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Case report
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Serum eye drops in treating recurrent corneal erosion syndrome

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Abstract

Background: Persistent recurrent corneal erosion syndrome (RCES) was successfully treated with plasma eye drops in a district hospital in Malaysia.
Case presentation: We report a case of a woman who presented with recurrent right eye pain and redness post trauma. She exhibited a chronic persistent epithelial defect despite multiple treatment modalities offered, which included medical and surgical intervention. She was initially treated with vigorous artificial tears, bandage contact lens application, and epithelial debridement; however, symptoms recurred. Significant improvement was seen 1 month after initiation of autologous serum eye drops and complete resolution was achieved following completion of this regime. No recurrence of symptoms was reported at 1 year after treatment completion.
Conclusion: The use of serum eye drops was shown to be effective in treating RCES.

Keywords: recurrent corneal erosion syndrome, serum eye drops

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Ubat titis mata serum dalam merawat sindrom hakisan kornea berulang

Abstrak

Latar belakang: Sindrom hakisan kornea berulang yang berterusan telah berjaya dirawat menggunakan ubat titis mata serum di sebuah hospital daerah di Malaysia.
Kes: Kami melaporkan satu kes pesakit yang mengalami gejala kesakitan mata kanan secara berulang dan kemerahan selepas trauma. Pemeriksaan menunjukkan kecacatan epitelium kronik yang berterusan walaupun pelbagai kaedah rawatan ditawarkan, termasuk rawatan perubatan dan pembedahan. Rawatan awal termasuklah penggunaan ubat titis mata buatan secara intensif, pemakaian kanta sentuh pembalut dan debridmen epitelium; namun gejala berulang. Peningkatan ketara dilihat satu bulan selepas rawatan menggunakan titisan mata serum autologous dimulakan, dan resolusi lengkap dicapai selepas selesai rejimnya. Tiada gejala berulang dilaporkan satu tahun selepas rawatan selesai.
Konklusi: Penggunaan titisan mata serum menunjukkan keberkesanan dalam merawat sindrom hakisan kornea berulang.

Kata kunci: sindrom hakisan kornea berulang, titisan mata serum

Introduction

Recurrent corneal erosion syndrome (RCES) is a common disorder worldwide first described in 1872 by Hansen as "intermittent neuralgic vesicular keratitis". It was later recognized as "recurrent erosion of the cornea" by Von Arlt in 1874 and was subsequently termed RCES in the current ophthalmic literature.[1] It is a chronic, relapsing, and debilitating condition characterised by recurrent episodes of pain, photophobia, watering, and blurred vision. It occurs due to poor adhesion of the corneal epithelium to its basement membrane.[2] Trauma is the most common factor, accounting for over half of the cases.[3] Of the cases reported, 87% involve the inferior third of the cornea.[3] RCES remains one of the most challenging conditions to manage despite advancements in corneal science. Most studies reported that recurrences occur during awakening or the rapid eye movement sleep phase.[4] The presence of superficial epithelial oedema from trauma may lead to poor epithelial adhesion. Hence, the opening of the eyelid or rapid eye movement produces a shearing force on the cornea epithelium, causing erosion.

Treatment options offered may range from simple conservative treatment to complex surgical intervention. Traditional measures include antibiotic eye drops,

vigorous preservative-free topical lubricants, cycloplegics, and oral analgesics to ease the pain. Using bandage contact lenses (BCL) may be beneficial as an adjunct to pharmacological therapies. Newer therapies include oral matrix metalloproteinase inhibitors, serum eye drops (SEDs), amniotic membrane grafts, and topical corticosteroids.[5] The reported use of SEDs for the treatment of persistent epithelial defects led us to consider its possible application in our patient, who presented with RCES despite undergoing multiple treatment modalities.

Case report

A 24-year-old woman who had multiple clinic visits presented to us with a complaint of eye pain and redness in the right eye for 3 days. She had a history of being hit by the edge of a car door on the side of her right eye before showing initial symptoms. At presentation, her best-corrected visual acuity (BCVA) was 6/12 in the right eye and 6/6 in the left eye. Slit lamp examination revealed a corneal epithelial defect with rough edges measuring 3 mm x 1.8 mm with fluorescein staining uptake in

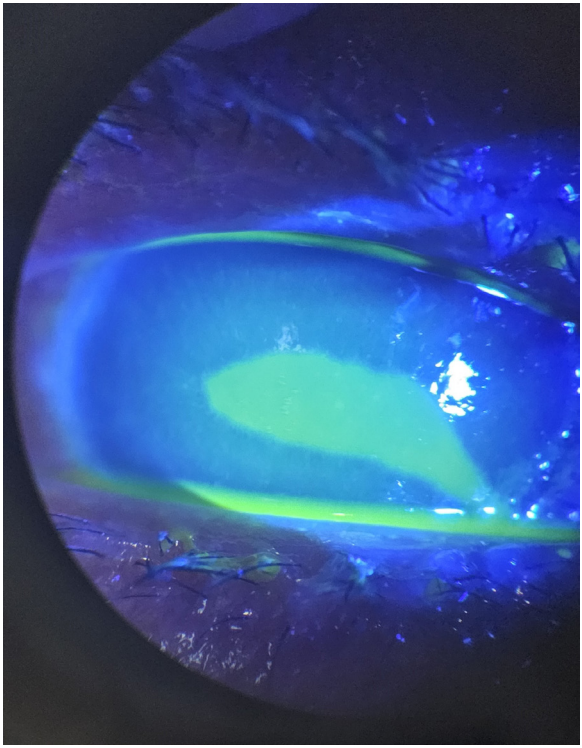

Fig. 1. Inferior epithelial defect.

the inferior region of the corneal surface, not involving the visual axis (Fig. 1). The anterior chamber was deep and quiet. Fundus was normal. Examination of the left eye revealed no significant findings. She had corneal epithelium debridement done twice; however, her condition did not improve. Therefore, the patient was treated as a case of RCES secondary to trauma.

The patient was given options for autologous SEDs treatment, and the procedures were explained. On follow-up 2 weeks after initiating of SEDs, her symptoms had improved. BCVA had improved to 6/7.5 in the right eye. Slit-lamp examination showed no epithelial defect (Fig. 2), with negative staining uptake (Fig. 3). SEDs application was continued every 2 hours for 2 months together

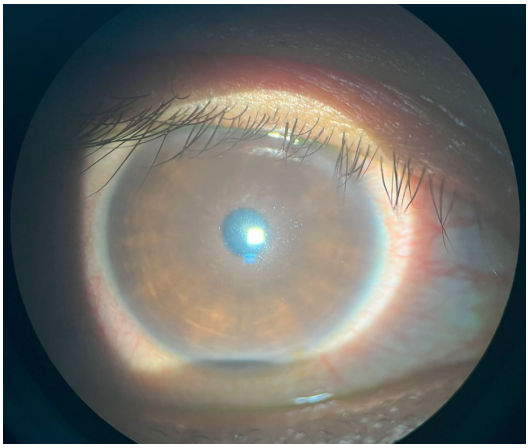

Fig. 2. Healed epithelial defect 2 weeks after treatment initiation of serum eye drops.

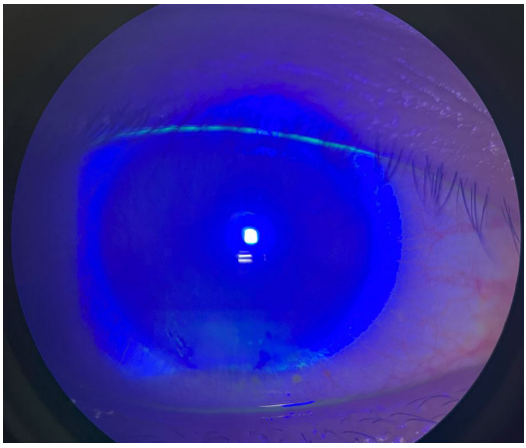

Fig. 3. Healed epithelial defect 2 weeks after treatment initiation of serum eye drops with negative fluorescent staining.

with a bandage contact lens. After 2 months, the regimen was tapered to 4 times daily for another 4 months. Upon reviewing the patient's condition 1 month after treatment initiation, her BCVA was 6/6 in the right eye, and symptoms had completely resolved. At the 1-year follow-up, she no longer had symptoms of RCES 1 year after completion of the 6-month treatment regime.

Discussion

Autologous serum was first introduced in 1975 by Ralph *et al.* to treat the ocular surface of patients with chemical burns using a mobile ocular perfusion pump.[6] Since then, it has been widely used to treat ocular surface diseases, including dry eye disease, Sjogren syndrome, persistent epithelial defects, exposure keratitis, recurrent corneal erosion, and Stevens-Johnson syndrome. Studies have documented that using blood-derived products has proven effective in treating corneal epithelial conditions. The effects of blood-derived products on the proliferation, vitality, and migration of corneal epithelial cells have been well-documented in both in-vitro and in-vivo experimental studies for the past few decades.[7]

Apart from supplementing the lack of tears, autologous SEDs also contain epitheliotropic factors that are essential for the restoration of damaged corneal epithelium, namely epidermal growth factor, transforming growth factor-beta1 (TGF-β), fibronectin, and platelet-derived growth factor-AB.[8] The presence of epitheliotropic factors, which are similar to those present in natural tears, makes it superior to lubricant eye drops.[9] The abundance of epitheliotropic growth factors aids in strengthening the epithelial adhesion complex, which is crucial to wound healing in the corneal epithelium. Based on these studies, the use of plasma eye drops was considered in our patient, who presented with a persistent epithelial defect despite being treated with both conservative and surgical methods.

SEDs are processed from whole blood through a centrifugation method. It can be obtained from the patient's blood (autologous) or donor blood (allogenic). At first, our patient used autologous SEDs. However, during the subsequent venesection, she experienced an episode of vasovagal syncope, and the procedure was abandoned. We then resorted to allogenic SEDs as an alternative. A pilot double-blind, randomised, crossover trial comparing autologous and allogeneic SEDs found no difference in efficacy.[10] Allogenic SEDs are assumed to be as effective as autologous SEDs in treating severe dry eye. We concur with this, as our patient reported improving symptoms using allogeneic SEDs. Lomas *et al.* found that treatment with both autologous and allogenic SED leads to a significant reduction in symptom severity based on the Ocular Surface Disease Index (OSDI) score. There was no statistically significant difference in OSDI score reduction between patients receiving autologous and allogenic SEDs.[11]

Tsubota *et al.* classified the efficacy of SEDs based on the time it took for epithelial defects to heal. SEDs were considered effective if the defect healed within 2 weeks, partially effective if healing was achieved in 1 month, and ineffective beyond 1 month. Based on the study, it was concluded that 43% of the total cases achieved complete resolution of the epithelial defect within 2 weeks, and 18% of cases resolved in 1 month. One-third failed to respond within the required duration.[12] Treatment with SEDs in our patient was considered effective as the epithelial defect had healed at the 2-week follow-up.

The dilution of SEDs also plays an essential role in determining its efficacy. Lekhanot *et al.* found undiluted SEDs to be more effective compared to diluted ones.[13] The rationale for diluting SEDs is to decrease the concentration of TGF-β in serum to a level equivalent to natural tears, as high TGF-β concentrations may possibly retard corneal epithelium healing, although there is no proven data. In our patient, undiluted serum eye drops were used since we believed that 100% serum eye drops would provide a higher concentration of growth factors and reduce the risk of contamination due to less serum manipulation. The major setbacks of using undiluted SEDs are the inconvenience of repeated venesection, a large volume of blood collection, and potential ocular irritation associated with the high viscosity of the eye drops. Regarding our patient, although undiluted 100% serum was used, there was no reported ocular discomfort or irritation.

We found no studies have determined SED therapy's optimal frequency and duration. The duration of treatment in studies ranges from 2 weeks to 6 months, which often coincides with the study duration.[14] No clear evidence suggests that more frequent instillation improves symptoms and clinical findings. The frequency and duration of treatment may vary depending on individual circumstances. Given its proximity to our case, we followed Lee *et al.*'s treatment regimen of 1 eye drop every 2 hours for 2 months, subsequently reduced to 4 times daily for the remaining 4 months, for a total duration of 6 months.[15] Another study by *Ziakas et al.* stated that a 6-month treatment regime was sufficient to keep patients symptom-free for at least 2.5 years.[16]

While effective in treating severe dry eye symptoms, SEDs have few limitations. Logistically, collecting blood and processing it into SEDs may result in a considerable waiting time for the patient. Additionally, patient-related factors such as poor venous access, low haemoglobin level, and fear of needles may become obstacles to collecting sufficient blood for autologous SEDs.[10] Meanwhile, allogenic SEDs might carry the risk of blood-borne disease transmission. Hence, all blood donations were tested for blood-borne diseases before processing into SEDs. Another primary safety consideration for SEDs is the risk of microbial growth during storage, as serum-based solutions are good growth media.[17] Microbial contamination remains a considerable risk in patients with compromised ocular surfaces.

Conclusion

In conclusion, blood-derived eye drops represent an exciting option for treating ocular surface disease. Our case highlights that using either autologous or allogenic SEDs proved very effective in treating RCES by resolving all symptoms in our patient at the 1-year follow-up. However, there is a clear need for a more detailed perspective involving larger studies with a more extended follow-up period to confirm our findings. Standardised treatment guidelines are needed to provide better evidence and implementation into daily clinical practice.

Declarations

Consent for publication
Informed consent was obtained from the patient to publish the data and images in this case report.

Competing interests
None to declare

Funding
None to declare.

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