Treatment of peripheral corneal ulcers by limbal conjunctivectomy

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Peripheral corneal ulcers can still pose difficult clinical problems despite therapeutic advances such as specific antimicrobial agents, collagenase inhibitors, heparin, ocular lubricants, biological adhesives, and soft contact lenses. This paper reports the healing of several types of progressive marginal ulcers after the excision and recession of adjacent limbal conjunctiva (limbal conjunctivectomy), in some cases after other modes of treatment had been unsuccessful.

Case reports

CASE 1, MOOREN’S ULCER

A 54-year-old Black woman developed a severely painful, largely non-infiltrative ulcer of the nasal left cornea. The ulcer had an overhanging central edge and progressed circumferentially during a period of one year to involve nearly the entire corneal periphery (Fig. 1a). Progression occurred despite treatment at various times with acetylcysteine drops, L-cysteine drops, topical and subconjunctival heparin, artificial tears, soft contact lens, a short trial of topical corticosteroids, and a trial without any treatment to minimize the possibility of overtreatment. Two years before we saw her, the patient had lost her other eye from a similar process despite heparin treatment and lamellar keratoplasty; the eye had been enucleated to relieve severe pain, although the ulcer had not perforated.

Ocular cultures and scrapings were negative or non-contributory. Extensive systemic examinations by internal medicine were negative on two separate occasions except for sporadic increases in immunoglobulins M and A. No other evidence was found to indicate the presence of autoimmune disease.

After all other therapeutic attempts had failed, we performed a 360° peritomy and made contiguous cryoapplications to the central and peripheral edges of the ulcer. The cryotherapy was performed with an Amoils cryosurgical retinal probe which reached temperatures of -40 to -50°C. Each application was maintained for 10 to 15 seconds. Fibrous tissue began to appear within the ulcer about one week later, followed in a few days by superficial vascularization. The ulcer had healed and epithelialized three weeks after surgery (Fig. 1b) and L-cysteine and heparin drops were continued for three weeks after it had healed. The ulcer has

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FIG. 1 (Case 1). (a) Moorén’s ulcer just before surgery. All medical treatment had failed to halt progression. (b) Complete healing of ulcer after peritomy and cryotherapy to ulcer edges.
fermentation tests confirmed the presence of ocular (and genital) *Neisseria gonorrhoeae*.

The corticosteroid-sulphonamide ointment was stopped, and treatment with systemic penicillin, topical bacitracin ointment, and L-cysteine drops was begun.

Six days later the eye was essentially white and repeat cultures were negative, but the ulcer was not improved and was thought to be deeper in some areas. We then excised a 4 to 5 mm strip of limbal conjunctiva adjacent to the ulcer and loosely recessed (without sutures) the remaining conjunctiva to a distance of about 1 cm from the limbus. The bacitracin and L-cysteine were discontinued. The ulcer showed early fibrosis three days after surgery and was healed and epithelialized 10 to 14 days after the procedure (Fig. 2b). The ulcer has remained healed for two years.

**CASE 3, RHEUMATOID ARTHRITIS**

A 64-year-old White woman had had severe, immobilizing rheumatoid arthritis for 17 years. Her general medications were salicylates, indomethacin, and ironized yeast. For six weeks she had complained of bilateral ocular discomfort and blurred vision, for which she was given an unknown eyedrop which provided slight and temporary symptomatic improvement.

Corneoscleral ulcerations, extending to about two-thirds of the corneoscleral thickness, were present bilaterally, nasally in the right eye (Fig. 3a) and nasally and temporally in the left eye (Fig. 3b). The ulcerations were essentially non-infiltrative, and there was no discharge. The eyes were not dry. Slit-lamp examination was not possible, but the anterior chambers were grossly clear.

Significant laboratory studies included radiological changes of rheumatoid arthritis, slightly decreased serum albumin, raised serum gamma globulin, raised serum immunoglobulins G and M, positive rheumatoid factor, and lupus erythematosus phenomenon (LE prep.), 2+ 'speckle' positive fluorescent antinuclear antibody, increased erythrocyte sedimentation rate, and normochromic normocytic anaemia by bone marrow examination.

We began ocular treatment for both eyes with L-cysteine drops, sulphacetamide drops, and artificial tears. Nine days later the ulcers were larger and deeper, and it was feared that perforation might be imminent. Two weeks after beginning our treatment bilateral conjunctivectomy with recession was performed adjacent to the areas of ulceration. Much of the excised conjunctiva was bulbar rather than limbal, since the ulcers extended on to the sclera. Postoperatively L-cysteine was stopped, but sulphacetamide and artificial tears were continued. A fibrous coagulum was apparent over all areas of ulceration four days after surgery: some of this material appeared to become fibrous six days after surgery. After eight days both eyes were healing well (Figs 3c, d), and the patient was discharged. Healing was soon complete, and there has been no recurrence during the subsequent two years.

**CASE 4, KERATOCONJUNCTIVITIS SICCA**

This 72-year-old White woman had been followed-up for two years for dry eyes in association with xerostomia...
and rheumatoid arthritis (Sjögren's syndrome). Artificial tears alone were insufficient; bilateral soft contact lenses were prescribed for full-time wear in conjunction with sulphacetamide drops and artificial tears. A diffuse cellular infiltration of the superficial stroma of each cornea appeared four days later. The lenses were discontinued, and treatment with topical gentamicin and bacitracin ointments and artificial tears was started. Small central epithelial defects developed bilaterally six days later. The left eye healed and its infiltrate cleared, but the right cornea suddenly perforated centrally. We applied cyanoacrylate glue and another soft contact lens (Fig. 4a), and the anterior chamber re-formed within minutes. The glue detached 10 days later, revealing a raised, vascularized scar over the site of perforation, but a large non-infiltrative ulceration developed along the entire nasal limbus (Fig. 4b).

Limbal conjunctivectomy with recession was performed (Fig. 4b), and a fibrinous coagulum with fine vascularization began to fill the defect two days later.

L-cysteine, artificial tears, and the soft lens were continued for a few more days. The eye healed (Fig. 4c) and has remained stable for 14 months. The corneal scarring and surface irregularities have cleared considerably (Fig. 4d).

**CASE 5, ROSACEA**

A 63-year-old White man was seen for a non-infiltrative ulcer of the inferotemporal periphery of the left cornea (Fig. 5). After onset about one month previously, he had been treated elsewhere with a topical corticosteroid-sulphonamide ointment for an unknown length of time. There was no history of rheumatoid arthritis or other autoimmune disease.

The typical findings of rosacea were present on the face—that is, erythema, papules, pustules, and telangiectases without comedones. There was clinical evidence of mild staphylococcal blepharitis bilaterally. Rosacea keratoconjunctivitis was present as shown by...
FIG. 4 (Case 4). (a) Cyanoacrylate adhesive and soft contact lens sealing corneal perforation in Sjögren's syndrome. (b) Adhesive has detached 10 days later revealing underlying scar. Marginal corneal ulceration has appeared along nasal limbus, and conjunctivectomy with recession has been performed. (c) Marginal ulcer healing 10 days after conjunctivectomy. (d) Final result seven months later.

dilated conjunctival vessels and peripheral vascularization of the cornea, worse below. The ulcer penetrated to slightly more than half of the stromal thickness.

Conjunctival scrapings were negative. Lid-margin cultures revealed a few colonies of Staphylococcus epidermidis.

We began treatment with topical acetylcysteine drops, lid scrubs, and bacitracin ointment to the lid margins. The referring physician performed limbal conjunctivectomy with recession, and the ulcer healed in about 10 days. No further ulceration has occurred in the succeeding one year.

CASE 6, THERMAL BURN

A 30-year-old Black man sustained first, second, and third-degree burns on the chest, face, and both eyes, from molten metal. The left eye was destroyed. The right cornea was opaque, and there was extensive conjunctival ischaemia and necrosis, worse below.

The left eye was eviscerated. The right eye was treated with topical antibiotics and cycloplegia, daily lysis of symblepharons, and the insertion of a plastic scleral shell for maintenance of the fornices. Two weeks later a marginal corneal ulcer appeared inferonasally. Topical acetylcysteine drops were started, but the ulcer deepened. Perforation was feared, so limbal conjunctivectomy with recession was performed one week after onset of the ulcer. Acetylcysteine drops were continued. Vascularization of the ulcer appeared within 10 days, and it was healed 19 days after the surgery. There has been no recurrence of ulceration.

CASE 7, RHEUMATOID ARTHRITIS

A 70-year-old White man had had rheumatoid arthritis for 40 years, for which he was taking only aspirin. One week before our examination he developed foreign-body sensation and photophobia of the right eye. No ocular treatment had been given.
We found a relatively quiet, non-infiltrative, ovoid, paralimbal ulcer superonasally; it extended to slightly more than half of the stromal thickness. There was mild hyperaemia and extension of the adjacent limbal vascular arcades. The anterior chamber showed 1+ flare and cells without keratic precipitates.

We performed limbal conjunctivectomy with recession and started topical L-cysteine drops. Two days later the ulcer had partially filled in coincident with further extension of the limbal vessels. We continued L-cysteine, and healing and vascularization progressed. Three weeks after beginning treatment the ulcer was healed without staining (Fig. 6), and it has remained stable over the intervening four months.

CASE 8, ULCER AFTER CATARACT SURGERY (POSSIBLE MOOREN’S ULCER)

An 81-year-old White woman had a slightly infiltrative marginal corneal ulcer in the area of interrupted catgut sutures which had been placed at the time of cataract surgery in the left eye, four months earlier. The referring ophthalmologist had previously tried treatment with topical corticosteroids and patching without success.

The ulcer extended from 10 to 2.30 o’clock superiorly and to about half of the stromal thickness. Treatment was begun with topical acetylcysteine and sulphacetamide drops, but one month later the ulcer was not improved. We then advised limbal conjunctivectomy with recession. This was performed by the referring ophthalmologist about one month later, at which time the ulcer had extended to the 7.0 o’clock position nasally and to the 5.0 o’clock position temporally. The procedure produced minimal or no improvement. The patient subsequently was treated elsewhere with placement of a conjunctival flap that also became involved in the ulcerative process, and finally with a graft of mucous membrane in conjunction with lamellar shaving of the remaining central island of corneal tissue. She has since been lost to follow-up.

Histopathology

All of the excised strips of conjunctiva showed moderate to large numbers of mononuclear cells and smaller numbers of PMNs infiltrating the subepithelial tissues. The mononuclear reactions consisted mainly of lymphocytes, although scattered monocytes were also present. All specimens except those from the case of rosacea (Case 5) and the thermal burn (Case 6) also contained moderate to large numbers of plasma cells; Case 5 did not contain plasma cells, and Case 6 had only rare ones. The conjunctiva from the case of ulceration after cataract surgery (Case 8) showed also scattered eosinophiles.

Conjunctiva was not available from the case of Mooren’s ulcer (Case 1), but we were able to examine the patient’s other eye, which had been previously enucleated. The subepithelial connective tissues and superficial sclera adjacent to the ulcer contained extensive infiltrates of lymphocytes and plasma cells, in about equal numbers, while the corneal ulcer itself showed only a few isolated lymphocytes.

Discussion

Aviel (1972) reported the successful treatment of four cases of Mooren’s ulcer by the empiric use of peritomy and cryoapplications to the ulcer edges, prompting us to resort to the same treatment in our Case 1 after all others had failed. Healing was rapid and complete, with no recurrence over a period of more than three years.

There was no ready explanation for the appar-
ently beneficial effect of this mode of therapy until
Brown (1972) incriminated the conjunctiva as a
source of collagenase and proteoglycanase, enzymes
that are capable of causing corneal ulceration by
producing destruction of corneal collagen and
ground substance. Brown (1972) also suggested
excision of limbal conjunctiva as a possible treat-
ment for Mooren’s ulcer and has since alluded to
the apparently successful use of this treatment for
rapidly progressing peripheral corneal ulcers and
scleromalacia (Brown, 1974). We thus began to
suspect that the successful outcome of our Case 1
may have been related more to peritomy and
conjunctival recession than to cryotherapy. In all
subsequent cases we have omitted cryotherapy
and have substituted conjunctival excision for
simple peritomy, with good results in all but one
instance (Case 8). Whether cryotherapy has any
value, alone or in combination with conjunctivec-
tomy, remains to be determined.

Bloomfield and Brown (1974) confirmed the
presence of, and partially characterized, a col-
lagenase produced by both normal and inflamed
rabbit conjunctiva. They thought that the con-
unctival epithelium was the major source of the
collagenase. They also cited unpublished studies
in which they detected collagenase and proteogly-
canase in conjunctiva adjacent to Mooren’s ulcers.

The precise origin of conjunctival or corneal
collagenase in any given clinical situation is un-
certain. Epithelium in contact with wounded
stoma (Brown and Weller, 1970), PMNs (Brown,
Weller, and Akiya, 1970; Brown and Hook, 1971),
and fibroblasts (Bloomfield and Brown, 1973) have
all been found to be capable of producing col-
lagenase under various experimental circumstances.
Factors that may initiate collagenase production
are also poorly understood. Presumably some
immunological or traumatic stimulus calls forth and
activates one or more of the above cell types. The
presence of plasma cells and lymphocytes in the
conjunctival tissues that were excised from our
cases suggests that humoral or cellular immune
phenomena are operative, although both of these
cell types are not infrequently found in subepi-
thelial conjunctival inflammation of various causes
and may be non-specific findings.

While removal of proteolytic conjunctival enzy-
mes or their cells of origin seems likely to be the
means by which conjunctivectomy exerts its
beneficial effect, this has not been proved. The
fact that the procedure causes bleeding, and that
serum is known to contain antillegenase factors
(Eisen, Bloch, and Sakai, 1970; Hook, Brown,
Iwanij, and Nakaniishi, 1971; Berman, Barber,
Talamo, and Langley, 1973), must also be con-
sidered. Another possible explanation is that the
surgical trauma simply stimulates vascularization,

fibrosis, or other non-specific aspects of inflam-
ation. If the elimination of conjunctival enzymes is
critical, it may be important to ensure that the
recessed conjunctiva does not grow to the limbus
again before re-epithelialization of the corneal
ulcer. In some cases the recessed conjunctiva may
need to be sutured to the sclera well posterior to
the limbus as is done in the bare-sclera technique
of pterygium surgery.

We do not advocate conjunctivectomy with
recession as primary treatment of every case of
marginal corneal ulceration. That the procedure
is not a panacea is clearly demonstrated by its
failure in Case 8 above. Moreover, marginal
ulcers comprise a heterogeneous group of diseases,
and many cases respond well to other modes of
treatment. Some types are self-limited and do not
require specific or enthusiastic therapy. A clinical
classification of marginal ulcers, which we have
found to be useful, is given in the Table. The
superficial infiltrative ulcers are normally self-
limited or respond well to topical treatment with
antibiotics or corticosteroids. Corticosteroids are
generally effective for the non-infectious types of
dep deep infiltrative ulcers, whereas these drugs tend
to worsen most of the ulcers of the deep non-
infiltrative group, probably because of corticosteroid
enhancement of collagenase activity. It is this last
group that seems to respond best to the use of
collagenase inhibitors, but not invariably so, and
Mooren’s ulcer is notorious for frequently resisting
all medical treatment. The results of conjuncti-
vectomy appear to be encouraging for this deep
non-infiltrative group, but we have had no experi-

Table Typical clinical characteristics of
peripheral corneal ulcers*

<table>
<thead>
<tr>
<th>Ulcer</th>
<th>Infiltrative</th>
<th>Non-infiltrative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial</td>
<td>Phlyctenule, Catarrhal infiltrate, Trachoma pusule, Gold hypersensitvity</td>
<td>Vernal ulcer, Neurotrophic and exposure ulcer</td>
</tr>
<tr>
<td>Deep</td>
<td>Wegener granulomatosis, Polyarteritis nodosa, Ulcerative colitis, Gonorrhoea, Bacillary dyssentery, Psoriasis, Bacterial and fungal ulcers</td>
<td>Rheumatoid arthritis, Lupus erythematous, Diffuse systemic sclerosis, Mooren’s ulcer, Chemical burn, Erythema multiforme, Osular pemphigoid, Radiation, Rosacea, Vitamin A deficiency</td>
</tr>
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*Herpes simplex, varicella-zoster, and vaccinia infections are variable and can exhibit any of the above patterns
†Polyarteritis and psoriasis ulcers can occasionally be non-infiltrative
‡Gonorrhoea and other typically inflammatory diseases can become non-infiltrative after treatment with antibiotics or corticosteroids
§Although Mooren’s ulcer typically begins and progresses with mild, grey, corneal infiltration, the cellular response is unimpressive for the degree of ulceration.
**Rosacea and vitamin A deficiency ulcers can be infiltrative, particularly with secondary infection or microblephary.
ence with the procedure for the deep infiltrative group. Additional knowledge and experience are necessary before we shall know the true value, indications, and mechanisms of action of conjunctivectomy.

Summary
We report the rapid healing of several cases of marginal corneal ulceration of various aetiologies after the excision of a 4 to 7 mm strip of adjacent limbal conjunctiva. After conjunctivectomy the remaining conjunctiva was loosely recessed (without sutures). In one case with coexisting scleromalacia, we excised strips of adjacent bulbar conjunctiva with equally good results. Some of the cases had failed to respond to other modes of treatment including topical collagenase inhibitors.

One case responded to peritomy and cryotherapy to the ulcer edges, but we have abandoned this treatment in favour of conjunctival excision.

Limbal conjunctivectomy with recession is presumed to act by eliminating conjunctival sources of collagenase and proteoglycanase.

Addendum
Since this paper was submitted for publication, two additional papers concerning the histopathology and conjunctival proteolytic enzymes of Mooren’s ulcer and the use of conjunctival excision as treatment have been published (Brown, S. I. (1975), *Brit. J. Ophthal.*, 59, 670 and 675).

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