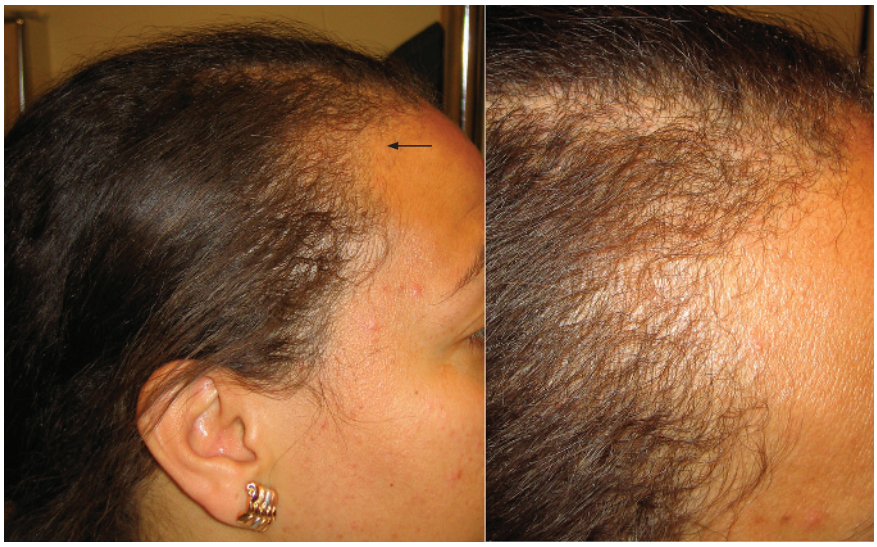

Figure 2 Topical Interferon Alopecia: Left, hair loss (arrow) from cranium is viewed at low and at higher magnification (right). Informed consent was obtained for publication of this figure.

patient consented to topical interferon-alpha therapy. The risks and benefits of therapy were explained in a discussion that adhered to the tenets of the Declaration of Helsinki and complied with the United States Health Insurance Portability and Privacy Act of 1996 (HIPPA).

Treatment involved placement of a punctal plug into the left lower eyelid followed by application of interferon-alpha eye drops (1-million units per millilitre four times per day for three months). She was taking no other medications during treatment. Ophthalmic examinations included a visual acuity determination, intraocular pressure measurement, slit-lamp examination and indirect ophthalmoscopy.

During her monthly examinations, a progressive reduction in tumour size and eyelid oedema was noted. However, at the end of treatment she complained of hair loss from her head temporally associated with topical interferon alpha therapy (fig 2).

Comment

Interferon induced a partial reduction in ALH and decreased eyelid oedema (a palliative treatment with no apparent ocular side effects). However, our patient noted scalp-alopecia during treatment.

Though hair loss is a known side effect associated with systemic interferon alpha administration, searching the National Library of Congress online database (PubMed) with the key words (interferon, eye cancer, conjunctiva, alopecia, Intron) revealed no other reported case of alopecia induced by interferon alpha eye drops. As seen after systemic interferon alpha administration, her hair has started to grow back.[9] However, it's reasonable to warn patients that alopecia can be associated with even the small dose used during topical interferon-alpha treatment of conjunctival tumours.

P T Finger, D Reichstein

From The New York Eye Cancer Centre, The New York Eye and Ear Infirmary, New York City, New York, USA

Correspondence to: Paul T Finger, MD, The New York Eye Cancer Centre, 115 East 61st Street, New York City, New York, USA 10021; pfinger@eyecancer.com

doi: 10.1136/bjo.2006.106930

Accepted 2 October 2006

Supported by The EyeCare Foundation, Inc., New York City, New York, USA. http://eyecarefoundation.org

Competing interests: The authors have no proprietary interest in any drugs used in this study.

Informed consent was obtained for publication of the person's details in this report.

References

1 **Erickson BA**, Harris GJ, Enke CA, *et al.* Periocular lymphoproliferative diseases: natural history, prognostic factors, and treatment. *Radiology*, 1992 Oct, **185**:63–70.
2 **Polito E**, Leccisotti A. Prognosis of orbital lymphoid hyperplasia. *Greafes Arch Clin Exp Ophthalmol* 1996;**234**:150–4.
3 **Coupland SE**, Hellmich M, Auw-Haedrish C, *et al.* Prognostic value of cell-cycle markers in ocular adnexal lymphoma: an assessment of 230 cases. *Graefes Arch Clin Exp Ophthalmol* 2004;**242**:130–45.
4 **Finger PT**. Topical chemotherapy for malignant conjunctival and corneal neoplasia. *Br J Ophthalmol* 2006;**90**:807–9.
5 **Boehm MD**, Huang AJ. Treatment of recurrent corneal and conjunctival intraepithelial neoplasia with topical interferon alfa 2b. *Ophthalmology* 2004;**111**:1755–61.
6 **Esquenazi S**, Fry CL, Holley E. Treatment of biopsy proved conjunctival intraepithelial neoplasia with topical interferon alfa-2b. *Br J Ophthalmol* 2005;**89**:1221.
7 **Schechter BA**, Schrier A, Nagler RS, *et al.* Regression of presumed primary conjunctival and corneal intraepithelial neoplasia with topical interferon alpha-2b. *Cornea* 2002;**21**:6–11.
8 **Guillot B**, Blazquez L, Bessis D, *et al.* A prospective study of cutaneous adverse events induced by low-dose alpha-interferon treatment for malignant melanoma. *Dermatology* 2004;**208**:49–54.
9 **Taliani G**, Biliotti E, Capanni M, *et al.* Reversible alopecia universalis during treatment with PEG-interferon and ribavirin for chronic hepatitis. *C J Chemother* 2005;**17**:212–4.
10 **Wilson MW**, Czechonska G, Finger PT, *et al.* Chemotherapy for eye cancer. *Surv Ophthalmol* 2001;**45**:416–44.

Bilateral symptomatic angle closure associated with a regular dose of citalopram, an SSRI antidepressant

Symptomatic angle closure (also called acute angle closure, AAC) is a rare complication in patients receiving antidepressant treatment. The main mechanisms of AAC proposed in the literature are through the antimuscarinic and the serotoninergic action of certain antidepressants[1] or through the development of choroidal effusions. In this unusual case, two different classes of antidepressants are highlighted, both of which seem to have had a direct effect of precipitating angle closure in our patient, but with differing timescales.

Case report

In December 2005, a 55-year-old Caucasian woman presented with a sudden onset of bilateral blurred vision, described as ''grey net curtain''. The symptoms lasted for a few hours and then the vision returned to normal, leaving her with a mild headache. Her medical history revealed depression and an episode of thyrotoxicosis in September 2005 for which she had radioactive iodine treatment. She was initially taking imipramine which was switched to citalopram 20 mg/day in July 2005 and thyroxine since September 2005. She wore hypermetropic glasses with a prescription of +3.75 D (dioptre) OD, +4.75 D OS, and had axial length measurements of 22.8 mm OD and 22.5 mm OS. On examination, visual acuities were 6/6 and both corneas were clear and intraocular pressures (IOPs), however, were measured at 56 mm Hg OD and 34 mm Hg OS.

The pupils were mid-dilated and showed a sluggish reaction to light. Gonioscopy revealed appositional angle closure >270° right and around 200° left. There was no significant cataract present in either eye. Optic discs had no features of glaucomatous damage.

The diagnosis of bilateral symptomatic (''sub-acute'') angle closure was made, and medical treatment was given according to our institutional protocol. The treatment consisted of intravenous acetazolamide 500 mg and G pilocarpine 2%, in addition to G apraclonidine and G levobunolol in both eyes. The above treatment brought the left IOP down to 18 mm Hg but the right eye required argon laser iridoplasty to achieve pressure control. These treatments were followed by bilateral Nd:YAG laser iridotomies. She was discharged with IOPs of 16 mm Hg right, 14 mm Hg left and patent iridotomies, and was prescribed G pilocarpine 2% and G prednisolone 1% both to be used in both eyes four times a day. With the consent of her doctor, she also stopped her citalopram tablets.

In subsequent follow-up visits, the topical pilocarpine was stopped and up to 3 months later she retained open drainage angles with no peripheral anterior synechiae, patent iridotomies and IOPs in the range of 15–16 mm Hg. During the same period, she developed increasing symptoms of a chronic anxiety disorder and her doctors restarted her on imipramine 25 mg/day on 9 May 2006. Fortuitously, she had a glaucoma clinic appointment 2 days later, at which point she was found to have over 270° appositional angle closure despite patent iridotomies, and IOPs measured at 28 mm Hg right and 23 mm Hg left. She was put on pilocarpine 1% twice daily

in both eyes and continued on imipramine until 7 July 2006. On the 7 July 2006, she was switched to mirtazepam 30 mg, which is her current antidepressant. IOPs and angles have now normalised, and she continues with her topical treatment.

Discussion

There have been reports of tricyclic antidepressants (such as amitriptyline and imipramine) being associated with angle closure largely through mydriasis of susceptible patients' pupils, mediated by an antimuscarinic effect.[2 3] A similar association was reported in six patients using paroxetine, which is a selective serotonin re-uptake inhibitor (SSRI) with a weak antimuscarinic effect.[4–8] Croos *et al*[9] have reported a case of bilateral angle closure after a citalopram and alcohol overdose. In a recent case report Zelefski *et al*[10] have highlighted the association of escitalopram with choroidal effusions and secondary angle closure. This has also been described extensively in association with the use of topiramate and is thought to be an idiosyncratic reaction to the drug. It usually manifests clinically within 2–4 weeks of administration.[11–14]

Although anterior chamber depth measurements and ultrasonography were not performed on our patient, the possibility of a choroidal effusion-related angle closure is unlikely as: (a) the visual acuity was normal on presentation; (b) there was no myopic shift; (c) the onset was delayed; and (d) the angle closure responded to conventional treatment with acetazolamide, miotics and peripheral iridotomies.

There is evidence of the presence of serotonin receptors in the human iris, cornea and ciliary body, but the effects of long-term SSRI administration on IOP or the angle are unclear. In animal studies, serotonin stimulation may cause mydriasis and have an independent effect in raising the IOP.[15 16]

The salient points in our case were that the episode of angle closure occurred 5 months after our patient started citalopram and also that there was a conspicuous relapse into angle closure 2 days after re-administration of imipramine, despite having patent iridotomies.

Although we have only an indirect indication of the tendency to angle closure (from axial length measurements and hypermetropic prescription), the sequence of events suggest a pharmacological factor influencing the course of disease. We propose a slow (possibly partially serotoninergic) effect on the iris and/or ciliary body attributable to citalopram given the delay in the onset of symptoms, and a more direct antimuscarinic effect of imipramine, which had an almost immediate effect.

From the current literature, the risk of angle closure related with the use of SSRIs appears small but can lead to significant morbidity. More laboratory-based studies are needed to further elucidate the long-term effects of SSRIs on the iris, angle and the IOP.

In reality, it is impractical to screen all the new patients on SSRIs for narrow angles. However, ophthalmic examination should be recommended in high-risk individuals before starting antidepressants and all patients need to be made aware of the symptoms of angle closure and the need for regular optometric eye examinations even in the presence of patent iridotomies.

P Massaoutis, D Goh, P J Foster
Moorfields Eye Hospital, London, UK

Correspondence to: P Massaoutis, Moorfields Eye Hospital, 19 Worfield St London, London SW11 4RB, UK

doi: 10.1136/bjo.2006.107185

Accepted 24 November 2006

Competing interests: None declared.

References

1 **Tripathi RC**, Tripathi BJ, Haggerty C. Drug-induced glaucomas: mechanism and management. *Drug Saf* 2003;**26**:749–67.
2 **Lowe RF**. Amitriptyline and glaucoma. *Med J Aust* 1966;**2**:509–10.
3 **Ritch R**, Krupin T, Henry C, *et al*. Oral imipramine and acute angle closure glaucoma. *Arch Ophthalmol* 1994;**112**:67–8.
4 **Levy J**, Tessler Z, Klemperer I, *et al*. Late bilateral acute angle-closure glaucoma after administration of Paroxetine, in a patient with plateau iris configuration. *Can J Ophthalmol* 2004;**39**:780–1.
5 **Eke T**, Bates AK. Acute angle closure glaucoma associated with paroxetine. *BMJ* 1997;**314**:1387.
6 **Browning AC**, Reck AC, Chisholm IH, *et al*. Acute angle closure glaucoma presenting in a young patient after administration of paroxetine. *Eye* 2000;**14**(Pt 3A):406–8.
7 **Bennett HG**, Wyllie AM. Paroxetine and acute angle-closure glaucoma. *Eye* 1999;**13**(Pt 5):691–2.
8 **Kirwan JF**, Subak-Sharpe I, Teimory M. Bilateral acute angle closure glaucoma after administration of paroxetine. *Br J Ophthalmol* 1997;**81**:252.
9 **Croos R**, Thirumalai S, Hassan S, *et al*. Citalopram associated with acute angle-closure glaucoma: case report. *BMC Ophthalmol* 2005;**5**:23.
10 **Zelefski JR**, Fine HF, Rubinstein VJ, *et al*. Escitalopram-induced uveal effusions and bilateral angle closure glaucoma. *Am J Ophthalmol* 2006;**141**:1144–7.
11 **Banta JT**, Hoffman K, Budenz DL, *et al*. Presumed topiramate-induced bilateral acute angle closure glaucoma. *Am J Ophthalmol* 2001;**132**:112–14.
12 **Craig JE**, Ong TJ, Louis DL, *et al*. Mechanism of Topiramate-induced acute-onset myopia and angle closure glaucoma. *Am J Ophthalmol* 2004;**137**:193–5.
13 **Levy J**, Yagev R, Petrova A, *et al*. Topiramate-induced bilateral angle closure glaucoma. *Can J Ophthalmol* 2006;**41**:221–5.
14 **Fraunfelder FW**, Fraunfelder FT, Keates EU. Topiramate-associated acute, bilateral secondary angle closure glaucoma. *Ophthalmology* 2004;**111**:109–11.
15 **Barnett NL**, Osbourne NN. The presence of serotonin (5-HT1) receptors negatively coupled to adenylate cyclase in rabbit and human iris/ciliary processes. *Exp Eye Res* 1993;**57**:209–16.
16 **Osborne NN**. Serotonin and melatonin in the iris/ciliary processes and their involvement in intraocular pressure. *Acta Neurobiol Exp* 1994;**54**(Suppl):57–64.

Ocular surface toxicity associated with topical interferon α-2b

Conjunctival intraepithelial neoplasia (CIN) has traditionally been managed with surgical excision, combined with cryotherapy, with a wide range of reported recurrence rates.[1] In cases of CIN that are too extensive to perform a complete surgical excision or in cases in which the surgical margins are involved, ophthalmologists are now using adjunctive topical antineoplastic agents such as mitomycin C[2 3] and interferon α-2b (IFNα-2b)[4–12] in place of, or in combination with, repeat surgical excision. Although the toxicity associated with the topical ophthalmic use of mitomycin C is well recognised,[13–15] IFNα-2b has been reported not to cause ocular surface toxicity.[4–12] We report a case of corneal toxicity, manifest as epithelial microcyst formation, associated with the use of topical IFNα-2b.

Case report

A 64-year-old man with a history of biopsy-proven CIN of the left eye presented to one of the authors (AJA) for evaluation. Twenty-two years earlier, he had undergone a superficial keratectomy and excision of a papillomatous conjunctival lesion from the left eye. Six years before presentation he had undergone a second superficial keratectomy, and a limbal conjunctival biopsy 3 years later demonstrated epithelial squamous cell carcinoma in situ. The patient was treated with a 4-week course of topical mitomycin C (0.02% initially, then 0.01%), which was discontinued secondary to poor tolerance.

On presentation, the patient's visual acuity was limited to counting fingers in the left eye secondary to a dense cataract. Unilateral 360° micropannus and scattered punctate epithelial keratopathy (PEK) were noted in the cornea of the left eye. Several foci of fine papilliform vessels were noted in the nasal and limbal bulbar conjunctiva (figs 1A,B); biopsy specimens taken from these regions demonstrated marked atypia of the epithelial cells, consistent with CIN, extending to the edges of the submitted specimens.

As the extensive conjunctival vascular abnormalities were too diffuse to perform a complete surgical excision, adjunctive topical treatment with mitomycin C was considered. However, given the previous poor tolerance of mitomycin C and concern about exacerbation of corneal limbal stem cell compromise secondary to the previous limbal keratectomies and mitomycin C-associated toxicity, the patient was started on topical IFNα-2b (1 million IU/ml; prepared from injectable powder mixed with preservative-free normal saline) four times daily. Four weeks later, diffusely

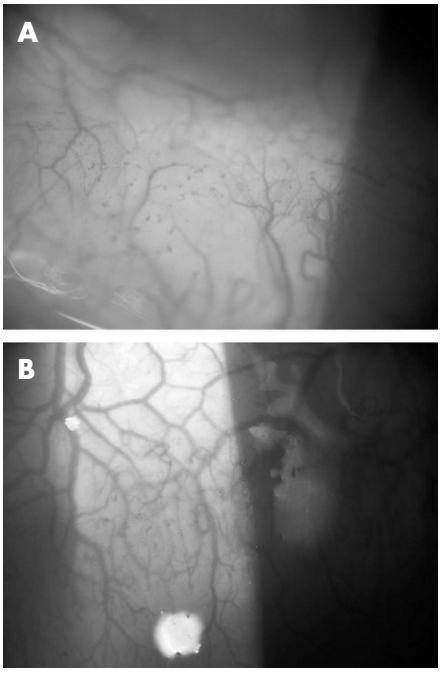

Figure 1 Slit lamp photomicrographs demonstrating fine corkscrew vessels in the inferonasal bulbar (A) and superior limbal (B) conjunctiva of the left eye.