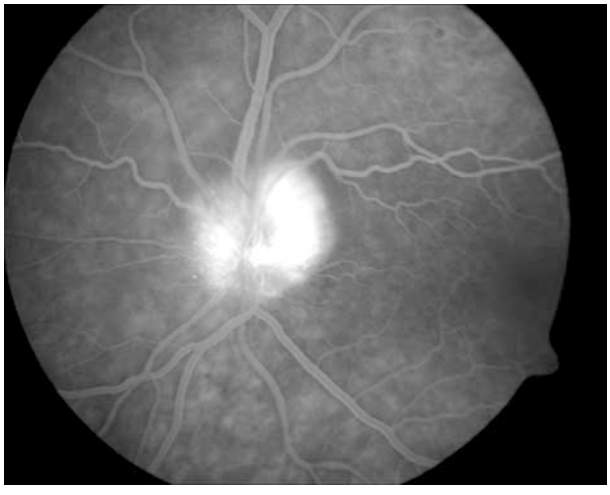

Figure 3 Fundus fluorescein angiography of left eye during acute phase of NAION showing diffuse disc hyperfluorescence.

fibrinogen levels, and cigarette usage.[7] The mechanism of action is thought to involve the reduced perfusion pressure in the posterior ciliary arteries supplying the optic disc, leading to ischaemia. Local factors such as structural predisposition to ischaemic damage by the presence of an optic disc with a small physiological cup (cup-disc ratio of less than 0.1), the classic 'disc at risk' (Burdle[8]), are thought to play an important role. Systemic circulatory factors are also thought to be involved in the development of critical ischaemia to the ONH. Systemic arterial or nocturnal hypotension may be a possible aetiology, especially in the context of a structurally crowded ONH. As with other PDE5 inhibitors, tadalafil is known to have systemic vasodilatory properties that may result in transient decreases in blood pressure,[9] which may be sufficient to serve as a trigger for ischaemia in the anatomically predisposed optic disc. As it is unknown whether the patient developed an erection or went on to participate in sexual activity, a steal phenomenon cannot be postulated as the cause of the hypotensive event to his optic nerve. By way of increasing local levels of NO, a potent vasodilator, disrupted auto regulation of microvasculature may also compromise ONH perfusion. Another potential mechanism is drug-induced potentiation of NO resulting in a toxic optic neuropathy.[1]

The association of tadalafil and NAION in a patient with no known systemic or local risk factors, combined with the lower dose of the drug, its greater selectivity for PDE5 and longer duration of action, may suggest that it is associated with a higher risk of the development of ONH ischaemia, compared to its predecessor. Although it is not possible to be confident about a causal association between tadalafil and NAION, this case, combined with previous reports of the condition in the context of PDE5 inhibitor usage, is strongly suggestive of one. The development of an animal model for NAION would provide an experimental paradigm in which to test the relationship between this poorly characterised condition and PDE5 inhibitors.

References

1 Pomeranz HD, Smith KH, Hart Jr WM, Egan RA. Sildenafil-associated nonarteritic anterior ischaemic optic neuropathy. *Ophthalmology* 2002; **109**(3): 584–587.
2 Dheer S, Rekhi GS, Merlyn S. Sildenafil associated anterior ischaemic optic neuropathy. *J Assoc Physicians India* 2002; **50**: 265.
3 Boshier A, Pambakian N, Shakir SAW. A case of NAION in a male patient taking sildenafil. *Int J Clin Pharmacol Ther* 2002; **40**(9): 422–423.
4 Gresser U, Gleiter CH. Erectile dysfunction: comparison of efficacy and side effects of the PDE-5 inhibitors sildenafil, vardenafil and tadalafil—review of the literature. *Eur J Med Res* 2002; **7**(10): 435–446.
5 Study 148–223: A double-blind, randomised, placebo controlled, four period crossover study to assess the effect of orally administered sildenafil (50, 100 and 200 mg) on visual function on healthy male volunteers. Viagra: Joint Clinical Review for NDA-20-895 Centre for Drug Evaluation and Research, FDA, Washington, DC, 1998, pp 160–161.
6 Padma-Nathan H. Efficacy and tolerability of tadalafil, a novel phosphodiesterase 5 inhibitor, in treatment of erectile dysfunction. *Am J Cardiol* 2003; **92**(9A): 19M–25M.
7 Ischaemic Optic Neuropathy Decompression Trial Study Group 666). *Characteristics of patients with NAION eligible for the Ischaemic Optic Neuropathy Decompression Trial. Arch Ophthalmol* 1996; **114**: 1366–1374.
8 Burdle RM. Optic disc risk factors for NAION. *Am J Ophthalmol* 1993; **116**: 759–764.
9 US Food and Drug Administration—Cialis. Department of Health and Human Services. Updated November 2003.

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Sir,

Optical coherence tomography-assisted localization of retained intraocular foreign body

Retained intraocular foreign bodies (RIOFB) represent a subset of ocular injuries that present complex surgical challenges to remove them successfully while attempting to preserve vision as well as the ocular architecture.[1]

Imaging modalities available to detect RIOFB include plain film X-rays, contact B-scan ultrasonography, CT scan, and MRI scanning.[2] This is the first report to the best of our knowledge describing the optical coherence tomography (OCT) findings for assessment of the depth of RIOFB on or within retina and associated macular status that may prognosticate the management.