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- Sir,  
**Peyronie’s disease following long-term use of topical timolol**
- Peyronie’s disease (PD) is characterised by formation of a localised fibrous plaque of the tunica albuginea of the penis, which results in varying degrees of pain and

angulation upon erection. This deformity frequently prevents sexual intercourse. Its aetiology is uncertain, but as with other fibrosing diseases it has been linked to the use of  $\beta$ -adrenergic receptor-blocking agents.<sup>1</sup> To our knowledge, we report the first case of PD secondary to the chronic use of timolol eye drops for the treatment of glaucoma.

### Case report

A 74-year-old Caucasian male attended the ophthalmology department for routine review of his primary open-angle glaucoma (POAG). He had been well controlled for the past 22 years with G.Timolol 0.25% twice daily with no adverse effects. Otherwise, he was taking no other medication and was a normotensive nonsmoker.

Automated static perimetry performed annually showed stable mild glaucomatous visual field defects. On examination at his latest visit, the visual acuity was 6/9 unaided in both eyes. Applanation tonometry revealed intraocular pressures of 18 mmHg OS and 19 mmHg OD, with optic nerve disc cupping of 0.7 and 0.6 respectively. Ocular examination was otherwise normal and routine follow-up was made.

The patient continued with G.Timolol, but presented again after the patient noticed a change in the shape of his penile erection, describing an angulation of the tip to the left and upwards with respect to the shaft, starting approximately one centimetre proximal to the base of the glans.

Over subsequent months, the deformity worsened, extending to 45° as measured by the patient. This was less apparent with his penis flaccid, but caused pain on erection, inability to perform intercourse, anxiety, and marital problems.

After reading the drug information sheet relating to his eye drops (Timoptol™, Merck Sharp & Dohme, York, UK), which cited PD as a side effect, he discontinued the drops and returned to clinic. He was then commenced on G.Lantanoprost nocte for intraocular pressure control. At 2 months from changing medication, the patient reported improvement in the angle of his shaft. After 2 years, the angle had halved, and sexual intercourse was achieved free from pain.

### Comment

Peyronie's deformity of the tunica albuginea of the penis is often only noticeable on erection, when a sharp and often painful angulation of the penis is revealed.

Epidemiological data on PD vary.<sup>2</sup> Levine<sup>3</sup> found an overall prevalence of 4.8% among a male cohort with a

mean angle of 21°, while Sommer<sup>2</sup> reported a prevalence of 3.2% among 4432 men, as defined by the presence of a palpable penile plaque. The triad of a palpable plaque, angulation, and painful erection was found in 1.04%. At autopsy, Smith<sup>4</sup> found either plaque or angulation in 23 out of 100 men examined. The true prevalence may be higher due to under-reporting of this embarrassing condition; physicians noted an increased incidence after a potential treatment became available in the form of sildenafil.

Numerous reports have linked  $\beta$ -blockers to fibrosing diseases. The chronic use of timolol and metoprolol eye drops has been reported to precede retroperitoneal fibrosis, which regressed after discontinuing the medication.<sup>5-8</sup> Similarly, reports of severe fibrosing side effects of practolol eye drops led to its withdrawal from use as glaucoma treatment. Rashes, nasal and mucosal ulceration, fibrous peritonitis, pleurisy, cochlear damage, and secretory otitis media occurred in some cases. In one case series, keratoconjunctivitis sicca, conjunctival scarring, fibrosis and metaplasia developed in 27 patients as an adverse reaction to practolol eye drops.<sup>9</sup> Symptoms and signs improved on withdrawal of the drug, but reduction of tear secretion persisted in most patients. However, no cases of PD have until now been reported as a result of the chronic use of topical  $\beta$ -blockers for glaucoma. In order to be certain that topical timolol caused PD in our patient, a rechallenge would have to be preformed. However, as this presents ethical dilemmas and alternative antiglaucoma therapy is as efficacious, we did not feel that this was appropriate.

Mechanisms involved in formation of these fibrotic plaques are unknown, but theories have been proposed. In this age group, reduced quality of erection predisposes to penile injury during sexual intercourse. Once injury has occurred to the tunica albuginea, an abnormal fibrotic plaque forms as a result of chronic inflammation.<sup>10</sup> This excessive fibrotic reaction relates to deposition of inappropriate collagen subtypes. Endogenous  $\beta$ -adrenergic agonists inhibit fibrosis by increasing the intracellular cAMP: cGMP ratio, thereby inhibiting fibroblast proliferation, a process itself inhibited by  $\beta$ -blockers. Histologically, a lymphocyte and plasmacyte infiltration of the perivascular space is seen, which is replaced by progressive fibrosis and substitution of elastic tissue with less distensible collagen type III, rich in glycine and alanine.<sup>7,11</sup>

The risk of PD with ocular (or systemic)  $\beta$ -blockers is unknown, but they are prescribed frequently to elderly males in whom PD is most common, and in most cases are used long term for the treatment of chronic disease. In our patient, it was noteworthy that PD started to resolve soon after discontinuing timolol eye drops. Prescribing clinicians should consider counselling

certain patients about this rare, under-reported and embarrassing complication of  $\beta$ -blockers, along with the more commonly encountered adverse effects.

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Sir,  
**Disciform keratitis and optic disc swelling in Kawasaki disease: an unusual presentation**

Kawasaki disease (KD) or mucocutaneous lymph node syndrome was first described by Tomisaku Kawasaki in 1967.<sup>1</sup> It is a disease of unknown aetiology and diagnosis

is based on characteristic clinical features. These include fever persisting for 5 days and at least four of the following five principal clinical features:

1. erythema and fissuring of lips, tongue, buccal, and pharyngeal mucosa,
2. polymorphous exanthema,
3. erythema and oedema followed by desquamation of the skin of palms and soles,
4. bilateral nonexudative conjunctival injection,
5. acute nonpurulent cervical lymphadenopathy.

Diagnosis can be made by the presence of fever and fewer than four principal symptoms when coronary artery disease is detected on echocardiography or coronary angiography.<sup>2,3</sup>

## Case report

An 11-year-old Caucasian male was admitted in the paediatric ward with a 5-day history of fever and rash on wrists and ankles. The rash became more widespread, involving his palms and soles and he also developed erythematous blisters on his lips and tongue with bilateral nonpurulent conjunctivitis. Laboratory investigation showed lymphocytosis ( $9.7 \times 10^9$  cells/l) and raised CRP (25 mg/l). No organism was identified on blood and urine culture, and anti-streptolysin titres as well as antibody screen for virus and mycoplasma were negative. He was managed as suspected KD and systemic signs responded well to treatment with intravenous immunoglobulin (IVIG) and high-dose aspirin. Echocardiogram showed normal function and no aneurysm was detected.

At ophthalmic referral on presentation, his visual acuity was noted as 6/6 in the right eye and 6/5 in the left eye. Anterior segment examination revealed diffuse bilateral nonpurulent conjunctival congestion, without any follicles or papillae and mild punctuate corneal staining. No anterior chamber or vitreous reaction was present and fundoscopy was normal.

After 3 weeks, he complained of cloudy vision in both eyes without any associated pain, redness, or photophobia. Vision was reduced to <6/60 in both eyes. He had no relative afferent papillary defect, and colour vision, measured with Ishihara plates, was intact. There was no conjunctival injection or discharge in either eye. Bilateral central stromal oedema with localised keratic precipitates and mild anterior chamber reaction characteristic of disciform keratitis was noted. Intraocular pressure was 10 mmHg OD and 12 mmHg OS by applanation. Fundoscopy revealed bilateral disc swelling without any other signs of inflammation in the posterior segment (Figure 1). A full neurological assessment excluded signs of increased intracranial