Ectopic conjunctivalisation in Stevens-Johnson syndrome

Samuel E Navon, Peter A D Rubin

Stevens-Johnson syndrome (erythema multiforme major) is a severe exfoliative vesiculobullous dermatitis accompanied by fever, inflammation of mucous membranes, and a severe purulent conjunctivitis. Late ocular complications are most commonly due to conjunctival cicatrisation resulting in symblepharon formation, trichiasis, conjunctival keratinisation, and keratoconjunctivitis sicca. This report describes an unreported phenomenon of ectopic conjunctivalisation of the eyelids in a case of Stevens-Johnson syndrome.

Case report
A 37-year-old black woman was referred for management of a non-healing lesion of her right upper lid after suffering a severe bout of Stevens-Johnson syndrome attributable to oral penicillin. During the acute phase of her illness she sustained 90% total body surface area a full thickness epidermal desquamation, including her eyelids, and required a 3 month hospitalisation in the burns unit of the Massachusetts General Hospital. Her dermatological recovery was complete with residual reticulated epidermal scarring except for a persistent lesion on her right upper and lower eyelids, which was very painful (Fig 1). The eyelid lesion appeared grossly as an ulceration and had been managed for 3 months before referral with topical antibiotics, steroids, lubrication, and vitamin A ointment with absolutely no change in the symptoms and appearance. Her remaining ophthalmic examination was unremarkable except for right upper and lower lid madarosis and occasional trichiasis. During the acute phase of disease, and at presentation, her ocular involvement was limited to only a mild conjunctivitis. There were no signs of more serious ocular surface disease such as forniceal foreshortening or symblepharon formation.

After referral to our service, a biopsy of the central portion of the lesion was performed. The specimen consisted of stroma with generalised fibrosis, areas of chronic non-granulomatous inflammation, a lining of non-keratinised stratified squamous epithelium, and occasional goblet cells (Fig 2). The histological diagnosis was conjunctival epithelium overlying an inflamed dermal base.

The ectopic conjunctiva of the upper eyelid was removed en bloc. Since the extensive scarring precluded any suitable donor sites for a full thickness skin graft a split thickness skin graft, harvested from the thigh, was used to cover the eyelid defect. This tissue matched the texture of her scarred eyelids. Four months after the grafting the patient noted complete resolution of the preoperative discomfort. At that time the graft was well healed but hyperpigmented. This pigmentation decreased over the next several months to result in a cosmetically satisfactory result (Fig 3).

Comment
Ocular complications of Stevens-Johnson syndrome are commonly a result of conjunctival
ectopic conjunctivalisation and consist of entropion, trichiasis and keratoconjunctivitis sicca. Less common sequelae include ocular cicatricial pemphigoid,\(^1\) corneal ulceration,\(^1\) chronic conjunctival inflammation,\(^1\) and a chronic progressive course of conjunctival keratinisation and corneal vascularisation leading to blindness.\(^1\) We report here for the first time a case of ectopic conjunctivalisation as a sequela to severe Stevens-Johnson syndrome. The ectopic epithelium was continuous with the palpebral conjunctiva of the right upper lid. In the normal eye, the mucocutaneous junction is located just posterior to the muscle of Riolan (the 'grey line').

We propose that epidermal sloughing of the upper eyelid that occurred in this patient was confluent with the mucocutaneous junction. This removed the normal boundary that exists between the palpebral conjunctiva and epidermis and allowed conjunctival epithelium to migrate beyond its normal borders. The ectopic conjunctival tissue was unresponsive to topical therapies and remarkably stable over 3 months, retaining a moist papillary appearance up until the time of biopsy.

There are several possibilities for the pathogenesis of ectopic conjunctiva. Weissman \textit{et al.}\(^4\) have recently measured DNA synthesis in conjunctival epithelium and found increased proliferation of basal epithelium cells in Stevens-Johnson syndrome. Such an increase could contribute to the development of ectopic conjunctiva. In addition, the inflamed dermal bed of the adjacent dermal wound might have provided an added stimulus for this exuberant conjunctival response. Ectopic conjunctivalisation has been reported in patients who suffered extensive burns to the face and eyelids.\(^7\) The abnormal growth of conjunctiva in these patients was probably due to the anatomical disruption of histological borders between the conjunctiva and skin. The cutaneous lesion of Stevens-Johnson syndrome and severe burns are very similar in that they both result in epithelial necrosis and desquamation. Thus, it is possible that our patient developed ectopic conjunctiva because of the involvement of her eyelid adjacent to conjunctiva rather than to any feature unique to the Stevens-Johnson syndrome.

Why is ectopic conjunctivalisation such an uncommon occurrence in the Stevens-Johnson syndrome? One possibility is that the conjunctiva is usually severely affected along with the skin. Our patient was quite unusual in the relative sparing of the conjunctiva, despite the severity and extent of the cutaneous lesions. This was documented throughout the acute phase of her illness by frequent ophthalmic examinations. The mild clinical involvement of the ocular surface of this patient further extends the similarity between this clinical presentation and that seen with severe facial burns. We postulate that when the eyelid epidermis of our patient was destroyed a relatively normal, and perhaps a hyperproliferative, conjunctiva was then able to migrate into the wound. We alert others to the possibility of ectopic conjunctivalisation in patients with non-healing eyelid lesions after Stevens-Johnson syndrome, especially when ocular involvement was mild compared with that of the surround skin.