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.

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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

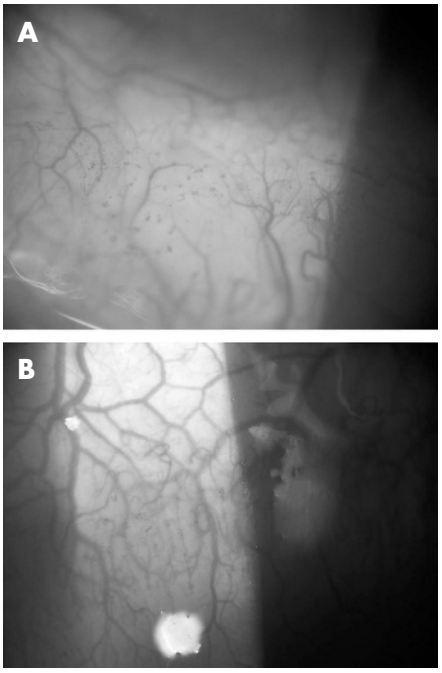

Figure 1 Slit lamp photomicrographs demonstrating fine corkscrew vessels in the inferonasal bulbar (A) and superior limbal (B) conjunctiva of the left eye.

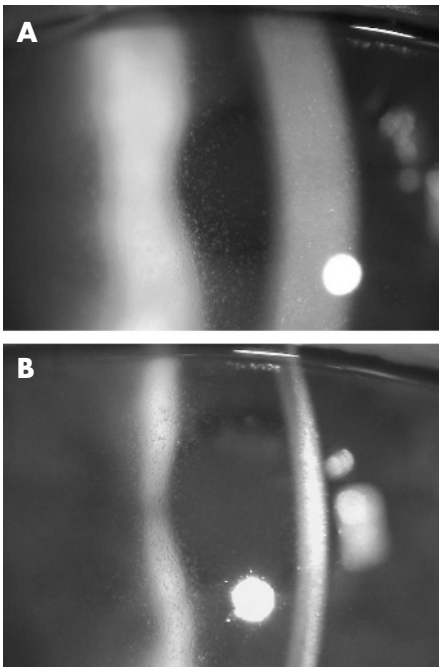

Figure 2 (A) Slit lamp photomicrograph demonstrating fine, diffuse, clear epithelial microcysts in the left cornea 4 weeks after instigating topical interferon α-2b treatment. (B) Scattered punctuate epithelial staining in the slit lamp beam, overlying, but not necessarily corresponding to, the epithelial microcysts.

distributed, clear corneal epithelial microcysts were noted, prompting discontinuation of the topical interferon (figs 2A,B). Following an uncomplicated cataract extraction, the corrected visual acuity improved to 20/30, limited by central PEK and persistent epithelial microcysts. At 1 year after treatment with topical IFNα-2b, the corneal epithelial microcysts were still present, as were the limbal papilliform vessels, although the patient declined additional therapy.

Comment

Interferons are a group of proteins that bind to surface receptors of target cells, triggering a cascade of intracellular antiviral and antitumour activities.[7 10] Previous reports have shown topical IFNα-2b, with or without subconjunctival IFNα-2b, to be very effective in the treatment of primary and recurrent CIN.[5–12 16 17] To the best of our knowledge, none of the 40 cases reported have documented associated corneal epithelial toxicity,[5–12 16 17] although after 2 weeks of treatment, four times a day, one patient developed mild PEK, which resolved after discontinuation of the topical interferon.[16] A transient follicular conjunctivitis has also been reported in five patients,[7 8] presumed by one author reporting four of these five cases to be related to the vehicle used in the topical IFNα-2b preparation,[7] as no evidence of corneal or conjunctival epithelial toxicity was demonstrated previously in an animal model.[4] As the topical IFNα-2b drops utilised by the patient reported here were prepared using only preservative-free normal saline, we may safely conclude that the observed corneal epithelial changes were not secondary to vehicle or preservative-related toxicity.

The development of corneal epithelial microcysts in the case reported here is evidence of the ocular surface toxicity that may be seen in patients treated with topical IFNα-2b. Corneal epithelial microcystic formation, identical to that noted in the patient reported here, has been reported with the use of systemic interferon treatment,[18] and is a well-recognised complication of the systemic administration of the antineoplastic agent cytarabine (Ara-C).[19 20] Corneal toxicity associated with high-dose systemic cytarabine is thought to be secondary to the inhibition of DNA synthesis in the rapidly dividing basal corneal epithelial cells.[20] Similarly, the antineoplastic actions of interferon involve immune-enhancing properties as well as inhibition of cellular proliferation.[21] An alternative mechanism that has been proposed to explain corneal epithelial microcyst formation in association with systemic interferon treatment is increased intercellular adhesion and altered corneal epithelial cell migration via an interferon-mediated increased expression of intercellular adhesion molecule-1.[18] The development of the epithelial cysts several weeks after the initiation of topical interferon treatment, whether through inhibition of DNA synthesis, alteration of epithelial cell migration or another mechanism, indicates that IFNα-2b-related corneal epithelial cell toxicity is the most likely explanation for the origin of the microcysts. Ophthalmologists should be aware of the fact that ocular surface toxicity may be associated with topical IFNα-2b treatment, and that it should be used judiciously in patients with corneal and conjunctival intraepithelial neoplasia.

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Periorbital xanthogranuloma after blepharoplasty

Periocular xanthogranuloma is a rare inflammatory condition characterised by histiocytes and Touton giant cells. It is encountered in several settings: juvenile xanthogranuloma, Erdheim–Chester disease (ECD) and necrobiotic xanthogranuloma. Recently, cases with an adult onset not associated with ECD have been described, with frequent involvement of the eyelids and orbit.[1–3] In this report, we describe a unique case of adult-onset periocular xanthogranuloma precipitated by blepharoplasty.

Case report

A 57-year-old woman was referred for persistent postoperative oedema/inflammation 18 months after bilateral upper and lower blepharoplasty. On the basis of a review of her medical record and a conversation with her cosmetic surgeon, there was no suggestion of disease before surgery: her periocular involutional changes were typical and no abnormalities were noted intraoperatively. Her initial postoperative course was unremarkable, with mild swelling/ecchymosis. In contrast with the ecchymosis, which resolved within 2 weeks, the oedema unremittingly progressed. No photographs were taken during the immediate postoperative period.

Examination revealed infiltration of all four eyelids, which were rubbery to palpation, bilateral blepharoptosis, palpably enlarged