RECURRENT CORNEAL EROSION: CLINICAL FEATURES

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SUMMARY

The clinical features of a group of 30 patients with recalcitrant recurrent corneal erosions (i.e. those who failed to respond to conventional therapy) were evaluated. Associated ocular and facial abnormalities were documented. Meibomian gland dysfunction was present in all patients as manifest by dropout and inspissation of the meibomian glands, reduced tear film break-up time and debris in the tear film. Dropout of meibomian glands was present in 25 (83%) patients and was maximum in the medial half of the lid in 21 (84%) of these 25 patients. Tear film break-up time was reduced in all patients, being instant in 7 (23%), between 1 and 5 seconds in 22 (74%) and between 10 and 15 seconds in 1 (3%) patient. Superficial corneal abnormalities were present in 28 (93%) patients as manifest by maps, dots and fingerprints. Facial abnormalities such as telangiectasia, rhinophyma and acne rosacea were present in 22 (73%) patients. The findings of our study suggest an association between recalcitrant recurrent corneal erosions and meibomian gland dysfunction.

Recurrent corneal erosions were first described in 1872 by Hansen[1] who termed the disorder 'intermittent neuralgic vesicular keratitis'. Von Szily[2] in 1900 gave a comprehensive account of the disorder and illustrated the principal features of the disease. Chandler[3] in 1945, in a fascinating account of the disorder, divided the syndrome of recurrent corneal erosions into a macroform and a microform.

The macroform is characterised by widespread loss of the corneal epithelium and severe symptoms. It is well described and easily recognised by ophthalmologists. Symptoms may take several days to subside. The macroform recurs at long intervals of weeks, months or years. The microform is characterised by a small area of epithelial loss and may easily be overlooked on clinical examination. The attacks are milder and of shorter duration than those of the macroform, but occur far more frequently – sometimes every night or morning.

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Recurrent corneal erosions can occur spontaneously, following superficial corneal injury or in certain corneal dystrophies.[4] Recurrent corneal erosions occurring in map, dot, fingerprint corneal epithelial dystrophy have been differentiated from the spontaneous and traumatic form.[5]

The purpose of this study was to evaluate the clinical features and lid disease in a group of patients with recalcitrant recurrent corneal erosions. We introduced the term 'recalcitrant recurrent corneal erosions' to denote those patients with recurrent corneal erosions who fail to respond to conventional therapy.

PATIENTS AND METHODS

Patient Selection

All consecutive patients with recurrent corneal erosions presenting the Birmingham and Midland Eye Hospital between April 1991 and October 1992 were considered for study entry. The criteria for inclusion were: (1) a history of recurrent corneal erosions, (2) the patient had been seen with a documented corneal epithelial loss, (3) persistent recurrent corneal erosions for 2 months, while using lubricating eye ointment every night. Patients with any corneal dystrophy other than map, dot, fingerprint dystrophy were excluded. Patients with systemic diseases known to be associated with recurrent corneal erosions, such as epidermolysis bullosa, were also excluded. All patients enrolled in this study were entered in a treatment trial for recurrent corneal erosions and are the subject of a subsequent report.[6]

At the initial study visit, details of age, sex, any history of trauma and previous ocular and medical diseases were recorded. The duration and nature of symptoms, and the frequency and type of recurrent corneal erosions were documented.

A complete ophthalmological examination was carried out, including best corrected visual acuity and indirect ophthalmoscopy. Slit lamp biomicroscopy was performed and the tear film assessed for the presence of debris. The cornea was examined using retroillumination to assess the presence of subtle abnormalities such as cysts, maps, dots and fingerprints. The site of corneal epithelial abnormal-

ities was assessed and recorded by a specially prepared scale placed over the proforma, dividing the cornea into thirds: inferior, middle and superior.

The meibomian glands were assessed with the technique of lid transillumination, using a scleral transilluminator. The number of meibomian glands was counted in each lower lid. Meibomian gland dropout was defined as mild, moderate or severe. The lid was divided into a medial and a lateral half. A count of between 10 and 12 meibomian glands per half-section was defined as mild dropout of the meibomian glands, between 5 and 10 meibomian glands per half-section was defined as moderate dropout and a count below 5 in each section was defined as severe dropout. The meibomian glands were assessed for the presence or absence of inspissation at the lid orifices.

Tear film break-up time (TBUT) was measured using one drop of preservative-free 2% sodium fluorescein prior to instillation of any other medication. A drop of fluorescein was instilled, and the interval between the last complete blink and the development of the first randomly distributed dry spot in the precorneal tear film measured using a stop-watch. Non-randomly distributed dry spots overlying localised areas of elevated epithelium were ignored when measuring the TBUT. The lids were not held for this procedure. TBUT was measured for both eyes and the two results averaged. The results of the TBUT were divided into five groups: instant, between 1 and 5 seconds, between 5 and 10 seconds, between 10 and 15 seconds and over 15 seconds. A TBUT of over 15 seconds was defined as normal.

The Schirmer test was performed, without the use of local anaesthetic. Aqueous production was measured 5 minutes following insertion of the filter paper and the result expressed in millimetres. A result of over 5 mm was defined as normal.

The facial features were examined and particular note taken of facial telangiectasia, rhinophymna, pustules and papules.

RESULTS

The results of this study are shown in Tables I–VII.

The age and sex distribution of the patients is shown in Table I. The type of erosion and the incidence of bilateral disease is shown in Table II. The nature of the initial precipitating injury is shown in Table III. A fingernail injury was the commonest form of injury identified. One patient underwent general anaesthesia for a minor procedure and subsequent to this developed a painful eye and developed recurrent corneal erosions. Two patients suffered from diabetes and 1 from rheumatoid arthritis. A positive family history of recurrent corneal erosions was identified in 2 patients: one 49-year-old woman had a daughter with recurrent corneal erosions and one 31-year-old man had an affected father.

All patients complained of pain associated with the development of a recurrent corneal erosion. In addition, 22 (74%) of 30 patients suffered from pain, photophobia and lacrimation, 4 (13%) from pain and photophobia, 3 (10%)

Table I. Age and sex distribution of 30 patients with recurrent corneal erosions

Females	17 (57%)
Males	13 (43%)
Age	27–77 years (mean 45 years)

Table II. Type of recurrent corneal erosion

Macroerosion and microerosion	23 (77%)
Mircoerosion only	6 (20%)
Macroerosion only	1 (3%)
Bilateral	9 (30%)

Table III. Causes of initial corneal abrasion in patients with recurrent corneal erosion

Fingernail	5 (16%)
Animal	2 (7%)
Plant	2 (7%)
Paper	2 (7%)
Metallic object	2 (7%)
Surgery	1 (3%)
None	16 (53%)
Total	30 (100%)

Table IV. Principal aggravating factor in recurrent corneal erosions

Tiredness	4 (13%)
Menopause	4 (13%)
Menstruation	2 (7%)
Alcohol	2 (7%)
Crying	1 (3%)
Pregnancy	1 (3%)
Lid abscess	1 (3%)
None	15 (50%)

Table V. Meibomian gland dysfunction in recurrent corneal erosions

Tear film debris	30 (100%)
Reduced tear film break-up time	30 (100%)
Meibomian gland dropout	25 (83%)
Meibomian gland inspissation	25 (83%)
Conjunctival injection	19 (63%)
Lid scales or collarettes	6 (20%)
Corneal pannus	3 (10%)

Table VI. Corneal abnormalities in recurrent corneal erosions

Microcysts	21 (54%)
Microcysts, fingerprints and maps	14 (36%)
Fingerprints	2 (5%)
Normal	2 (5%)
Total	39 (100%) eyes

[a]Of 30 patients, 21 had unilateral recurrent corneal erosions and 9 had bilateral recurrent corneal erosions, giving 39 affected eyes.

Table VII. Cutaneous facial abnormalities in patients with recurrent corneal erosions

Telangiectasia	22 (73%)
Pustules or papules	4 (13%)
Rhinophyma	3 (10%)
Normal	8 (27%)
Total	30 (100%) patients

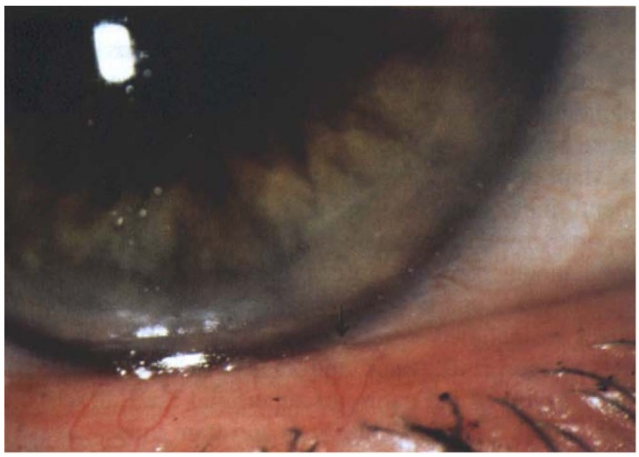

Fig. 1. *Meibomian gland dysfunction in recurrent corneal erosions, with tear film debris, meibomian gland inspissation (arrow) and conjunctival injection.*

Fig. 2. *Meibomian gland dropout in recurrent corneal erosions. A 31-year-old man with recurrent corneal erosions. Meibomian glands can be seen transilluminated (arrows) through the lid. There is moderate fallout of the meibomian glands medially (open arrow).*

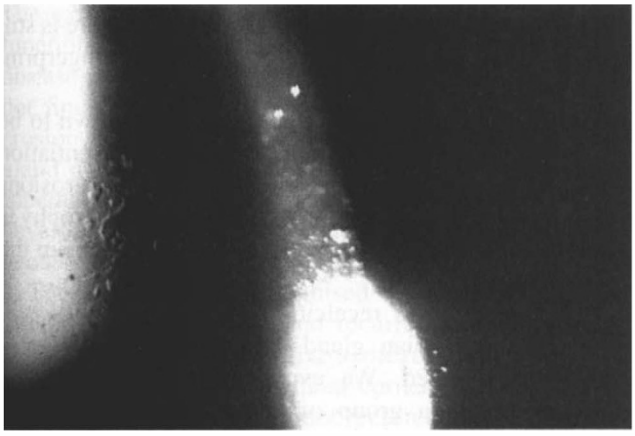

Fig. 3. *Corneal abnormalities in recurrent corneal erosions with microcysts and fingerprints.*

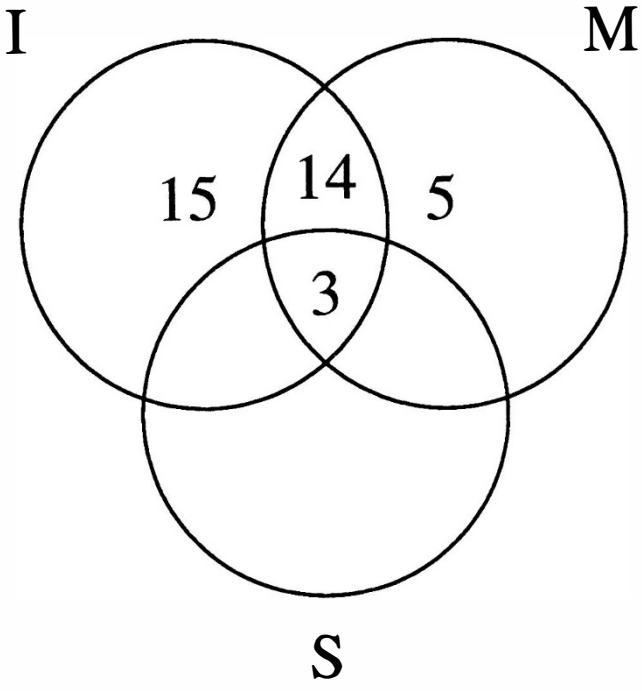

Fig. 4. *Distribution of corneal abnormalities in recurrent corneal erosions. The majority of abnormalities were situated in the inferior and middle of the cornea. Superior involvement was always accompanied by involvement of the entire cornea. Thirty-nine eyes had recurrent corneal erosions and 2 had no corneal abnormality. I, inferior third of the cornea; M, middle third of the cornea; S, superior third of the cornea.*

experienced pain and lacrimation and 1 (3%) patient experienced pain only.

Symptoms occurred either during the night or on waking. On waking, 17 (56%) of 30 patients suffered a sharp pain accompanied by lacrimation. Five patients (17%) suffered symptoms only at night and were woken from their sleep with pain. Eight patients (27%) had a combination of the above and had symptoms during the night and also on waking. Specific factors which could precipitate and aggravate recurrent corneal erosions were identified in half the patients (Table IV). Of the 17 women in the study, 7 (41%) identified hormonal events such as menstruation, pregnancy and menopause as aggravating factors which precipitated an increased number of recurrent corneal erosions.

Ocular examination revealed meibomian gland dysfunction in all 30 patients (Table V). Microscopic tear film debris was present in all patients (Fig. 1). Tear film break-up time was reduced in all patients, being instant in 7 (23%), between 1 and 5 seconds in 22 (74%) and between 10 and 15 seconds in 1 (3%) patient.

The number of meibomian glands was reduced in 25 (83%) of the 30 patients (Fig. 2). Meibomian gland dropout was severe in 3 (12%) patients, moderate in 8 (32%) and mild in 14 (56%) patients. Meibomian gland dropout was located medially in 21 (84%) patients, laterally in 1 (4%), and in 3 (12%) patients the entire lid was affected (Fig. 2). The orifices of the meibomian glands were inspissated in 25 (83%) of 30 patients (Fig. 1).

Lid scales and collarettes around the hair follicles were present in 6 patients. Bilateral superficial corneal vascularisation, located superiorly was present in 3 patients. The aqueous component of the tear film, as assessed by the

Schirmer test, was normal in 29 patients. The aqueous component of the tear film was abnormal in 1 patient and the Schirmer test was 4 mm in the right eye and 6 mm in the left.

Corneal examination revealed microcysts, fingerprints and maps in 28 (93%) of 30 patients (Table VI, Fig. 3). All 9 patients with bilateral recurrent corneal erosions demonstrated corneal abnormalities in both eyes. In unilateral cases of recurrent corneal erosions, no corneal abnormality was present in 2 (5%) patients. Corneal cysts, seen in 21 (54%) of 39 eyes, were the commonest corneal abnormality, and cysts were also seen in combination with maps and fingerprints in 14 (36%) eyes. Fingerprints only were present in 2 (5%) eyes.

In the 21 patients with unilateral recurrent corneal erosions, 7 (33%) patients had corneal abnormalities in the fellow eye. Examination of the fellow eye in these patients demonstrated fingerprints in 4 (57%) of 7 eyes, microcysts in 2 (29%) eyes and microcysts and fingerprints in 1 (14%) eye.

The distribution of the corneal abnormalities was noted to be predominantly in the inferior third of the cornea, and although superior involvement did occur, this was always in the presence of inferior corneal involvement (Fig. 4). Fifteen (41%) of 37 affected eyes demonstrated corneal abnormalities in the inferior third of the cornea, in 14 (38%) the inferior and middle third of the cornea was involved, in 5 (13%) the involvement was limited to the middle third of the cornea, and in 3 (8%) eyes there was involvement of the entire cornea.

Twenty-two (73%) of 30 patients demonstrated facial abnormalities seen in acne rosacea. Cutaneous telangiectasia, rhinophyma, pustules and papules were noted (Table VII). Eight (27%) patients had no facial abnormality.

DISCUSSION

Recurrent corneal erosions occur spontaneously, following trauma, or in association with corneal dystrophies and secondary to certain systemic diseases.[4]

Epithelial, stromal and endothelial corneal dystrophies have all been described in association with recurrent corneal erosions.[4] These inherited recurrent corneal erosions may be subclassified into two main groups.[4] Epithelial corneal dystrophies associated with recurrent corneal erosions include Francheschetti type, epithelial rosette dystrophy, map, dot, fingerprint dystrophy (epithelial basement membrane dystrophy) and Meesman's dystrophy. Other corneal dystrophies associated with recurrent corneal erosions include Reiss-Buckler's dystrophy and the stromal dystrophies, macular, granular and less commonly lattice dystrophy. Endothelial dystrophies may be complicated by recurrent corneal erosions in the later stages when there is corneal decompensation and oedema.

The pathogenesis of recurrent corneal erosions associated with inherited corneal dystrophies and systemic diseases such as epidermolysis bullosa differs from that associated with spontaneous or traumatic recurrent corneal erosions.[7,8] These diseases were excluded from our study. In our opinion, recurrent corneal erosions occurring in map, dot, fingerprint dystrophy may have a similar pathogenesis to the spontaneous or traumatic form and these patients were therefore included in the study.

Map, dot, fingerprint dystrophy, also known as basement membrane epithelial dystrophy, was initially reported by Cogan,[9] who described repeated attacks of spontaneous recurrent corneal erosions associated with a variety of superficial corneal changes. The corneal changes included epithelial microcysts, bleb patterns, nets, fingerprints, lines and maps. Brown and Bron[10] further defined the nature of superficial lines, describing mare's-tail lines, fibrillary lines and tram lines.

Laibson and Krachmer[11] identified 20 kinships with the map, dot, fingerprint dystrophy. A dominant mode of inheritance was proposed but this failed to explain the predominance of women affected with the disorder. Others have questioned this mode of inheritance; Werblin *et al.*[12] felt that the family association was spurious. There is still debate about the inheritance of map, dot, fingerprint dystrophy.[4]

Traumatic recurrent corneal erosions are known to be associated with epithelial microcysts. The differentiation between the traumatic form of recurrent corneal erosions and that associated with map, dot, fingerprint dystrophy is made on the finding of fingerprints, nets and blebs in the latter condition.[13]

The association of recalcitrant recurrent corneal erosions and meibomian gland dysfunction has not previously been noted. We evaluated ocular and facial abnormalities in a group of patients with recalcitrant recurrent corneal erosions and found that all patients with recalcitrant recurrent corneal erosions had meibomian gland dysfunction.

Meibomian gland dysfunction was manifest by dropout and inspissation of the meibomian glands, debris in the tear film, and reduced tear film break-up time. Dropout of the meibomian glands was present in 25 (83%) of 30 patients. Tear film break-up time was reduced in all patients. Meibomian gland dysfunction is associated with acne rosacea; we demonstrated facial abnormalities seen in association with acne rosacea in 22 (73%) of 30 patients.

We found the corneal abnormalities present in recalcitrant recurrent corneal erosions to be located principally in the inferior and middle thirds of the cornea. Other investigators have also documented this finding.[5] No explanation has been advanced, however, to explain this finding.

Seven (41%) of the 17 women in the study identified hormonal factors such as menstruation, pregnancy and the menopause as causing a worsening of the recurrent corneal erosions. The relationship of recurrent corneal erosions to menstruation has been noted previously but has remained unexplained.[13] The stimulus for secretion of lipid by the meibomian glands is not fully known. It is assumed that the secretion of meibomian glands is modulated by the levels of plasma sex hormones, as the meibo-

mian glands are sebaceous glands and the role of sex hormones in the modulation of sebaceous secretion is well known.[14]

Meibomian gland dysfunction is, we believe, implicated in the pathogenesis of recalcitrant recurrent corneal erosions. The evidence for this view is as follows:

1. Meibomian gland dysfunction was present in a group of patients with recalcitrant recurrent corneal erosions.
2. Patients with recalcitrant recurrent corneal erosions respond to treatment of the associated of the meibomian gland dysfunction.[6]
3. Corneal abnormalities associated with recurrent corneal erosions are located in the inferior and middle third of the cornea, that part of the cornea that has maximum contact with the tear film.
4. Women identify hormonal changes as increasing the frequency of recurrent corneal erosions. Meibomian glands are believed to be modulated by sex hormones.

The exact mechanism by which meibomian gland dysfunction may be implicated in the pathogenesis of the disease is unknown. It is possible that pre-existing map, dot, fingerprint dystrophy and associated recurrent corneal erosions may be aggravated by accompanying meibomian gland dysfunction. Alternatively, meibomian gland dysfunction may predispose susceptible individuals to the development of recurrent corneal erosions either spontaneously or in response to trauma.

This previously unrecognised association of meibomian gland dysfunction and recurrent corneal erosions lends a whole new perspective to the role of the tear film in the pathogenesis of superficial corneal disorders. It has allowed us to treat recalcitrant recurrent corneal erosions successfully.[6] Further research into this aspect of the disorder may lead to clarification of the pathogenesis of recurrent corneal erosions and superficial corneal disorders.

Key words: Macroerosion, Meibomian gland, Meibomian gland dysfunction, Microerosion, Oral tetracycline, Recurrent corneal erosion.

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