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Management of Recurrent Corneal Erosions: A Stepwise Approach

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Recurrent corneal erosions syndrome (RCES) is a common disorder characterized by recurring episodes of corneal epithelial breakdown.[1] Symptoms include pain, tearing or redness typically worse upon awakening or overnight during rapid eye movements (REM) sleep. Severe episodes can last for days, leading to epithelial defects and corneal scarring. Recurrences can be frequent and debilitating for patients. The aim of this review is to summarize the current medical and surgical methods available to treat RCES.

Etiology

The two most common causes of RCES are trauma and epithelial basement membrane dystrophy (EBMD) **(Figure 1).**[2] Within the trauma group, fingernail trauma is the most common. Other frequent modalities of trauma include those from paper, tree branch and mascara brush injuries. Other predisposing factors include corneal dystrophies such as lattice and Reis-Bücklers dystrophy, dry eye, meibomian gland disease, rosacea, and diabetes.[2]

The mechanism likely involves abnormal hemidesmosomes and anchoring filaments, leading to poor adhesion of corneal epithelium to the underlying stroma.[1] Epithelial trauma results in defective adhesion complex formation, while EBMD is characterized by an abnormal and multilaminar basement membrane that leads to poor adhesion. Patients with RCES, especially those with meibomian gland disease and rosacea, have also been found

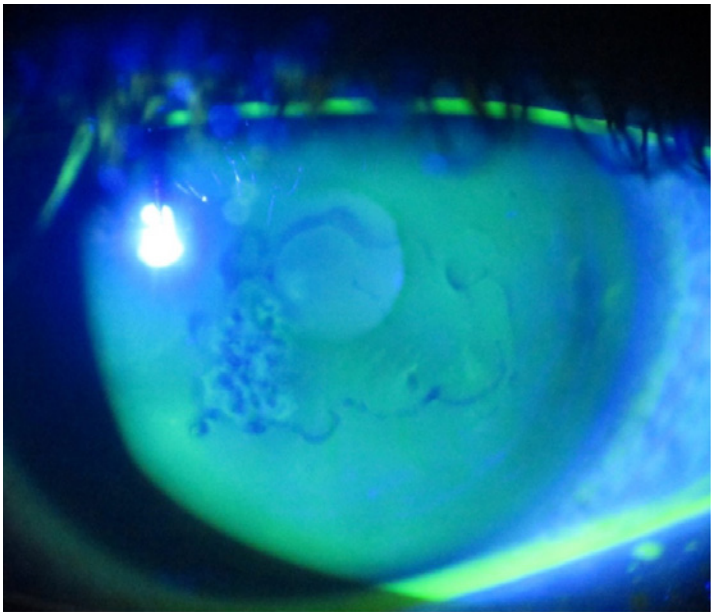

Figure 1. Slit lamp photograph demonstrating negative staining in epithelial basement membrane dystrophy; courtesy of Dr. Clara C. Chan.

to have higher levels of matrix metalloproteinases (MMPs) in tear fluid, which promotes cleavage of collagen and adhesion proteins.[3] In addition, dry eye may contribute to RCES by increasing adhesion between the lids and corneal epithelium. The shearing forces from rapid opening of the eyelid can lead to corneal erosions.

Medical Treatment

There is a wide range of treatment options available; treatment can be approached in a stepwise fashion with the objective of improving epithelial and basement membrane adhesions. Most patients can be managed initially with medical therapy **(Figure 2).**

First-line treatment includes lubrication and the application of nightly ointment. The choice of additional treatment depends on patient preferences while targeting the underlying ocular comorbidities such as dry eyes and meibomian gland dysfunction (MGD).

Acute period

Typically, patients presenting with an acute erosion are initially treated with antibiotic ointment/drops and artificial tears. Depending on the severity of the episode, patching, bandage contact lenses (BCLs) or cycloplegic eye drops can be added for comfort. A BCL acts as a mechanical barrier from the debridement action of the eyelid and provides a scaffold for healing. A prophylactic antibiotic is subsequently added to prevent microbial keratitis.

Chronic period

Lubrication and hypertonic saline

Lubrication with preservative-free artificial tears and lubricating ointment at nighttime is first-line treatment. Ointment at nighttime helps to prevent the eyelid from adhering to the corneal epithelium. A hypertonic saline ointment can also be used, which reduces epithelial edema and promotes epithelial adherence.[1] This protocol is typically continued for 6-12 months to allow the adhesion complexes to rebuild.

MMP inhibitors

Oral tetracycline and topical steroids inhibit MMP, which is thought to be involved in the cleavage of

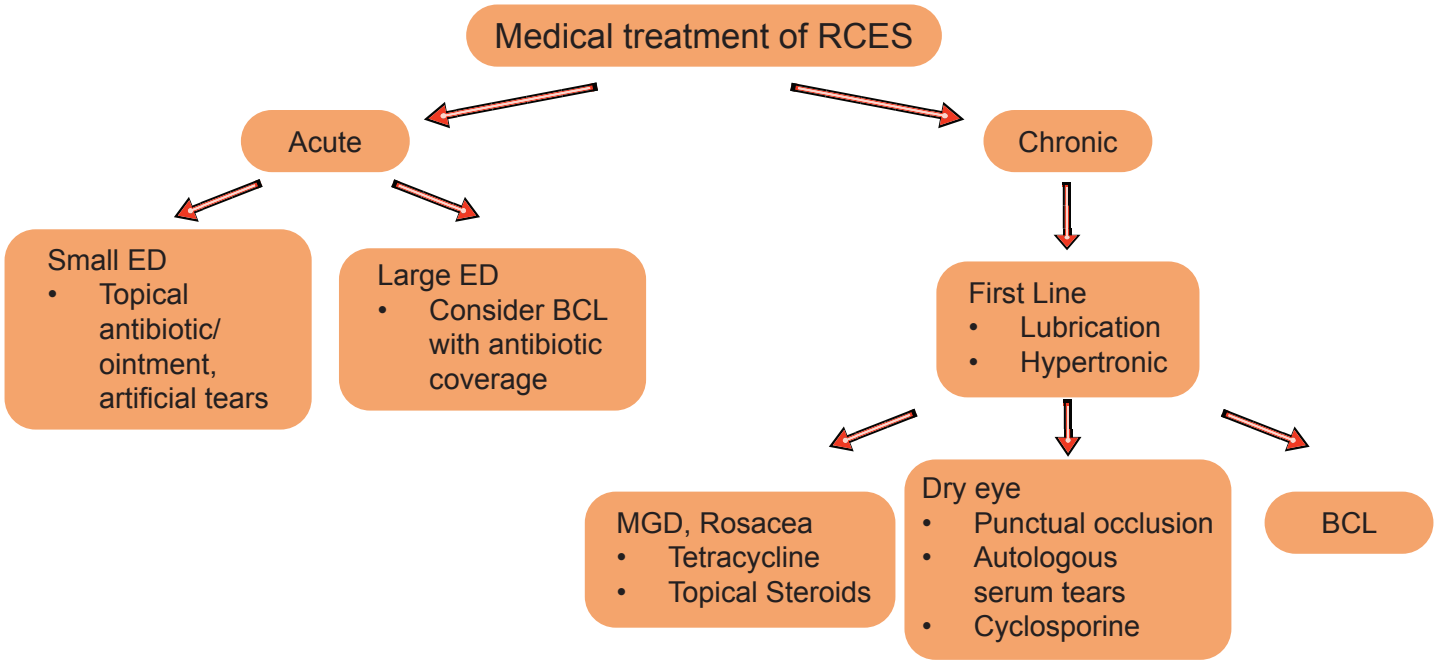

Figure 2. Medical treatment options for recurrent corneal erosion syndrome (RCES); courtesy of Yelin Yang, MD
RCES= recurrent corneal erosions syndrome; ED= epithelial debridement; BCL= bandage contact lenses; MGD= meibomian gland dysfunction

adhesion proteins. A combination of doxycycline 50 mg twice daily for 2 months and topical steroid used three times daily for 2-4 weeks was found to be effective in eyes with recalcitrant recurrent erosions.[4,5] Doxycycline may be particularly beneficial in patients with MGD and ocular rosacea as it inhibits lipase production. Patients with these conditions tend to accumulate higher levels than normal of lipases from colonizing bacteria; this creates toxic free fatty acids that negatively impact epithelial membrane healing.[5] Associated blepharitis should also be treated with lid hygiene and warm compresses.

Punctal occlusion

Punctal occlusion may be useful in patients with chronic dry eye where lubrication alone is insufficient. This increases the tear lake and may promote more rapid healing.[1]

Serum tears

Autologous serum tears contain proteins such as fibronectin, epidermal growth factor and Vitamin A, which promote epithelial migration and anchorage.[6] They have been used in patients failing conventional therapy such as lubrication, hypertonic solution, anterior stromal puncture (ASP), and BCL.[6,7] They are typically administered for 3-6 months, at a dose of 4-6 times daily with a tapering course. Clinical studies have demonstrated favourable results, with a reduction from 2.2 recurrences per month pre-treatment to 0.028 recurrences per month post-treatment.[7] Long-term clinical studies have reported a recurrence rate of 15% over a follow-up period of 12 months.[6]

Topical cyclosporine

Topical cyclosporine can be helpful in patients with chronic dry eye by improving tear film quality and goblet cell numbers, thereby reducing the mechanical friction that can lead to erosions. It has been used in patients with refractory RCES and persistent epithelial defects in a small case series.[8]

BCL

In addition to treating large erosions in the acute period of RCES, a BCL maybe be applied for an extended period of time for up to 3 months. The lens should have a flat base curve and high oxygen permeability.[1] Clinical study results are varied, with some studies reporting favourable results. Conversely, a randomized clinical trial demonstrated no results difference between topical lubricants and extended wear BCLs.[9,10] BCLs are more likely to be helpful in patients with evidence of active erosions with fluorescein staining, without significant MGD or ocular rosacea. Close follow-up is important due to the risk of microbial keratitis, and coverage with topical antibiotic is indicated. The percentage of basal cell membrane occupied by hemidesmosomes has been shown to increase for 6 weeks before stabilizing. As a result, it has been suggested that a minimum of 6 weeks of BCL wear is recommended to allow sufficient epithelial basement membrane remodelling.[9]

Surgical Treatment

Various surgical options are available for patients who fail conservative therapy **(Table 1).** It has been estimated that approximately 50% of patients with RCES may require surgical intervention.[2]

ASP is a procedure that can be performed in office. A bent 25- or 27-gauge needle is used to make superficial punctures through the Bowman's layer approximately 0.5 mm apart **(Figure 3).** The superficial punctures are thought to promote formation of firmer adhesions between the epithelium and basement membranes.[1] ASP tends to be used for peripheral lesions not involving the central visual axis as it can induce scarring if performed overly aggressively. Previous clinical studies have reported recurrence rates between 17% and 40% following ASP alone.[2,11] ASP can be combined with epithelial debridement to reduce recurrence. When combined, a recurrence rate of approximately 29% has been reported at mean follow up of 1.4 years.[12]

In epithelial debridement (ED), loose epithelium is removed to promote healing from the healthy edge.[13,14] It is typically removed with a rounded blade; subsequently, a BCL is put in place to promote re-epithelialization with topical antibiotic coverage. This is helpful for cases with loose epithelium that is freely mobile. However, ED as monotherapy has a high recurrence rate as it does not address the abnormal basement membrane, and typically it is insufficient for dystrophic cases presenting with RCES.

To reduce recurrence, ED can be combined with diamond burr polishing. Diamond burr is applied to the debrided area for approximately 10 seconds to gently polish the Bowman's membrane. This creates a slightly rough surface to which the new epithelium can adhere and may lead to more rapid re-epithelialization.[15] In addition, the polishing may stimulate reactive fibrosis, which allows stronger

Surgical treatment	Advantages	Disadvantages	Recurrence rate
ASP (can be combined with ED)	In-office, low cost	Leaves scar, avoid lesions in visual axis	17%-40%[2,11,12]
Epithelial debridement	Low cost	Not sufficient for dystrophy	18%-56%[2,15]
Epithelial debridement + Diamond burr polishing	Lower recurrence	Higher risk of haze	4%-25%[2,16,17]
Epithelial debridement + Alcohol delamination	Low cost, lower recurrence	Risk of toxicity, newer technique	8%-26%[18,19]
PTK	Lower recurrence	Cost, laser required Higher risk of haze Refractive shift	10%-36%[21-23]

Table 1. Surgical treatment options for recurrent corneal erosion syndrome (RCES); courtesy of Yelin Yang, MD
ASP= anterior stromal puncture ; PTK= phototherapeutic keratectomy

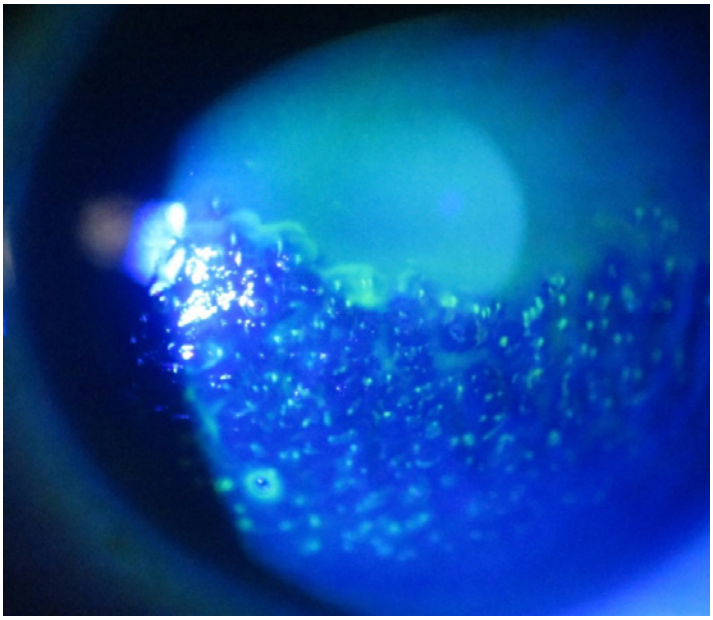

Figure 3. Slit lamp photograph demonstrating superficial punctures in anterior stromal puncture; courtesy of Dr. Clara C. Chan.

adhesion of the epithelium to the stroma. Clinical studies have reported recurrence rates following diamond burr polishing at between 4% and 25%.[2,15,16] However, vigorous polishing is not recommended as it can damage the Bowman's layer and cause reactive scarring.[1] Risk of corneal haze has been reported in up to 40% of cases following diamond burr polishing.[15] However, the majority of cases are mild and improve over time, with only 4% demonstrating persistent haze at 6 months.[15] Caution should be exercised when performing this procedure and only a large diameter brush should be used to avoid irregular astigmatism or excessive stromal thinning.

Alcohol delamination is a technique that is thought to create a smooth epithelial surface for healing and facilitate epithelial attachment.[17] Twenty percent alcohol is applied to the epithelium for approximately 40 seconds, followed by copious irrigation and removal of the epithelium.[17] Small clinical studies suggest that the recurrence rate with alcohol delamination is 8%-26%.[17,18] However, there is a risk of toxicity with the use of alcohol, along with reduced viability of the epithelial cells, and greater inflammatory markers have been demonstrated in *in vitro* studies.[19] Additional long-term clinical studies are needed to validate this technique.

In phototherapeutic keratectomy (PTK), excimer laser removes the Bowman's layer and outer 5-10 μm of stroma to create a smooth surface. This allows the epithelium to regrow with a stronger attachment, and new basement membranes/ hemidesmosomes have been shown to form within 2 weeks.[13] The recurrence rate with PTK is comparable to that of diamond burr polishing, reported at between 11% and 36%.[20-22] Deeper ablations can be associated with corneal haze and refractive shift.[13] Lower energy, a larger treatment zone and slight hyperopic treatment can be used to minimize the refractive shift.

Comparison between surgical treatments

Decision-making regarding the type of intervention to use is multifactorial, involving considerations of risks, costs, equipment availability, surgeon preferences, and the nature of the pathology. For peripheral lesions not involving the visual axis, ASP can be attempted. For erosions involving the central cornea, ED combined with diamond burr, alcohol delamination, or PTK can be performed with low rates of recurrence. In comparison, PTK involves the use of a laser and may be less accessible due to its cost.

Conclusion

RCES is a challenging condition that can have significant impact on patient quality of life. There are multiple treatment options available. Topical lubrication and nightly ointment are first-line treatments, while additional medical treatments such as MMP inhibitors, BCLs and cyclosporine can be used for patients with underlying ocular comorbidities or those wishing to delay surgical intervention. The optimal approach to surgical treatment is to tailor it to the patient, bearing in mind the nature of the pathology, risks of the procedure, costs and facilities available. With appropriate therapy, most patients can achieve long-term resolution.

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