Nocturnal lagophthalmos and recurrent erosion

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Corneal exposure due to incomplete lid closure is a widely recognized complication of conditions such as facial palsy, lid deformity, proptosis, and coma. It is less well known that corneal exposure can occur during sleep in subjects who have normal voluntary lid closure. This diagnosis was made when patients presented with the characteristic history of ocular pain or discomfort occurring after sleep, associated with corneal epithelial lesions in the interpalpebral zone.

Incidence and presentation

A total of 102 patients believed to have suffered corneal exposure during sleep were collected over a two-year period. Sixty-eight cases were examined personally and details of those remaining were provided by colleagues working in the same department.

The ages of the patients ranged from 17 to 82 years (average 42). Attacks had started at the age of 13 years in one patient, but for the whole series the incidence was highest in the third decade and slowly declined with increasing age.

Patients typically presented early in the day within a few hours of waking with their symptoms. The symptoms consisted of soreness, pricking discomfort or sharp pain in one eye, often associated with watering and sometimes blurred vision. Some patients had awoken during the night with pain in one eye. Symptoms were most pronounced immediately after their onset and tended to improve spontaneously during the course of the day. The appearance of symptoms in both eyes together was uncommon, and in the eight patients in whom this occurred, symptoms were always more marked in one eye than the other.

PREVIOUS ATTACKS

The number and pattern of attacks experienced by different patients varied. In 53 patients the presenting episode was their first and only attack, while in 18 there was a history of one or two previous

attacks. Thirty-one patients had experienced multiple attacks during a period varying from months to as long as 16 years in one case. A few patients in this last group gave a history of attacks occurring on several mornings in succession.

ROLE OF ALCOHOL

The only factor of possible aetiological significance revealed by history was the taking of alcohol. Fifty-two patients admitted to having drunk alcohol during the previous evening, but in 19 the amount of alcohol involved was small. Twelve patients were calculated to have consumed the equivalent of between 50 and 100 ml pure alcohol, and 11 patients had taken between 100 and 200 ml alcohol. Another 10 patients stated that they had been drinking heavily or had drunk more than usual. An association between alcohol and nocturnal lagophthalmos was recognized by four patients, all with a history of multiple attacks.

Family history

There was a family history of sleeping with the eyes open in five patients, representing four separate families.

A 29-year-old woman had had persistent symptoms of nocturnal lagophthalmos for seven years, affecting mainly the left eye. Her brother had seen her sleeping with this eye partly open, and taping shut the lids at night gave relief from her symptoms. While in hospital for investigation three years ago she had been seen to sleep with the left eye partly open. Next morning a small area of punctate epithelial keratopathy had been visible in the interpalpebral zone of the left cornea. A neurological examination had been normal.

The 24-year-old brother of this patient attended the casualty department recently with the symptoms and signs of nocturnal lagophthalmos. He had drunk the equivalent of 110 ml alcohol the previous evening and awoken the next morning with a sore right eye. There was no history of previous attacks.

A 31-year-old man, in whom symptoms of nocturnal lagophthalmos had occurred intermittently for 1½ years, was seen after waking at 4.0 am with a sharp feeling in the right eye. Examination revealed corneal

epithelial microcysts in the interpalpebral zone. The patient and his three daughters were all known to sleep with one or both eyes open at times.

A 42-year-old man gave a history of waking in the night with sore eyes for 15 years. Attacks occurred several times a year, on two or three nights in succession. He had attended the hospital frequently and the records for each visit showed punctate staining of both lower corneae. The patient, his father, his two sisters, and his son and daughter were all known to sleep with their eyes partly open.

A 54-year-old woman attended the hospital on two occasions in the past year with nocturnal lagophthalmos of first the left and then the right eye. She had been observed by her daughter to sleep with one eye open. The patient's mother and two aunts were also known to sleep with their eyes open.

In addition to these patients with a family history, a further six patients had been told that they tended to sleep with their eyes open. Thus a total of 11 patients who attended with nocturnal lagophthalmos had been observed on one or more occasions to sleep with one or both eyes partly open. It is noteworthy that in many of these patients, and in particular the relatives of those with a family history, failure to close the eyes during sleep was not necessarily followed by symptoms. Whether or not corneal exposure occurs must depend upon the presence or absence of Bell's phenomenon (see below).

DESCRIPTION

As anticipated from the history, examination revealed involvement of only one eye in most cases, although bilateral corneal changes were seen on at least one occasion in 18 patients.

There was usually mild to moderate hyperaemia of the affected eye, but some eyes were not injected at all. However, the most important diagnostic finding was an area of epithelial disturbance located in the interpalpebral zone of the cornea. The lesions, which could easily be overlooked without the aid of a biomicroscope, consisted of punctate epithelial keratopathy (PEK) combined with epithelial microcysts. The PEK lesions were visible by focal illumination as greyish flecks and stippling which stained well with rose bengal but poorly, or not at all, with 2 per cent fluorescein dye. The epithelial microcysts were visible only by retroillumination and did not take up stain. The proportion of PEK to microcysts varied in different patients and some lesions consisted mostly of PEK while in others microcysts predominated.

Basically the epithelial disturbance took the form of a horizontal band, in some cases this was patchy and incomplete, running across the lower cornea (Figs 1, 2). The width of this band varied in different patients from a narrow line of less than $\frac{1}{2}$ mm wide to a broad strip 4 or 5 mm wide. Sometimes, instead of a single band of epithelial lesions there were two horizontal lines. In some patients, examination of the apparently uninvolved eye revealed a few groups of microcysts

FIG. 1 *Area of partial thickness epithelial loss in centre of a band of rose bengal staining. Patient awoke with a sore eye after drinking the equivalent of 180 ml alcohol the previous evening*

FIG. 2 *Irregular double band of rose bengal staining. Slightly curved upper border of lesion conforms to shape of upper lid margin*

situated below the centre of the cornea. Extension of rose bengal staining on to the adjacent bulbar conjunctiva was uncommon even in cases in which a wide and well-defined corneal band ran from limbus to limbus.

In three patients a discrete grey faceted lesion was seen in the centre of a band of scattered PEK lying in the interpalpebral zone (Fig. 1). The central lesion stained strongly with 2 per cent fluorescein as well as with rose bengal dye and was thought to represent partial thickness epithelial loss.

Two other patients in whom nocturnal lagophthalmos was diagnosed presented on a different occasion with an area of complete epithelial loss (macroform recurrent erosion).

A 20-year-old man who was seen after waking with a sore right eye gave a history of a similar episode one year previously. Examination showed two horizontal

strips of rose bengal staining across the lower cornea. After treatment with chloramphenicol ointment and a pad the eye was symptom-free next day and the cornea no longer stained. Four months later he again awoke with a painful right eye and was found to have an oval area of epithelial loss below the corneal centre. The eye was padded but the patient failed to attend the next day.

A 39-year-old man presented with a six-month history of waking intermittently at about 3.0 am with pain in the left eye. This usually occurred after drinking six or seven whiskies. Examination showed minimal injection of the left eye and epithelial microcysts situated below the centre of each cornea but which were more marked on the left where a faint punctate stain was visible with 2 per cent fluorescein dye. Two years previously he had attended the casualty department after waking with a sore left eye. There was an area of epithelial loss in the interpalpebral zone of the left cornea and a faint epithelial irregularity extending across the right cornea. The left-sided erosion healed in 48 hours.

In many subjects, when blinking was prevented by restraining the upper lid, the tear film overlying the epithelial lesions broke down after 10 to 15 s (Fig. 3). This caused existing areas of PEK to become greyer and more readily visible and sometimes resulted in the appearance of similar greyish areas in parts of the interpalpebral cornea which had looked normal when the tear film was intact. Re-formation of the tear film resulted in rapid disappearance of these greyish areas.

Schirmer's test was performed on 22 patients, although the assessment of adequate tear production with this test is unsatisfactory because of the great variation encountered in normal individuals (de Roethth, 1953). Tear production was much reduced (less than 5 mm of wetting in 5 min) in four cases. All the patients

FIG. 3 Same case as Fig. 2 (unstained). Tear film breakdown over lesion when blinking is prevented. Patient was unaware of nocturnal lagophthalmos but saw his 18-year-old son sleeping with his eyes open

had suffered multiple attacks and two of them demonstrated rose bengal staining of the bulbar conjunctiva on one or more visits. In the remaining 18 patients, 15 mm or more of wetting was recorded from the affected eye. In those patients on whom Schirmer's test was not performed the tear film was judged to be normal in appearance and rose bengal drops caused copious tearing in most cases.

Treatment and course

Patients were treated according to the severity of their symptoms. Chloramphenicol ointment was prescribed and the eye was padded in cases in which symptoms were marked. Most patients were given chloramphenicol ointment to be used at bedtime. All patients who were seen next day were symptom-free or almost so, and the cornea had healed in most of them. In a few cases some residual epithelial lesions were still visible but these consisted predominantly of microcysts. Several patients subsequently experienced further attacks of nocturnal lagophthalmos despite the use of chloramphenicol ointment at night. However, most patients prone to recurrent attacks felt that the ointment did reduce the incidence of these attacks.

Discussion

Direct proof that the corneal lesions described in this paper were caused by exposure during sleep was obtained in only one case, although 10 other patients had been told that they sometimes slept with their eyes open. The failure to obtain such a history from the remaining patients is not surprising since most people are not observed while asleep. Even if the eyelids had been partly open during sleep a gap of 2 to 3 mm could have passed unnoticed on casual inspection, particularly in poor light.

Incomplete lid closure during sleep has however been reported by a number of authors. Fuchs and Wu (1948) described this phenomenon in China where it is not uncommon. In Bombay, Lebas (1956) encountered patients with bilateral opacification of the lower portion of the corneae which he ascribed to sleeping with the eyes half open. Likewise Mueller (1967) observed children and adults in Ethiopia who slept with their eyes open 3 to 4 mm. He surmised that this habit might in some cases produce the oval opacities on the lower third of the cornea seen in patients submitted for keratoplasty. Recently, Howitt and Goldstein (1969) in the USA described a patient, known to sleep with her eyes open, who awoke with a foreign body sensation and demonstrated punctate staining of the inferior third of both corneae. Clearly this

case resembles the patients described in the present paper.

Corneal exposure will not occur if the eyes are rotated upwards during sleep, although the lids remain open. In his paper describing the motions of the eye Bell (1823) implied that during sleep the eyes are always turned upwards, this being the state of rest. In fact, Bell's phenomenon is not a constant finding during sleep. Hall (1936) examined the position of the eyes in 234 sleeping subjects and Bell's phenomenon was present in only 42 per cent. The eyes were directed straight ahead in 44 per cent and in the remainder the eyes were deviated to one side (8.5 per cent) or turned down (5.5 per cent). Hall also noted that subjects were not consistent with regard to Bell's phenomenon which might be present one night and absent the next, or vice versa.

The characteristic history given by the patients provided further evidence for the occurrence of nocturnal lagophthalmos. Thus the onset of symptoms is directly related to sleep, and once patients are awake symptoms slowly subside spontaneously. Identical symptoms may be encountered in subjects who are known to have impaired lid closure. Examples of this were seen in a patient with unilateral dysthyroid lid retraction combined with restricted elevation of the eye, and in another patient in whom unilateral congenital ptosis had been overcorrected surgically. Despite an obvious and constant cause for poor lid closure in both these patients their symptoms of nocturnal lagophthalmos occurred only intermittently, as in the patients described in this paper with normal voluntary lid closure.

Finally, the morphology and nature of the corneal lesions themselves strongly suggest that they are the result of exposure. Incomplete or partially healed lesions may take the form of a few groups of PEK scattered across the lower cornea (Fig. 4) or a collection of epithelial microcysts (Fig. 5). Viewed in isolation the aetiology of this type of epithelial disturbance is not immediately obvious. Well developed lesions, however, consist of a greyish, stippled, horizontal band lying in the interpalpebral zone, and closely resemble Ayoub's description of desiccation keratitis (Ayoub, 1944). It is curious that in half of Ayoub's cases only one eye was involved although the condition developed during the daytime. The predominantly unilateral nature of the lesions seen in nocturnal lagophthalmos is equally puzzling and remains unexplained.

The differential diagnosis of nocturnal lagophthalmos includes dendritic ulcer, incomplete blinking, and the microform of recurrent erosion.

A dendritic ulcer had been diagnosed on one or more occasions in the past in three patients who subsequently re-attended with nocturnal lagoon-

FIG. 4 *Non-specific punctate staining with rose bengal. Patient awoke twice during night with a sore eye. Seen 9 months previously with bilateral microform recurrent erosions*

FIG. 5 *Macrophotograph showing corneal epithelial microcysts by iris retroillumination. Patient awoke with a sore eye and misty vision. No previous episodes*

phthalmos. In two of these patients the epithelial lesions had been carbolized producing, in one case, a corneal nebula. Examination of the hospital records made at that time suggested that nocturnal lagophthalmos would have been a more appropriate diagnosis. In a fourth patient the initial diagnosis of dendritic ulcer was changed to nocturnal lagoon-

phththalmos when another doctor saw the patient. The corneal lesions in all four cases were situated in the interpalpebral zone, being shown as a horizontal band of stippling in three cases, and recovery was rapid in every case. It seems unlikely that any of these four patients ever had a dendritic ulcer. It can be difficult to distinguish between a dendritic ulcer and the dendritiform figure produced during the healing stages of an epithelial disturbance. Thus in a further four patients the epithelial lesions were described as 'pseudodendritic' or 'not typically dendritic'.

Corneal staining associated with incomplete blinking has been reported in 55 out of 300 subjects who were examined before being fitted with contact lenses (Korb and Korb, 1970). 2 per cent fluorescein dye showed diffuse blotchy staining of the peripheral cornea inferiorly, unlike the pattern seen in nocturnal lagophthalmos, and no symptoms were described.

Recurrent corneal erosions occur in two forms which are distinguished by the severity and duration of the symptoms and by the epithelial changes. This was recognized by von Reuss (1898) and emphasized by Chandler (1945) who introduced the terms macro- and microform. The microform, which is more common, is characterized by the sudden onset of pain or discomfort in one eye, rarely both, which either wakes the patient from sleep or starts when the eyes are opened in the morning. Some patients notice blurred vision at the start of an attack (Franke, 1906). Symptoms subside spontaneously within minutes to hours. Depending on the facilities available and the time elapsing after the onset of symptoms, corneal examination may reveal no abnormalities (Grandclément, 1888; von Reuss, 1898; Stood, 1901; Franke, 1906), tear film disturbance when the upper lid is restrained from blinking (Peters, 1904), localized irregularities of refraction visible by skiascopy (Szili, 1900), or superficial greyish dots or flecks (Salus, 1922; Procksch, 1926) associated with microcysts (Vogt, 1930; Chandler, 1945; Bron and Tripathi, 1973) and situated below the corneal centre. Although a history of previous trauma to the affected eye is often obtained from patients with recurrent erosion, in a considerable number of cases the microform is not preceded by trauma (Szili, 1900; Franke, 1906; Salus, 1922; Procksch, 1926; Lemoine and Valois, 1930; Spektor, 1931; Chandler, 1945; Brown and Bron, 1976). Recurrences of the microform are both more frequent than the macroform and more persistent since attacks may recur for many years. The application of ointment to the eyes at night is an established prophylactic measure which greatly reduces the incidence of recurrences (von Reuss, 1898; Stood, 1901; Chandler, 1945; Thygeson, 1959).

The micro- and macroforms are thought to represent the two ends of the recurrent erosion spectrum (von Reuss, 1898; Hirsch, 1898; Szili, 1900; Salus, 1922) and both forms can occur in the same patient. Thus the microform may immediately precede the macroform in the same eye (Stood, 1901; Procksch, 1926; Brown, 1975), or both forms may appear simultaneously, one in each eye (Procksch, 1926; Brown, 1975). The frequent episodes of the microform which are encountered in some patients may be interspersed with occasional attacks of the macroform (von Reuss, 1898; Hirsch, 1898; Szili, 1900; Brown and Bron, 1976). Finally, careful examination of the epithelium surrounding a macroform erosion sometimes reveals the presence of microcysts (Bron and Tripathi, 1973; Brown and Bron, 1976), a characteristic feature of the microform.

The striking similarity between the symptoms and corneal lesions of nocturnal lagophthalmos and the microform of recurrent erosion suggests that these two conditions are identical. In this case it is likely that the macroform of recurrent erosion is also initiated by corneal exposure during sleep. This would explain why recurrences are almost invariably situated in the interpalpebral zone, but not necessarily at the exact site of the original injury in post-traumatic cases (Hirsch, 1898; Szili, 1900; Chandler, 1945; Thygeson, 1959).

Examination of the corneal lesions seen in nocturnal lagophthalmos suggested that epithelial damage might have been caused in two different ways. In most patients it appeared that evaporation of the precorneal tear film had produced desiccation of the exposed corneal epithelium. Less commonly, the lids had apparently become stuck to the cornea when the tear film and lid margin secretions dried up. Movement of the lids or globe on waking had then disrupted the superficial layers of the corneal epithelium. Thus in several patients the corneal lesions consisted of two horizontal lines of PEK parallel with the lid margin (Fig. 6). Previous authors believed that adhesion between the corneal and tarsal epithelia could cause a recurrent erosion (von Reuss, 1898), particularly when the eyes were opened abruptly (Hirsch, 1898; Szili, 1900). Physical difficulty in opening the eyes in the morning accompanied by the onset of pain is sometimes described by patients with recurrent erosion (Stood, 1901; Hine, 1951; Bron and Tripathi, 1973; Brown and Bron, 1976). The prophylactic effect of ointment applied to the cornea at night tends to confirm the importance of exposure in the aetiology of recurrent erosion. One would expect that ointment, by augmenting the naturally-occurring oily layer of the precorneal tear film, would greatly reduce evaporation from the exposed cornea (Mishima and Maurice, 1961). This property is the

FIG. 6 Two incomplete horizontal bands of rose bengal staining believed to represent position of upper and lower lid margins during night. Patient drank 10 or 12 pints of beer and awoke with a sore eye next day

only factor common to the wide variety of ointments (Borlanolin, cocaine, iodoform, boric, chloramphenicol, 5 per cent NaCl) which have been recommended for the treatment and prophylaxis of recurrent erosion.

The mechanism whereby corneal exposure during sleep produces a recurrent erosion is believed to be that of damage to the superficial squamous cells of the epithelium. There is evidence that these cells represent the main barrier to the passage of tear film fluid into the epithelium (Tripathi and Bron, 1973). Exfoliation of the superficial squamous cells has been described in recurrent erosion (Tripathi and Bron, 1972) and epithelial oedema is a feature of both the traumatic (Goldman, Dohlman, and Kravitt, 1969) and the non-traumatic (Tripathi and Bron, 1972) forms of recurrent corneal erosion.

It is suggested that nocturnal lagophthalmos, by causing desiccation or disruption of the superficial epithelial cells, results in the development of epithelial oedema which, together with the epithelial damage, constitutes a microform recurrent erosion. Less commonly, fluid may accumulate beneath the epithelium to form a bulla, the rupture of which produces a macroform recurrent erosion.

The normally firm adhesion of the epithelial

basement membrane to Bowman's layer may become loosened for reasons which are usually not clear, although it is known that oedema can facilitate epithelial separation (Tripathi, 1972). In post-traumatic recurrent erosion a deficiency of the basement membrane has been implicated as being a cause of the epithelial separation (Goldman and others, 1969) but in a case of non-traumatic recurrent erosion the basement membrane was found to be intact (Tripathi and Bron, 1972). It is interesting that even when the epithelium is only loosely attached, the development of a recurrent erosion is by no means inevitable. Thus Szili (1900) was able to remove almost the entire epithelium without difficulty from several asymptomatic patients who had a history of recurrent erosion whom he examined from between ten days to six weeks after their last attack. Despite the lack of epithelial adhesion demonstrated in these patients accumulation of tear film fluid beneath the epithelium was presumably prevented by the presence of an intact epithelial barrier. Damage to this barrier may be followed by bulla formation as in the patient with a history of recurrent erosions in the right eye (Salus, 1922). Soon after tonometry had been performed on this eye it became painful and a bulla was seen which subsequently ruptured. It is suggested that a commoner form of epithelial damage predisposing to macroform recurrent erosions is that caused by nocturnal lagophthalmos.

Summary

The symptoms and corneal changes caused by sleeping with one or both eyes open are described in 102 patients. The clinical picture is identical to that of the microform recurrent erosion. The close relationship between the micro- and macro-forms of recurrent corneal erosion suggests that the latter condition is also precipitated by nocturnal lagophthalmos.

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