Recurrent Epithelial Erosion—cause of sudden pain and eye irritation

INTRODUCTION
Mr B, a 50-year-old male, presented for assessment following referral by his GP for investigation of reported “progressing severe ocular pain”.

The patient had begun suffering the onset of sudden pain in either eye approximately two years previously. He described the pain as being moderate to severe, mainly at the severe end of the scale. The condition had been slowly increasing in frequency as time progressed.

The onset of pain was either on waking in the morning or prior to waking in the early morning. The level of pain was enough to cause the patient to wake at 3 to 4 am. The pain was persisting for approximately 10 to 15 minutes then abating; however the eye would remain irritated during the rest of that day. The presentation could be in either eye without a definite pattern.

The patient was using topical Livostin drops twice a day prophylactically which appeared to moderate both the incidence and the severity of the condition.

Previous ocular history
The patient reported that his vision was generally good apart from the onset of presbyopia some years ago. He was using hobby glasses for reading.

The patient reported an incidence of possible trauma approximately two years ago involving galvanized iron flakes.

Medical history
The patient reported his general health to be “average” and was not taking any prescribed systemic medication. He reported no history of allergies

Family medical and ocular history
The patient’s family history was unremarkable.

General examination showed uncorrected distance vision to be 6/9 binocularly. Fundus examination showed the posterior pole was unremarkable and the intraocular pressures were normal.

Slit-lamp bio-microscopy showed the presence of a corneal epithelium basement membrane dystrophy. Also present were areas of slight superficial punctate epithelial staining in the left eye.

The last reported incidence of pain was in the left eye. The presence of bilateral blepharitis was noted.

DIAGNOSIS
The signs and symptoms, together with the history given, led to the diagnosis of recurrent epithelial erosion in the presence of map-dot-fingerprint dystrophy.

The absence of significant corneal defect allows the elimination of more serious corneal concerns such as a corneal ulcer, herpes simplex virus infection, or peripheral corneal thinning. As a non contact lens wearer mechanical trauma from contact lens wear can be excluded.

Corneal map-dot-fingerprint dystrophy is by far the most common corneal dystrophy and is named from its characteristic appearance under the slit lamp.
DISCUSSION

The corneal anatomy consists of five layers; the epithelium, Bowman’s layer, the stroma, Descemet’s membrane, and the endothelium.

The endothelium consists of a single cell layer of hexagonal cells. This layer plays a vital role in the hydration level of the cornea. With age the number of these cells decreases and as they do not regenerate the surrounding cells expand to fill the space.

Descemet’s membrane is composed of a fine lattice work of collagen fibers. The membrane consists of two layers; an anterior banded layer and a posterior non-banded layer.

The stroma makes up the majority of the cornea, approximately 90 percent of its thickness. It is primarily made of regularly orientated layers of collagen fibrils whose spacing is maintained by proteoglycans ground substance with keratocytes spread between its layers.

Bowman’s layer is the superficial layer of the stroma. Its is a cellular structure and does not regenerate if damaged.

The epithelium consists of three basic cell types. Firstly there are the single basal columnar cells attached to the stroma through the epithelial membrane and Bowman layer by hemidesmosomes. These provide the firm anchor points for the epithelium to remain attached to the cornea.

It appears that these anchor points are affected in recurrent epithelial erosions.

The basal cells are regenerated via migration from limbal stem cells thus damage to those limbal stem cells by trauma can markedly affect the epithelium’s ability to remain healthy and viable.

Next there two or three rows of wing cells which, as the name suggests, have thin “wing like” extensions.

Then there are two layers of long and thin surface cells jointed by bridges. The surface area of the outermost surface cells is increased by microvilli which facilitate the adsorption of mucus providing an effective base for the tear layer above. After a life span of a few days the superficial cells are shed onto the tear film.

As the epithelium has excellent regenerative properties the epithelium replaces itself within several days.

Recurrent epithelial erosion is a common clinical disorder characterized by repeated spontaneous breakdown of the corneal epithelium. The pathomechanism of this breakdown is due to the abnormalities of the adhesion complex between the corneal epithelium and the stroma.

The corneal epithelium basement complex is responsible for the tight adhesion of the basal cell layer of the epithelium to the underlying stroma. Recurrent epithelial erosions are commonly caused by superficial corneal trauma and may also occur in certain corneal dystrophies such as Cogan microcystic dystrophy which is also known as map-dot-fingerprint dystrophy. This condition is neither familial nor progressive.

Recurrent epithelial erosions develop in about 10 percent of patients, usually after the age of 30 years of age. The simultaneous occurrence of bilateral recurrent epithelial erosions would strongly suggest map-dot-fingerprint dystrophy involvement.

Reidy, Paulus, and Gona (2000) reviewed the associated factors of 104 patients with recurrent epithelial erosion. They found a history of trauma in 45 percent of patients, the presence of epithelial basement membrane dystrophy in 29 percent of patients, and 17 percent of patients had both a history of trauma and evidence of epithelial basement membrane dystrophy.
Bentley et al (2001), using a canine model, proposed that corneas with chronic corneal epithelial defects are lacking a normal basement membrane structure in the region of the epithelial defect.

Steele (1999) observed that the hemidesmosomal attachment between the basement membrane and basal cells completely disappears outward from the epithelial defect margin. The re-establishment of these tight adhesions to the underlying stroma is an important pre-requisite for the stability of regenerated corneal epithelium. Thus it could be presumed that in recurrent epithelial erosion these tight adhesions do not re-establish correctly.

During sleep the tear layer thins and at this time areas of poorly adhered epithelium may become attached to the surface of the tarsal conjunctiva of the upper lid. Areas of adhered corneal epithelium can pull away from the basement membrane of the cornea during periods of REM sleep or with the opening of the upper lid on waking causing the recurrent epithelial erosions.

The intermittent onset of erosions would depend on the level of adhesion of the abnormal areas of corneal epithelium and there would be no specific pattern to the occurrence of these erosions.

**MANAGEMENT**

The first line in medical treatment of recurrent epithelial erosion is the use of lubricants.

In the present case with only slight to moderate epithelial defects the preferred regime would be initial treatment using unpreserved artificial tears between 4 to 8 times a day and the use of ointment at night.

In addition, improved lid hygiene using heat compresses, lid scrubs and massage to reduce the Blepharitis.

Should more aggressive treatment of the Blepharitis be needed, the use of a topical antibiotic such as Doxycycline should be considered especially if there are reasonably sized corneal defects present.

The aim of lubricant treatment would be to achieve a period of three months without a occurrence of an erosion before tapering of the regime would be considered.

Jackson (1960) estimated the incidence of recurrence to be 1:150 cases following traumatic erosion. Heyworth et al (1998) found a significant number of patients with recurrent erosion syndrome were still symptomatic 4 years from initial review.

Other non-medical treatments have been used for recurrent epithelial erosions. These include; anterior stromal micropuncture, YAG induced epithelial adhesion, excimer laser phototherapeutic keratectomy, diamond burr superficial keratectomy, extended wear bandage lens, and corneal epithelium debridement of loose epithelium.

Bourges et al (2002) note that in the 12 to 18 months post treatment by excimer laser phototherapeutic keratectomy there was no recurrence of erosions in 94.7 percent of the treated eyes. Soong et al (2002) proposed that Diamond Burr Superficial Keratectomy is also a safe and effective method of treating recurrent epithelial erosion and a good alternative to phototherapeutic keratectomy and anterior stromal micropuncture.

Therapeutic contact lenses were in the past considered to be an inferior treatment option due to the high complication rates. However with the advent of the new generation of silicon hydrogel extended wear contact lenses, views on the effectiveness and safety of that option may well need revising.

If the medical treatments outlined do not achieve a resolution in cases of recurrent epithelial erosions then referral for a non-medical treatment such as phototherapeutic keratectomy should be considered.

It should be noted that treatment with Livostin is not commonly recommended for the condition but Mr B was adamant that if he ceased the regime of Livostin drops twice daily then the condition was exacerbated.
The effect of Livostin in this case can be considered in two ways.

The first is that the drops are merely providing a form of lubrication that is only sufficient to prevent the condition worsening but is not sufficient to enable the condition to improve.

If this premise is correct, then the suggested regime with the more viscous lubricant of unpreserved artificial tears used more often during the day and application of ointment at night should markedly improve the situation for the patient. Ultimately, this treatment should enable a more complete resolution of the condition but may not prevent recurrence.

The second factor to consider with the effectiveness of the Livostin in controlling but not resolving the condition is the question of whether the antihistamine effect of Livostin is moderating the course of the recurrent epithelial erosions. There appears no evidence for or against this possibility.

The remaining concern in this case is that there is a known increase in prevalence of recurrent epithelial erosion in the presence of map-dot-fingerprint dystrophy. As Mr B suffers both conditions full resolution may not be achievable.

For example, in a 4-year review of 117 patients with recurrent erosion syndrome Heyworth and his colleagues found nearly 60% of all the cases were still symptomatic after 48 months, with attacks occurring at a median frequency of 60 days.

Patients with epithelial basement membrane dystrophy (EBMD) were more likely to be symptomatic than those with a traumatic aetiology. 75% of those with EBMD were symptomatic after 48 months compared to 46% with a traumatic aetiology.

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