Sir,

Limbal stem cell deficiency: a clinical chameleon
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Limbal stem cell deficiency has recently been increasingly implicated as a cause of ocular surface disease including pterygium.[1,2] Limbal stem cells act as a physiological barrier to the ingress of conjunctival cells across the cornea.[3] Deficiency leads to conjunctivalisation of the cornea, with the epithelium being of conjunctival phenotype typified by goblet cells, surface irregularity, and vascularisation.[3] Limbal stem cells may become depleted by a wide range of pathological processes affecting the ocular surface including topical medications, ultraviolet, and ionising radiation.[3] A major iatrogenic factor that has been proposed is prior ocular surgery in the region.[4] We present a case history showing the clinical relevance of the above aetiological factors and the major ongoing impact to a patient of minor limbal stem cell deficiency.

Case report

A 64-year-old man of Indian origin presented with left corneal scarring secondary to presumed old trachoma, and a moderate-sized left nasal pterygium. He had a history of chronic sun exposure in his youth. The left corrected visual acuity was 6/24 having undergone routine phacoemulsification and intraocular lens implantation 1 year before. He was felt to be a good candidate for left penetrating keratoplasty but would first need pterygium excision with conjunctival autograft harvested inferiorly. This was performed successfully (Figure 1a) and 3 months later he underwent a left penetrating keratoplasty.

At day 1 postoperatively he was noted to have a donor corneal epithelial defect in the inferonasal quadrant (Figure 1b), but no leak. Topical cyclosporin drops and intensive topical preservative-free steroids were immediately commenced. However, no healing occurred and the epithelial defect persisted. The epithelial defect resulted in marked stromal swelling. By 1 month postgrafting, there was a wound leak in the same area, with anterior synechiae. The swelling reduced with the application of a bandage contact lens, although the leak did not seal. The inferonasal cornea became progressively more macerated and this precluded suturing to seal the leak, as the sutures would have cheesewired through the graft. Thus 5 weeks following corneal grafting, he underwent a left redo penetrating keratoplasty, this time with limbal stem cell grafting from the same cadaveric donor as the cornea.

Postoperatively, intensive antirejection therapy was started.[5,6] An identical inferonasal epithelial defect was noted again on day 1 postgrafting. By day 2 this had enlarged, but by day 3 was diminishing in size and had fully resolved only 4 days following grafting (Figure 2). The patient made a steady recovery and his drops including immunosuppressives were gradually weaned. No recurrence of the epithelial defect has since been noted at follow-up. At 1 year postregrafting and limbal stem cell transplant, visual acuity was 6/12 in the left eye after correction with a contact lens.

Comment

While clinicians should be aware of the recently recognised implications of limbal stem cell deficiency, they must also be made aware of the potentially dramatic consequences of minor limbal stem cell deficiency.

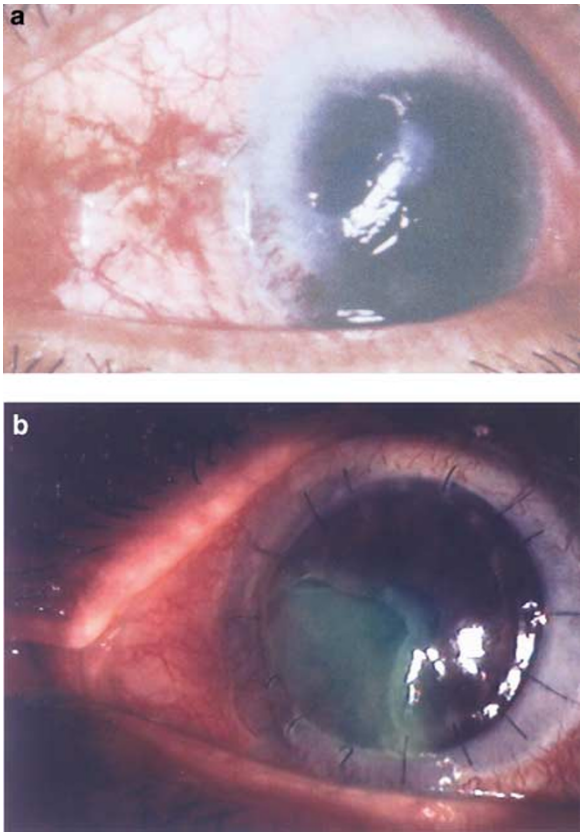

Figure 1 Anterior segment before and after original corneal transplant: (a) Colour photograph of anterior segment 1 day following excision of nasal pterygium with conjunctival autograft. (b) Colour photograph of anterior segment 1 day following penetrating keratoplasty showing inferonasal defect in the donor corneal epithelium.

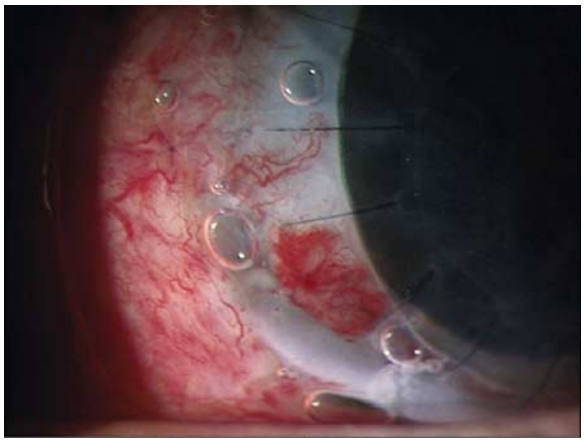

Figure 2 Colour photograph of anterior segment 4 days following redo penetrating keratoplasty with limbal stem cell graft. The functioning limbal stem cell graft is seen in the inferonasal limbus of the recipient eye, together with intact donor corneal epithelium.

Limbal stem cell deficiency is likely to have arisen in this patient owing to a combination of ultraviolet light exposure, pterygium formation, trachoma, and previous ocular surgery.

When taking a conjunctival autograft, some authors consider it important to take tissue from as near the limbus as possible in order to include some stem cells that can help towards replacing the relative deficiency in the area of the pterygium.[3] However, such an autograft is unlikely to act by this mechanism as the stem cells are located deep in the Palisades of Vogt in the anterior corneal stroma and would therefore not be included in the conjunctival autograft.[7] In this case, conjunctival autograft alone was insufficient to prevent a persistent epithelial defect from developing after penetrating keratoplasty.

After repeat corneal grafting, a similar inferonasal epithelial defect occurred. This then healed rapidly as a wave of epithelial cells migrated centripetally from the limbal stem cell graft. The epithelial defect has not since recurred, but long-term immunosuppression has been required.

Limbal stem cell deficiency is a recently described phenomenon that is implicated at the cellular level in the aetiology of ocular disease.[3] However, perhaps owing to its relatively recent recognition as a clinically important phenomenon, to our knowledge there is no other specific example in the literature of such minor limbal stem cell deficiency being documented to give rise to such serious clinical complications in a patient. This may have been because attention has not been drawn to the significance of even relatively minor degrees of limbal stem cell deficiency, making it easily overlooked in clinical practice, and thereby hard to causally link to clinical complications, particularly major ocular morbidity.

However, this unusual case makes it lucidly clear from the site of involvement that this patient had a minor degree of limbal stem cell deficiency at the site of successful pterygium excision and autografting, which gave rise at the same site to a persistent epithelial defect and its attending complications after corneal grafting. This was relieved by grafting limbal stem cells to the site of deficiency. This case suggests that it is important that the clinical significance of minor degrees of limbal stem cell deficiency not be underestimated, and that minor degrees not be overlooked as they can be associated with potentially disastrous consequences. Thus, where corneal transplantation is being considered, it is imperative that a search be actively initiated for evidence of even minor limbal stem cell deficiency from the outset. A history of ultraviolet light exposure as is found in outdoor labourers and individuals who have lived in equatorial climates, and prior surgery should be sought, and the significance of any concomitant pathology such as pterygium or trachoma is duly noted.

This case also suggests the interesting possibility of a role for prophylactic primary limbal stem cell grafting, undertaken at the time of corneal grafting, where even minor deficiency is suspected. However, further clinical evidence such as this interesting case would be required to debate this issue. It is hoped that this letter will draw attention to the possibility that minor, and thereby possibly underestimated or missed, limbal stem cell deficiency is a potential cause of serious ocular morbidity in patients undergoing corneal grafting. In this context, it is hoped that this report will stimulate other surgeons to analyse and if relevant report the potential reasons for any similar complications they may have had. This would help clarify the strength of association between minor limbal stem cell deficiency and such serious complications, and whether this justifies prophylactic limbal stem cell grafting in patients undergoing corneal grafts. Alternatively, it is possible that such an association, while documented in this patient, is genuinely extremely rare.

Thus, following corneal grafting in such patients, surgeons should be aware of the possibility that a persistent epithelial defect, with its associated complications, may have arisen because of undetected and or underestimated minor limbal stem cell deficiency. Careful, vigilant follow-up is needed. Till further evidence is available that there is a role for prophylactic limbal stem cell grafting for minor deficiency, it is at this stage of management that in select cases limbal stem cell grafting should be contemplated, but balanced with the potential side effects of immunosuppression.

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Sir,

Accelerated growth of a primary orbital schwannoma during pregnancy

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Primary orbital schwannomas are rare, accounting for about 1% of orbital tumours.[1,2] There is a known association with neurofibromatosis.[2–4] Typically, they arise from the first division of the trigeminal nerve (supraorbital and supratrochlear branches).[1,2,5] A typical presentation may occur as a single cystic lesion in the orbit[6] or as a schwannoma arising from the optic nerve itself.[7] We present a case of a primary orbital schwannoma with accelerated growth during pregnancy, which was positive for progesterone receptors. To the best of our knowledge, this is the first time hormone receptors have been found in such tumours.

Case report

A 38-year-old Caucasian lady presented initially with a 1- to 2-year history of a slowly progressive right-sided proptosis, which worsened significantly during her pregnancy. On examination, she had 11 mm of axial proptosis with normal optic nerve function. She had no trigeminal or other cranial nerve involvement. Systemic examination was normal and there was no family history of neurofibromatosis. MRI scan showed an extensive, moderately enhancing lesion, which masked the optic nerve (Figure 1a and b).

An orbital biopsy was subsequently carried out, histology of which suggested a diagnosis of schwannoma/neuroleimoma. Surgical treatment with the associated risks were discussed with the patient.

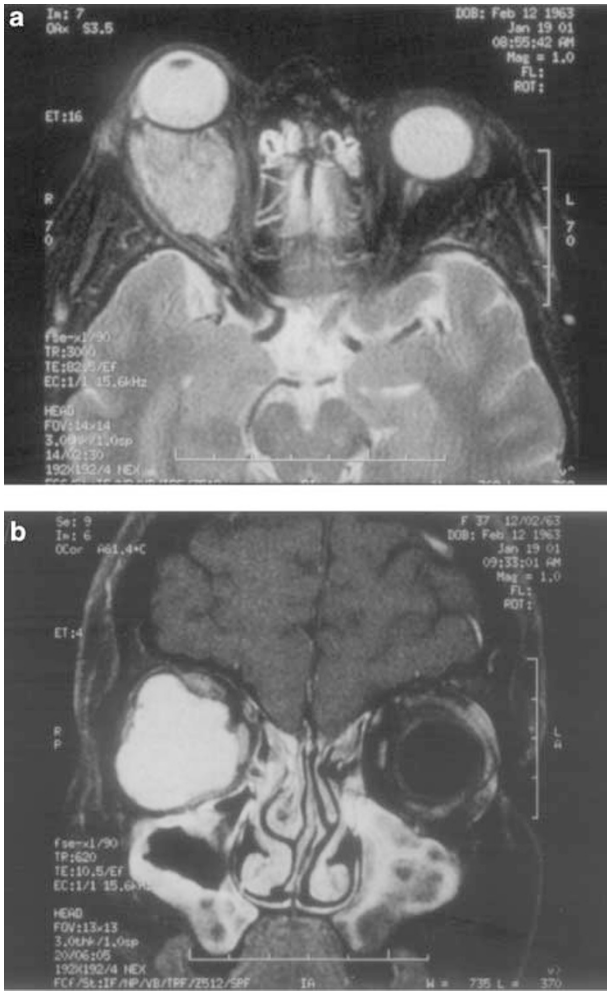

Figure 1 (a and b) Axial and coronal MRI (T2-weighted) scans showing a large enhancing mass in the right orbit. The optic nerve is masked by the lesion.