Sir,

Limbal stem cell deficiency and xeroderma pigmentosum: a case report

Aim

To report limbal stem cell deficiency in a case of xeroderma pigmentosum that was successfully managed by limbal transplantation and penetrating keratoplasty.

Methods

Interventional case report.

Result

A 28-year-old male with xeroderma pigmentosum had an adherent leucoma with 120° conjunctivalization in the left eye. Corneal impression cytology supported the clinical diagnosis of partial limbal stem cell deficiency. At 1 year after living-related conjunctival limbal allograft, followed by penetrating keratoplasty, the ocular surface was stable and vision had improved to 20/40.

Conclusion

Limbal stem cell deficiency could be considered as an ocular manifestation of xeroderma pigmentosum, suggesting the need for a close follow-up and limbal transplantation procedures if required.

Xeroderma pigmentosum, an autosomal recessive dermatosis, results in cutaneous pigmentary abnormalities and multiple malignancies,[1] and may have neurologic and systemic manifestations.[2] Ocular manifestations of this disease include ocular surface squamous neoplasia, neovascularization, and keratitis.[3]

We report a case of xeroderma pigmentosum presenting with features of partial limbal stem cell deficiency in one eye managed by limbal allotransplantation followed by a penetrating keratoplasty, that restored ocular surface stability and vision.

Case report

A healthy 28-year-old male diagnosed with xeroderma pigmentosum presented with diminished vision in both eyes, of several years duration. There was no prior history of exanthematous fever. He had been treated elsewhere for malignant lesions of the skin and nose. In the left eye, his best visual acuity was 20/400. An adherent leucoma was present in the lower one-third of the cornea with 120° conjunctivalization (Figure 1a). In the right eye, his vision was reduced to accurate projection of rays due to a dense vascularized corneal scar. Both eyes had normal lids, conjunctiva, and adequate tear meniscus. Dense corneal scars precluded the view of the remaining anterior and posterior segments. Systemic examination revealed no abnormalities other than hyper- and depigmented lesions of the skin in exposed areas. The differential diagnosis in the left eye included ocular surface squamous neoplasia and partial stem cell deficiency. Impression cytology revealed goblet cells in the inferior quadrant (Figure 2a) with squamous metaplasia in other areas of the cornea (Figure 2c). Adequate goblet cells were noted on the conjunctival surface (Figure 2b). There was no evidence of dysplasia in the epithelial cells. He was diagnosed as having partial limbal stem cell deficiency, and was advised a living-related conjunctival limbal allograft. His unaffected father volunteered to be the donor. After informed consent, the donor tissue was transplanted inferiorly over 0600 h. Histopathology of the excised pannus confirmed conjunctivalization of the cornea and excluded dysplastic changes (not shown). We followed the immunosuppressive regimen described by Tsubota.[4] After 3 months when the ocular surface was stable (Figure 1b), a corneal transplant was done. At the last visit, a year following penetrating keratoplasty, his best visual acuity was 20/40. The corneal graft was clear and the inferior limbal graft has been accepted (Figure 1c).

Comment

In xeroderma pigmentosum, there is a deficiency of the enzymes responsible for repairing UV light-induced DNA damage.[1] Persistence of unrepaired DNA results in somatic mutations, leading to neoplasias. The manifestation of limbal stem cell deficiency in this patient prompted us to speculate that exposure of the limbal stem cells to UV radiation might lead to permanent damage or dysfunction of these cells, or alteration of the stromal microenvironment.

Our patient had features of partial LSCD with 120° conjunctivalization inferiorly. Since ocular surface squamous neoplasia is frequently noted in XP patients, impression cytology aided in exclusion of this entity. The presence of stem cell deficiency could result in a failed corneal graft; therefore, we decided to do a limbal transplant, followed by penetrating keratoplasty. Partial LSCD can be managed conservatively, by repeated mechanical debridement,[5] or amniotic membrane transplantation.[6] However, the success of these procedures is determined by the presence of healthy residual limbal stem cells. In a patient of xeroderma pigmentosum with high susceptibility to UV radiation-

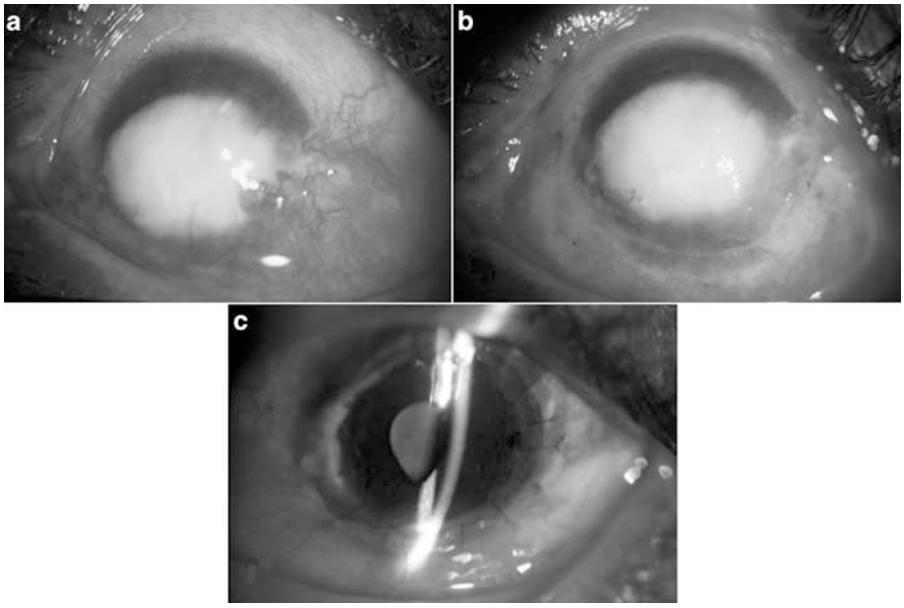

Figure 1 (a) Clinical picture of the left eye shows an adherent leucoma with 120° conjunctivalization of the inferior quadrant. (b) At 3 months after a living-related conjunctival limbal allograft, the ocular surface was noted to be stable and there was no recurrence of conjunctivalization inferiorly. (c) Clinical picture of the left eye 3.5 months after PKP, showing a clear and compact corneal graft, with a stable ocular surface and no evidence of conjunctivalization.

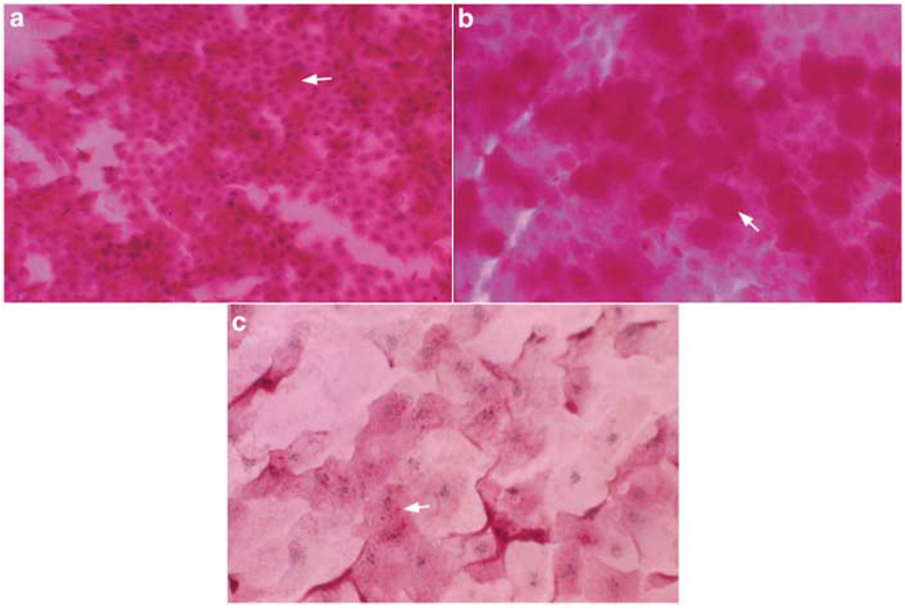

Figure 2 (a) Impression cytology from inferior quadrant of cornea showing epithelial cells interspersed with few goblet cells (arrow) characteristic of conjunctivalization of the cornea due to limbal stem cell deficiency (periodic acid Schiff stain, ×125). (b) Impression cytology of conjunctiva of the same eye showing a sheet of conjunctival epithelial cells with multiple goblet cells (arrow). (periodic acid schiff stain, ×500). (c) Impression cytology of nasal quadrant of the left cornea, showing singly scattered polygonal cells with low nuclear-cytoplasmic ratio and pink keratohyaline granules (arrow) in the cytoplasm, indicative of squamous metaplasia. There were no goblet cells noted. (periodic acid schiff stain, ×125).

induced damage we anticipated a permanent damage to the residual limbal stem cells and therefore preferred a living-related conjunctival limbal allo-transplant. We support the belief that a penetrating keratoplasty after restoration of ocular surface stability is more beneficial, as has been advocated earlier.[7,8] A simultaneous procedure may result in delivery of less antigenic load to the recipient by utilizing the same donor for both limbal

and corneal transplants, and in preservation of the transient amplifying cells.[9] The poor long-term outcome following simultaneous limbal transplantation and penetrating keratoplasty has prompted the recommendation of a staged procedure with a 1-year gap.[8] Though a stable ocular surface and good vision have been attained following these surgeries, the inherent pathology remains. Photoprotective measures have been advocated and the patient has been cautioned about the possible development of ocular or cutaneous manifestations of XP described earlier. Indefinite immunosuppression remains necessary to ward off limbal allograft rejection.[10] The patient is on low doses of cyclosporine ensuring serum trough levels of 50 ng/ml, regular assessment of renal and hepatic parameters, and on close follow-up in conjunction with an internist.

In summary, limbal stem cell deficiency may be one of the ocular manifestations of xeroderma pigmentosum, necessitating a high degree of suspicion and early surgical intervention to prevent visual disability.

References

1 Lever WF, Schaumberg-Lever G. *Histopathology of the skin*, Vol 6. JB Lippincott Co.: Philadelphia 1990; pp 72–73.
2 Kraemer KH, Lee MM, Scotto J. Xeroderma pigmentosum. Cutaneous, ocular and neurologic abnormalities in 830 published cases. *Arch Dermatol* 1987; **123**: 241–250.
3 Calonge M, Foster CS, Rice BV, Baer JC. Management of corneal complications in xeroderma pigmentosum. *Cornea* 1992; **11**(2): 173–182.
4 Tsubota K, Toda I, Saito H, Shinozaki N, Shimazaki J. Reconstruction of the corneal epithelium by limbal allograft transplantation for severe ocular surface disorders. *Ophthalmology* 1995; **102**: 1486–1496.
5 Dua HS. The conjunctiva in corneal epithelial wound healing. *Br J Ophthalmol* 1998; **82**: 1407–1411.
6 Anderson DF, Ellies P, Pires RRTF, Tseng SCG. Amniotic membrane transplantation for partial limbal stem cell deficiency. *Br J Ophthalmol* 2001; **85**: 567–575.
7 Croasdale CK, Schwartz GS, Malling JV, Holland EJ. Keratolimbal allograft: recommendations for tissue procurement and preparation by eye banks, and standard surgical technique. *Cornea* 1999; **18**: 52–58.
8 Ilari L, Daya SM. Long-term outcomes of keratolimbal allografts for the treatment of severe ocular surface disorders. *Ophthalmology* 2002; **109**(7): 1278–1284.
9 Rao SK, Rajagopal R, Sitalaksmi G, Padmanabhan P. Limbal allografting from related live donors for corneal surface reconstruction. *Ophthalmology* 1999; **106**: 822–828.
10 Daya SM, Bell RWD, Habib NE, Powell-Richards A, Dua HS. Clinical and pathological findings in human keratolimbal allograft rejection. *Cornea* 2000; **19**(4): 443–450.

M Fernandes[1], VS Sangwan[1] and GK Vemuganti[2]

[1]Cornea and Anterior Segment Service
LV Prasad Eye Institute, Hyderabad, India

[2]Ophthalmic Pathology Service
LV Prasad Eye Institute, Hyderabad, India

Correspondence: M Fernandes, MS
LV Prasad Eye Institute, LV Prasad Marg
Banjara Hills, Hyderabad 500 034, India
Tel: +91 040 23608262
Fax: +91 40 23548271
E-mail: fernandes@lvpei.org

Eye (2004) **18,** 741–743. doi:10.1038/sj.eye.6700717

Sir,

Intramuscular lipoma of the eyelid: a case report

Lipomas are common, benign tumours composed of mature adipose tissue. The majority are located subcutaneously around the torso, neck, and proximal limbs.[1] Intramuscular lipoma is a curious subgroup located within muscles, which can invade locally in a diffusely infiltrative pattern.

Intramuscular lipomas of the small muscles of the head and neck are reported only rarely. One previous report has identified intramuscular lipoma involving an eyelid,[2] and one recent report describes an intramuscular lipoma within a medial rectus muscle.[3] We describe a further case of an intramuscular lipoma affecting an eyelid.

Case report

A 77-year-old man presented with a left upper eyelid mass that had slowly enlarged since first being noticed 3 years previously (Figure 1). He had no pain, diplopia, or impaired vision on that side. On examination the mass was subcutaneous, soft, fatty, and nontender to palpation, and there was no proptosis or globe deviation.

The mass was biopsied under local anaesthesia without complication. During the procedure, it was noted that the lesion extended deep in to the orbital septum adjacent to the medial orbital wall.

The histological examination of the specimen (Figure 2) revealed lobulated groups of mature adipocytes surrounding groups of skeletal muscle fibres and individual muscle fibres, providing the diagnosis of an intramuscular lipoma. The presence of muscle fibres within this lesion refutes the diagnoses of orbital fat prolapse or classical lipoma.

At follow up 3 months postoperatively, the cosmetic appearance of the eyelid is very satisfactory. There is no residual mass, and the patient is asymptomatic.