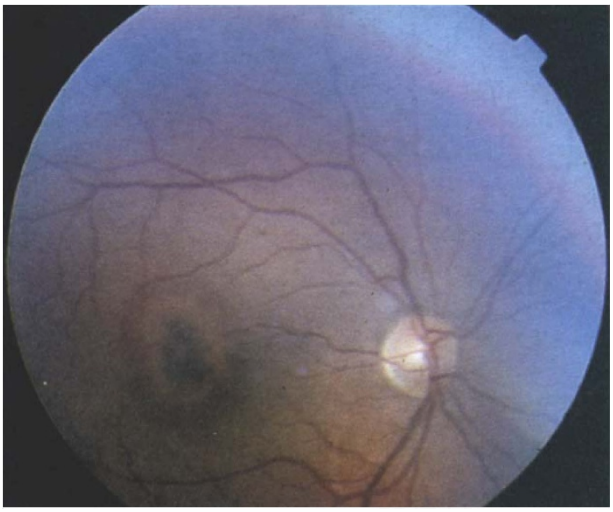
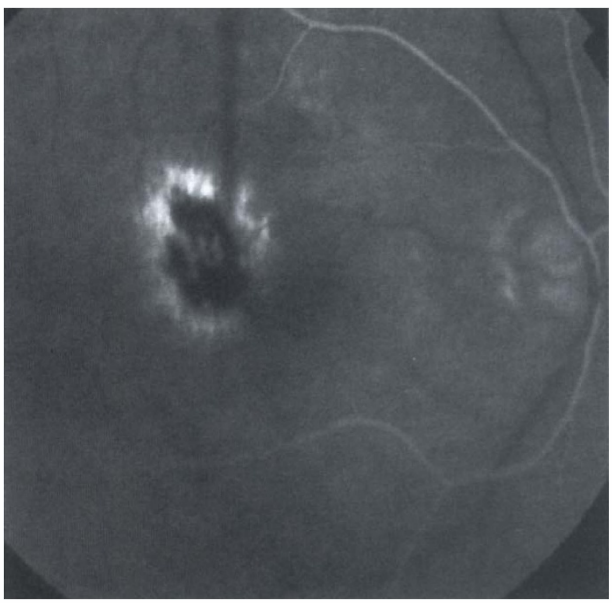


(a)



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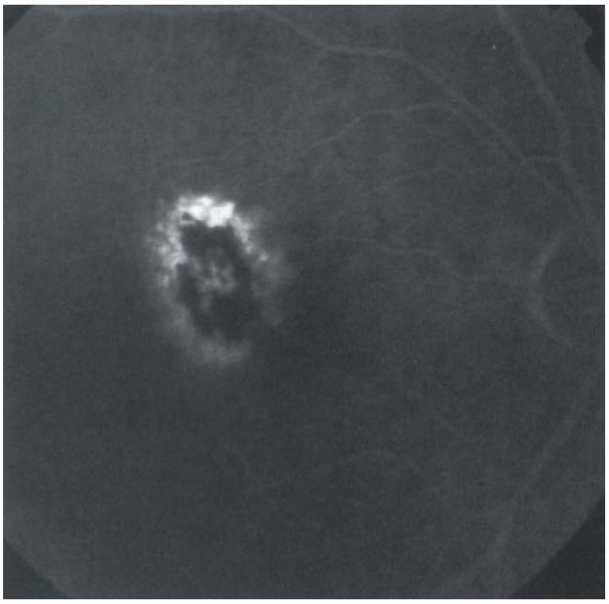

(c)

Fig. 2. *(a) Fundus photograph of the right eye demonstrates a grey subretinal lesion beneath the fovea with surrounding retinal pigment epithelial atrophy. (b) Fluorescein angiogram of the right eye in the early phase (20.8 s) shows early lacy hyperfluorescence, representing an area of classic subfoveal choroidal neovascularisation. (c) The late-phase angiogram (3.06 min) reveals progressive leakage and a surrounding area of retinal pigement epithelial atrophy.*

ocular injury and was possibly precipitated by the associated ocular ischaemia. Ischaemia may play a role in the development of choroidal neovascularisation.

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Sir,

Permanent corneal limbal stem cell dysfunction following radiotherapy for orbital lymphoma

We present a patient with unilateral stem cell deficiency following the administration of 4600 cGy in 21 fractions for a high-grade malignant B cell lymphoma of the orbit. The stem cell deficiency occurred without acute manifestations of radiation-induced toxicity to the cornea

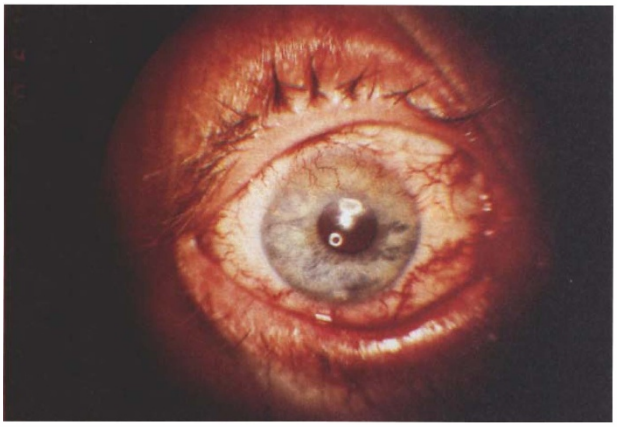

Fig. 1. *Photomicrograph of the right eye showing 'conjunctivalisation' of the superior and inferior cornea and adjacent large-bore conjunctival vessels.*

or conjunctiva. Conjunctivalisation was associated with changes in cytokeratin expression, confirmed by immunocytochemistry on impression cytology samples.

Case report

A 31-year-old man presented with a painful swelling in the right orbit and slight blurring of vision. There was a tender mass in the superomedial quadrant of the right orbit displacing the globe laterally. The Snellen visual acuity was 6/5. A computed tomogram (CT) showed the mass extending to the right orbital apex. A biopsy revealed a high-grade malignant B cell lymphoma (lymphoblastic lymphoma).

His vision was deteriorating rapidly so emergency radiotherapy of 3600 cGy in 16 daily fractions was given with a direct anterior field on a 6 MeV linear accelerator. The patient's eye was kept open to avoid build-up effect of radiation on the conjunctiva and cornea. Because there was still residual disease on completion of radiotherapy an additional 1000 cGy was given with the same field arrangement. Repeat CT showed the orbit to be free of lymphoma.

Four years later the patient returned with reduced visual acuity of 6/36, N36 and symptoms of ocular irritation. Slit-lamp examination showed enlarged conjunctival vessels and superficial vascularisation of the upper and lower thirds of the right cornea (Fig. 1). There was no keratinisation of the tarsal conjunctiva and the eye was not dry on Schirmer testing. The diagnoses of radiation-induced stem cell deficiency and cataract were proposed.

Impression cytology specimens were collected for immunocytochemical staining for cytokeratin (CK) expression (Fig. 2). Immunostaining for CK3, which is regarded as a marker for advanced corneal epithelial differentiation, was positive centrally, suggesting a corneal phenotype. Immunostaining for CK19 was positive superiorly from 9 o'clock to 3 o'clock, suggesting a conjunctival phenotype. At the lower border of the specimen there was a mosiac of CK3 and CK19 staining. There were also numerous neutrophils representing an area of chronic inflammation.

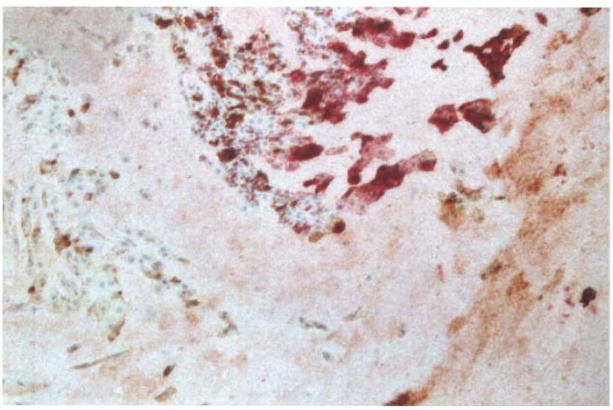

Fig. 2. *Photomicrograph of immunohistochemically stained epithelial cells from an impression cytology specimen. CK3 in corneal epithelium stains brown (horseradish peroxidase), CK19 in conjunctival epithelium stains red (acid phosphatase); haematoxylin counterstain. Magnification* ×100.

Removal of a right posterior subcapsular cataract by phacoemulsification and lens implantation improved the visual acuity to 6/9. However, the patient's symptoms of photophobia and ocular irritation persisted despite the use of topical lubricants.

Comments

Radiation-induced complications to the eye and ocular adnexa have been recognised since the late nineteenth century. Although cataract and radiation keratopathy are well known,[1] we are unaware of previous reports of persistent limbal stem cell dysfunction. The side-effects of a given dose of radiation are different depending the fraction size, dose rate, period over which it is administered and the cellular kinetics of the target and bystander tissues.[2] With 1000 cGy fractions, keratitis and corneal oedema can be expected after approximately 3000 cGy; if similar fractions are used 5000 cGy can be tolerated.[1] Fujishima and colleagues' case of temporary limbal stem cell deficiency occurred after 6100 cGy; symptoms began only 3 days after the completion of radiotherapy and resolved after 4 months with conservative treatment.[3] Cytokeratin expression was not examined.[3] In our case 4600 cGy administered over 21 sessions did not result in acute corneal complications, but there was clinical evidence of persistent limbal stem cell deficiency later and associated changes in expression of cytokeratin markers. The delay in presentation may be a consequence of the special regulation of stem cell mitotic activity[4] so that damage to DNA only manifests when stem cells replicate to maintain the stem cell pool.[4] Previous reports of limbal stem cell deficiency have also noted that the presentation may be delayed for more than 3 years.[5]

Limbal stem cells are required to proliferate and differentiate in a coordinated fashion for the ultimate replacement of normal corneal epithelium.[3–5] When the stem cells are severely damaged the conjunctival epithelium extends across the limbus onto the cornea. Clinically this 'conjunctivalisation' is manifested by a disturbed corneal surface, ocular irritation and later

chronic inflammation, stromal scarring and reduced visual acuity.[4,5] Impression cytology, with immunocytochemistry for CK expression, can be used to examine the phenotypic changes associated with 'conjunctivalisation'.[6,7] A change from CK3 expression to CK19 expression over the cornea suggests change from corneal to conjunctival phenotype.[6,7] These two populations normally meet at the limbus.[7]

The limbal stem cell population can be restored by limbal stem cell grafting.[8–10] Autologous grafting is generally preferred over allogenic grafting, which may suffer rejection without the use of immunosuppressive agents.[9] This has traditionally been achieved by taking two free limbal grafts (60 mm^2) from the healthy eye.[8,9] However, our patient was unprepared to take the risk of decompensating the normal left cornea. Recently a new technique using cells cultivated *in vitro* from 1 mm^2 biopsies of healthy limbal stem cells have generated enough epithelium to cover the entire corneolimbal surface.[10] These cells have been shown to retain their corneal phenotype for at least 2 years.[10] This technique offers another option for patients with bilateral stem cell deficiency or where the patient is unwilling to risk decompensating the unaffected eye.

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Sir,

Allergic contact fingertip dermatitis secondary to proxymetacaine in an ophthalmologist

We report a case of allergic contact fingertip dermatitis secondary to proxymetacaine sensitivity. This is a rare and infrequently reported problem, which can cause difficulties in clinical practice. Specialists with chronic hand eczema should consider seeking specialist dermatology advice.

Case report

In January 1999 a right-handed 45-year-old female consultant ophthalmologist began to suffer itching of the middle fingertip on her left hand. The problem progressed and caused thickening of the periungal skin and onycholysis of the distal nail plate. The fingertip became increasingly erythematous with painful fissuring, crusting and occasional bleeding (Fig. 1). Scrubbing the hands for theatre and wearing surgical rubber latex gloves exacerbated the symptoms. The affected finger was used to hold down the lower eyelid whilst applying drops to patients' eyes (Fig. 2). The symptoms worsened in the evening after working in the ophthalmology clinic.

The ophthalmologist began using her index finger for holding the eyelid down whilst applying eye drops, because of increasing pain in the middle finger. Similar symptoms started to develop on this finger within 7 days. The patient had no prior dermatological history, except for a past history of allergic contact dermatitis to epoxy resin, which developed from exposure occurring in tissue processing for electron microscopy. There was no personal or family history of atopy. The condition continued to worsen and use of the fingers was severely limited because of the intermittent bleeding and pain.

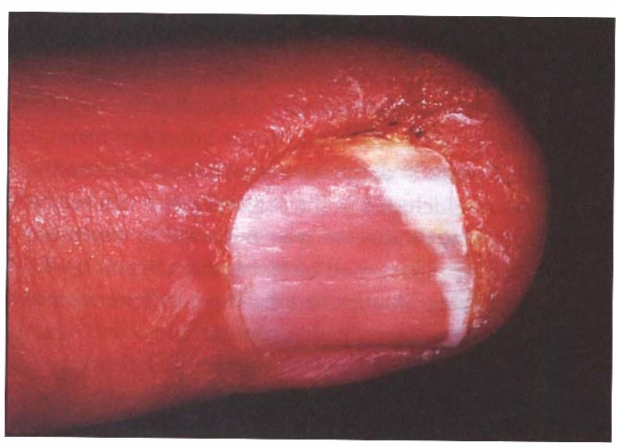

Fig. 1. *Right middle fingertip showing allergic contact dermatitis secondary to topical proxymetacaine eye drop application.*