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Sir,

Severe Reversible Ocular Anterior Segment Ischaemia Following Topical Trifluorothymidine (F3T) Treatment for Herpes Simplex Keratouveitis

Anterior segment ischaemia can result from vascular disease, ophthalmic surgical procedures, hyperviscosity syndromes and disseminated intravascular coagulopathy.[1,2] An acute ischaemic reaction in the anterior segment following long-term topical trifluorothymidine (F3T) treatment has previously been reported in the literature with conjunctival neovascularisation, band keratopathy and iris atrophy.[3] The reversible nature of F3T-induced ischaemia has not previously been documented.

We report a case of severe anterior segment ischaemia in a patient with known sarcoidosis using topical F3T for recurrent herpes simplex keratouveitis which improved on withdrawal of the topical medication. Conjunctival biopsy showed non-specific inflammatory features with no evidence of vasculitis.

Case Report

A 43-year-old man with past history of sarcoidosis, recurrent episodes of anterior uveitis in the left eye, and a 16 year history of recurrent herpes simplex dendritic keratitis in the right eye developed injection and irritation of the right eye. The patient had no previous history of trauma or ocular surgery to the right eye. Initially visual acuity was 6/18 on the right and 6/5 on the left. Herpes simplex keratouveitis was diagnosed clinically. Due to prior hypersensitivity to acyclovir, treatment with F3T five times a day, betamethasone q.i.d. and atropine b.d. was initiated. The treatment regime was reduced to F3T t.i.d. after 1 month but increased again to the initial frequency due to worsening keratitis.

Over the ensuing 1 month the patient developed generalised corneal oedema with ischaemic changes starting in the tarsal conjunctiva and progressing to 360° of ischaemia of the right anterior bulbar conjunctiva and sclera (Fig. 1). The inferior tarsal conjunctiva also became ischaemic. The visual acuity in the right eye deteriorated to count fingers at 50 cm. There was a large central corneal epithelial defect extending beyond the inferior limbus onto the bulbar conjunctiva. The anterior chamber had a moderate flare. Intraocular pressure by Goldmann

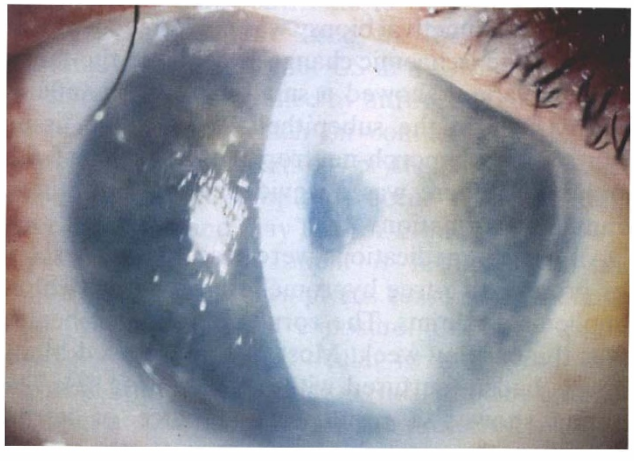

Fig. 1. *Generalised corneal oedema and limbal ischaemia.*

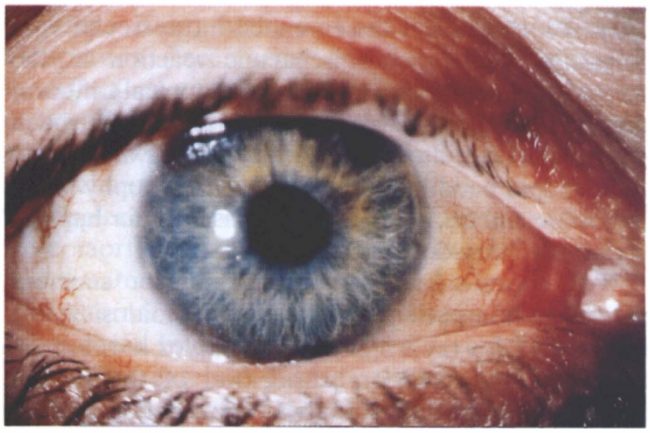

Fig. 2. *Resolution of the generalised corneal oedema and reperfusion of the occluded vasculature following discontinuation of the topical F3T treatment.*

applanation tonometry was 32 mmHg in the right eye and 18 mmHg in the left. Examination of the posterior segment revealed no active inflammation. Examination of the left eye was normal. Fluorescein angiography of the anterior segment of the right eye showed non-perfusion of large areas of anterior bulbar conjunctiva and episclera without sectorial ischaemia of the iris.

Results of laboratory investigations including a full blood count with differential, serum fasting glucose, sedimentation rate, C-reactive protein, clotting profile, autoantibody screen, anticardiolipin antibody, anti-neutrophil cytoplasmic antibody (ANCA), syphilis serology, circulating immune complexes, complement components and liver function tests were all within normal limits.

Angiotensin converting enzyme (ACE) level and ionised calcium were minimally raised. Serum creatinine and urea were marginally elevated. The 24 hour urine collection for detection of proteinuria was negative. The patient was reviewed by the renal physicians who felt that these results were consistent with established nephrocalcinosis and sarcoidosis. Ocular and carotid ultrasound examinations were normal.

Bulbar conjunctival biopsy was performed within 1 month of the ischaemic changes starting in the tarsal conjunctiva and showed a small increase in inflammatory cells in the subepithelial connective tissue with some polymorph-neutrophil infiltration of the epithelium. There was no evidence of vasculitis or granuloma formation.

All topical medications were discontinued except for preservative-free hypromellose drops and chloramphenicol minims. The corneal epithelium healed over the ensuing week. Most of the occluded blood vessels had re-perfused within 5 days (Fig. 2). The cornea showed a residual appearance of vortex epitheliopathy, probably secondary to the limbal insult. The visual acuity returned to the level of vision prior to the recent episode of herpetic keratouveitis.

Discussion

Anterior segment ischaemia can result from a systemic vasculitis such as polyarteritis nodosa, Wegener's granulomatosis, sarcoidosis or temporal arteritis.[1,2] Although our patient had a previous history of sarcoidosis, features consistent with a systemic vasculitis were not apparent on conjunctival biopsy.

Known toxic effects of topical F3T include punctate epithelial keratopathy, follicular conjunctival hypertrophy, punctal occlusion, conjunctival cicatrisation,[4] and inhibition of corneal epithelial wound healing.[5] Long-term use of F3T as a trigger of conjunctival ischaemia[6] and anterior segment ischaemia[3] has previously been postulated. We believe that the rapid recovery on withdrawal of the topical medication and the non-specific inflammatory features on the conjunctival biopsy in this case indicate that either the atropine or the F3T was responsible for the ischaemic changes. No prior reports exist in the literature that long-term use of atropine causes anterior segment ischaemia. Therefore, a toxic effect of topical F3T appears to be the most likely explanation for the severe reversible anterior segment ischaemic changes observed in this patient.

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Sir,

Ocular Exposure to CS Gas: The Importance of Correct Early Management

After assessment by 16 police forces,[1] all but two of the 43 forces in England and Wales[2] are now being issued with CS gas. Given this, and the growth in illegal usage, the prevalence of ocular injury from this agent seems destined to increase. We report the presentation and management of six patients simultaneously exposed to CS gas and review the current literature.

Case Report

The six individuals were affected when an illegally held substance, presumed to be CS gas (*O*-chlorobenzylidene malononitrile), was sprayed into the doorway of a public house. Two were hit by the spray directly, the other four being affected as the agent drifted into the bar. All six were rapidly transferred to Southampton Eye Unit where they underwent standard treatment for CS gas exposure of avoiding contact with water, or other irrigating solutions, and placing in a well-ventilated area. Electric fans were employed to increase airflow across the eye and facilitate the vaporisation of any dissolved gas.

Ocular examination 30 minutes later revealed only slight conjunctival injection. In particular the periorbital skin was undamaged, the pH was neutral in all 12 eyes, corneal sensation was normal and the anterior chambers quiet. One apparently paradoxical finding was a decreased tear break-up time (of 6–9 seconds) in the eyes of the four individuals indirectly affected, compared with normal in the two individuals receiving spray direct to the face. The following day all were asymptomatic with no respiratory or dermatological sequelae.

Despite a strong smell of CS vapour, no member of staff suffered any ill effects. No specific protective measures were taken other than opening the windows to improve ventilation.

Discussion

CS gas was developed at the Chemical Defence Experimental Establishment at Porton, England in the 1950s. The white crystalline substance was initially placed in a canister with an explosive device which, upon detonation, formed a smoke of suspended particles. Further development resulted in the product being micronised and mixed with an anti-agglomerant (CS_1) or treated with silicone water repellent (CS_2), a form which remains potentially active as a dust for several weeks.[3]

Tear gas, used world-wide for crowd control, is the common term for a group of some 15 chemicals otherwise referred to as 'harrassing agents' on account of their ability to cause temporary disablement. The most common are *O*-chlorobenzylidene malononitrile (CS gas), 1-chloroacetophenone (CN gas) and dibenzoxazepine (CR gas). Toxicology data are scant as much of the research has been military and some classified as secret,[4] but all are irritant to skin, eyes and respiratory tract.

CR gas is the most potent lacrimator, but has few systemic effects.[5] CN gas is the most toxic and a constituent of the self-defence spray Mace; deaths from asphyxiation or pulmonary injury have been reported. CS gas is 10 times more potent as a lacrimatory agent than CN but with less toxicity: studies amongst volunteers noted rapid cessation of all symptoms within minutes of removal from exposure. The British Secretary of State for the Home Department in 1969[3] concluded that 'whilst exposure to CS gas can be lethal in the form of toxic pulmonary damage leading to pulmonary oedema, such an occurrence would only be at concentrations that were several hundred times greater than exposure dosage that produces intolerable symptoms' which would force the individual to leave the vicinity. In times of conflict such evasive action may not be possible and in May 1988 the Federal Laboratories Inc. in the USA suspended sale of the agent.[6]

Until recently United Kingdom mainland police forces had used CS gas only during the Toxteth riots of 1981.[7] However, in March 1996, despite earlier deferral when a police officer suffered ocular burns,[8] more than 2000 officers in 16 authorities in England and Wales were issued with CS gas in a 6 month trial. No proven fatalities have occurred, but CS gas has been implicated by the media in the death of one individual during an aggravated arrest.[1]

Illegally acquired CS gas has a concentration of 0.2%, with large amounts of propellants and solvents[9] which may contribute to the symptoms. The 'CS gas Incapacitant' used by the police force[5] contains a 5% solution of CS in a solvent of methyl iso-butyl ketone propelled by nitrogen. The solvent is an ocular irritant which on contact with the skin causes tingling, irritation, erythema, drying and blistering. Initial symptoms occur up to 8 hours after exposure and may last for a week.

If the correct treatment is instigated, in the majority of cases all symptoms cease 15–30 minutes after withdrawal from exposure. Contrary to the general rule of copious ocular irrigation following chemical injury,[10] evaporation (facilitated by a fan or air from a cold hairdryer) is the preferred management. Irrigation simply prolongs the severe burning sensation.[11]