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CASE SERIES

Sir,

Successful management of three consecutive cases of recurrent corneal erosion with botulinum toxin injections

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Recurrent erosion can be an enigma. The idiopathic form almost always occurs in the morning and often disrupts working life. It engenders great anxiety. Dry eye and other symptoms are common apart from the agonising acute episodes. These episodes mean absence from work.

There are many treatments for recurrent erosion. Patients are often started on topical lubricating agents and topical desiccating agents. They are often unsuccessful and their failure has frequently been the reason for referral to the author for therapeutic contact lenses. These are probably the most common form of treatment and one that the author has found successful in the past. The therapeutic soft contact lenses have to be worn for several months. Such patients need constant medical supervision and continuing minor complaints, in the absence of typical painful erosions, are common.

Markedly invasive treatments are practised, for example, anterior stromal puncture,[1] phototherapeutic keratectomy,[2] and diamond burr superficial keratectomy.[3] There is an extensive literature on these.

Case reports

Case No. 1

In December, 2000, this patient started to try to wear monthly replaceable soft contact lenses for cosmetic reasons. She only achieved five hours a day tolerance.

On 1st January 2001, she attempted to take out the left lens one evening, but did not realise that it had fallen into a basin. She then asserted that she put her nail into her left cornea, thinking that she still had to remove the lens, and suffered ensuing pain. The next morning she visited her optician in great pain and was sent to a major eye hospital in London. She was seen to have an abrasion of the left cornea with a surrounding area of heaped-up epithelium, in its lower third and extending to about half the width of the cornea in this area. She was treated with Oc. chloramphenicol t.d.s., together with Oc. Lacrilube nocte.

One month, to the day, later on 2 February 2001, she awoke with pain and discomfort, this time in her right eye. She returned to the major eye hospital, where she was again treated with Oc. chloramphenicol and Lacrilube, for a right corneal abrasion, again in the lower half of the cornea.

After 2 weeks, she had a flare-up in her left eye and was seen by her optician. She revisited the major eye hospital again on 15 February 2001, at 0138 hours, in agony. An area of 'unhealthy epithelium' was seen in the inferior third of the left cornea. On this occasion, a nurse anaesthetised the left eye and patched it. Viscotears t.d.s. together with Lacrilube nocte were prescribed. She attended again at 0800 hours in the morning of 16th February, and a specialist registrar debrided the corneal epithelium in the area after anaesthetising the cornea. She subsequently attended her general practitioner, who referred her to a consultant ophthalmologist, who in turn referred her to the author for treatment with therapeutic soft contact lenses. No characteristic microcysts were seen on the right cornea, which did not stain with fluorescein. The left cornea showed punctate staining in its inferior third.

The author advised her that she should be treated with bilateral continuous wear therapeutic soft contact lenses, which would be worn for several months. She informed the author that she could not possibly do this. After an explanation, the author obtained her permission to inject the superior orbicularis muscles with Dysport (botulinum toxin A). Four areas, two nasal and two temporal (Figure 1), were injected with 0.025 ml of the standard solution (500 U in 2.5 ml saline). This was a very small dosage.

She returned on 29 March 2001, and said that she had been very happy for 2 weeks. She had been prompted to close one eye overnight with Blenderm tape (3 M) on one occasion, and it was better the next day. At this consultation, she said that she had awakened with a sore eye that morning, but she was obviously not in great distress. The author increased the dosage of Dysport to the superior obicularis muscles by giving a further 0.025 ml to the two temporal sites and a further 0.05 ml. to the two nasal sites. Further injections of 0.025 ml were given to the forehead — two on either side, one above the other.

The next day, 30 March 2001, she returned with a red right eye that showed a deep fluorescein stain. The eye was not painful. She was treated with Gut. Exocin (ofloxacin), 4 hourly.

She returned on 31 May 2001. She told the author that she had not had to Blenderm tape the eyes for 9 weeks, but that problems had increased in the previous two weeks and that her left eye was sore since the previous night. On this occasion, there was a small erosion in the lower half of the left cornea. Botulinum toxin injections were again given by injecting 0.05 ml. into all four injections sites.

The author saw her again on 12 July 2001, after a period of about 6 weeks. She told him that she had had no episodes of pain, but that in about 80% of days, both

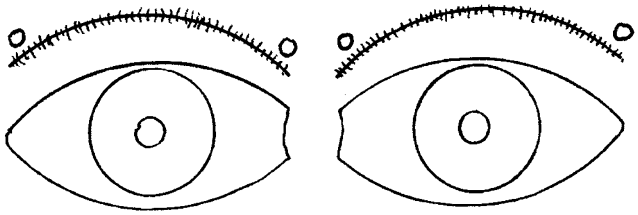

Figure 1 Temporal and nasal sites for injection, above the eyebrow lashes. The needle should be directed temporally when injecting at the temporal sites and nasally when injecting at the nasal sites. This minimises the possibility of creating lid ptosis. An optimum dose would appear to be 0.1 ml of the standard solution of Dysport (Ipsen Ltd) to each of the four sites.

lids, mainly the left, felt as if they were stuck to the eye. She had to rub the lids to release them. On this occasion, a faint punctate staining with fluorescein was seen in the lower third of the right eye. Botulinum toxin injections were repeated as at the previous visit.

She was seen again on 23 August, after a period of $4\frac{1}{2}$ weeks, and related how she had had no trouble up to the penultimate week. In the last week, the lids had been stuck down in the mornings and stung on opening, but calmed down in half an hour. At this time, the botulinum injections were repeated as in the previous visit.

On 27 September 2001, she returned saying that she had had only one 'stuck-up' episode since the previous visit and had had no problems in the morning. At this time, the botulinum toxin injections were repeated as in the previous visit.

She attended again on 5 November 2001, and reported that she had had no problems. On this occasion, the botulinum toxin dosage to the two nasal sites was increased to 0.1 ml. The temporal sites were injected as before with 0.05 ml toxin.

She was seen again on 20 December 2001, 14 February 2002, 7 May 2002, and 15 August, 2002, and on all occasions reported no problems. The botulinum toxin injections were repeated as they were on 5 November 2001.

The author telephoned the patient at the end of December 2002, and she reported that she had no problems with her eyes.

A further telephone call to the patient on 23 March 2003 revealed that she had had no further problems at all.

She telephoned the author on 14 July 2003 and said that she wished to try to wear cosmetic contact lenses again and would be making an appointment with the author.

Case No. 2

A further bilateral case of recurrent erosion was referred to the author on 18 July 2001. Her trouble had started when feeding her daughter on the preceding February. The daughter had allegedly scratched the left cornea and the patient had to attend the Casualty Department at the local hospital. Anaesthetic drops were instilled and the eye was bandaged. However, the patient had to take the bandage off after the anaesthesia wore off because of increased discomfort. It took 36 h for the eye to feel normal. After this she had mild discomfort on some mornings and she applied a lubricant. At the beginning of March 2001, she had a further severe episode in the left eye and had to hold the eye open, as well as she could, for 24 h until she saw her general practitioner, who prescribed Gutt. Fucithalmic and pain killers. She had to go to the local hospital eye casualty where again a bandage was applied, which she had to remove after 1 h. She then started to put Viscotears in the left eye on returning for the night, having tried Lacrilube without success.

In May 2001, her baby allegedly scratched the right eye. After this occurrence she had a severe episode of corneal erosion in this right eye and had to take a week off work.

The left eye continued to feel sore in the morning, and in this month of May (2001) she woke up in the middle of one night with an erosion in the left eye and had to attend the local hospital.

She was referred to the author on 18 July 2001. No microcysts were noted in either eye. Botulinum toxin injections were given. The dosage was 0.05 ml of the standard solution of Dysport in the four areas as depicted in Figure 1, plus a further two of 0.025 ml to the frontal muscles, in the middle of either side of the forehead. She was seen again on 30 July, and reported that seven nights after the previous appointment she had had a mild attack in the right eye in the morning, but nothing else.

She was seen again on 8 August 2001, and reported two mild attacks in one or the other eye. Botulinum toxin injections were repeated by giving 0.5 ml to each of the four areas in Figure 1. This means that the dosages given at the first injections were increased to 0.1 ml after a short period of 20 days. (The effect of the toxin lasts for about $3\frac{1}{2}$ months.)

She was seen again on 3 September 2001, and reported slight discomfort in the morning for the previous 4 days. The corneas were clear, except for a linear fluorescein

stain in the lower third of the left eye, which appeared after a considerable time and then vanished. At this time, she announced she was pregnant and so the botulinum toxin injections could not be repeated.

The author telephoned her on 5 May 2002, and she told him that she had had no trouble since her last appointment on 3 September 2001.

She reattended on 26 September 2002, and related to the author how she had started, in the previous 3 weeks, to have trouble in the middle of the night. This, however, usually cleared in 2 h with the use of Viscotears. At 3 weeks prior to the visit, she had taken a flight to Germany, and this state of affairs occurred in both eyes 36 h afterwards and lasted for 2 h. Again, she used Viscotears. She told the author that she often found it difficult to open her eyes in the morning and felt them dry. However, she said that since her last appointment, the botulinum toxin had cured the opening problem. The dryness was a new feature in the previous 3 weeks. On examination, rapid drying (4 s) was seen in the lower third of the right cornea and a small discrete stain was seen in the lower third of the left cornea. At this time, she was breast-feeding her new baby, so botulinum toxin injections could not be given. However, after a week in which the baby had been switched to bottle-feeding, botulinum toxin injections were again given, 0.10 ml being used in the four areas shown in Figure 1 together with 0.025 ml in the middle of each side of the forehead.

She reattended on 14 October 2002, relating that on the night of 7 October she had awakened in the middle of the night with discomfort in the right eye. It took about an hour until she managed to fall asleep, and when she awakened in the morning it was uncomfortable for about an hour. She was seen to have crusts on her lashes, and rapid drying (5 s) in the lower third of the left cornea. Some telangiectasis was noted on the lid margins. There were ample thick lower tear wedges. At this examination, she had not used make-up and was seen to have phymas of both cheeks with slight overlying telangiectasis. These were also present on the nose. A diagnosis of mild rosacea was made and she related that her father had rosacea affecting his nose and cheeks. She was treated with Caps. doxycycline.

The author telephoned her on 5 January 2003, and she reported that she sometimes felt her eyes dry in the morning, but had had no pain or acute problems

A further telephone call on 9 March 2003 revealed that she had had one episode lasting only an hour about a week previously. It occurred in the middle of the day and she thought that she may have rubbed her eye. She did not think it was serious enough to merit more toxin.

She reattended on 4 August 2003 and reported that her eyes had been uncomfortable for 2 months and had been painful in the mornings for half an hour. A mound of microcysts was found in the lower third of each cornea. Botulinum injections were given (0.1 ml) to each of the four sites shown in Figure 1.

Case No. 3

This patient was seen by the author on 6 August 2002. He is an airline pilot working on a passenger aircraft. His real trouble had started in February 2002, but for the previous 2 months his right eye had felt sore in the mornings. The symptoms worsened and the eye became very red and wept uncontrollably. Moving the eye, in one direction or the other, exacerbated the pain. He consulted his general practitioner, who referred him to a consultant ophthalmic surgeon. Some medication was put in the eye and it was patched. Within 24 h, he was asymptomatic. Some ulceration was noted after this and he was off work for about 18 days, by which time the ulceration had disappeared. The eye was comfortable for about 6 weeks, but slowly, at the beginning of May, 2002, the symptoms and soreness in the mornings returned. Hypromellose gave temporary relief. He was later advised to use Lacrilube, which helped to ease the morning symptoms. However, when he started work again, he could not use Lacrilube at night because it affected his vision the next day. He reverted to Hypromellose in the morning and this kept the symptoms at bay for about a month. The symptoms worsened in July when he had another extremely painful episode. This involved another 3 weeks off work.

He was referred to the author, by a consultant ophthalmologist, on 6 August 2002. Botulinum toxin (Dysport) injections were given. The temporal areas were given 0.05 ml and the nasal areas 0.1 ml of the standard solution, as demonstrated in Figure 1.

He was seen again on 2 September 2002. He noticed that a very slight left ptosis had developed 10 days after the injections. No other person noticed it. He related that he had had no redness or acute problem in the right eye, but one morning he had had a soreness lasting 10–15 min after getting up. He had not missed any days flying. He did report that 2 weeks previously the left eye had felt sore when he was blinking, as if there was an eyelash in the eye, but this had become better. He could be seen to have crusts on the lashes and there was a slight hyperaemic infiltration of the palpebral conjunctivas. Caps. doxycycline was prescribed. At this visit, further injections of 0.05 ml. of Botulinum toxin were given to the two temporal sites, twenty seven says after the previous injections to these sites.

He was seen again on 18 September 2002, and related that he had had no problems and that the slight left ptosis had lifted. Further injections of botulinum toxin

were given on 10 October 2002. The dosage was 0.1 ml in each of the four zones shown in Figure 1.

He was seen again on 8 January 2003, and again reported no problems of discomfort. However, he drew attention to, and was seen to have, crusts on his lashes. Gutt. Fucithalmic was prescribed for application to the lid margins at night. The botulinum toxin injections were repeated using 0.1 ml in each of the four areas shown in Figure 1.

A telephone call from the author on 23 March 2003 revealed that he had had no further painful erosions, but that he was using Viscotears at night and when flying, as his eyes felt dry in the morning.

He returned on 3 April 2003, relating that he had had no further trouble but would like the author to repeat the previous injections as a precaution. This was done.

Discussion

The salient fact emerging from these three cases is that none of them had a typical acutely painful recurrent erosion, requiring emergency treatment and absence from work, after the initial botulinum toxin injections.

Case No. 1 was undoubtledly started on a dosage that was too small. Symptoms persisted, but a typical acute erosion was not experienced. It would appear that the optimum dosage for the standard dilution of Dysport in the four sites is 0.10 ml (Figure 1).

The rationale for the use of botulinum toxin was explained to the patients before gaining their consent to the injections. Their attention was drawn to the fact that typical recurrent erosions occur in the morning on awakening. It was conjectured that rapid eye movements described in sleep[4] might be involved in the pathology. According to David Maurice, over 7000 scientific papers have been written on this subject since 1966. These papers have been the domain of disciplines ranging from psychology to neuropharmacology. He states that the condition has not received attention from ocular physiologists.[5]

A prospective study of 42 patients has demonstrated an abnormally high prevalence of 'absent' or 'weak' Bell's phenomenon in patients with recurrent erosion as compared to a control group of 189 patients. Patients without a predisposing factor for their recurrent erosions had a 78% prevalence of abnormal Bell's phenomenon. Those with an epithelial, or basement membrane, dystrophy had a 55% prevalence.[6]

Normal lid closure is mainly affected by Riolan's muscle, which is located in the posterior part of the lid margin and is not part of the orbicularis muscles.[7] Mackie[8] has demonstrated that abnormal blinking, with eye closure leads to an absence of Bell's phenomenon. By abnormal blinking he meant blinking with the addition of orbicularis muscle action. In an accompanying film to the presentation of the paper, he showed that 'peering', that is markedly closing the lids in a sphincter-like fashion, with the help of the orbicularis muscles, abolished Bell's phenomenon. The author demonstrated Bell's phenomenon and how it was altered by orbicularis action in the patient.

It is just possible that orbicularis movement is present in some cases of rapid eye movements during sleep, thus exacerbating the problem with Bell's phenomenon.

Further work needs to be carried out on the role of botulinum toxin in the treatment of recurrent erosion, in particular to the optimum dosage that should be used and the optimum sites for the injections. There is a case for an ocular physiologist to investigate rapid eye movements during sleep.

These results compare very favourably with those that are obtained with therapeutic soft contact lenses and the problem of corneal infections is avoided. Great caution has been advocated in the use of contact lenses in recurrent erosion.[9]

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