Cultivated oral mucosal epithelial transplantation (COMET) andpenetrating keratoplasty in long-standing severe ocular surface injury

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SUMMARY

Ocular chemical injury is a true ophthalmic emergency requiring immediate medical intervention. Damages can be devastating and potentially resulting in blindness, corneal perforation and phthisis bulbi. We describe here a successful treatment outcome in a patient who sustained Roper-Hall Grade 4 injury to both eyes. Patient received medical therapy followed by serial ocular surgeries with eventual visual recovery in one eye from counting finger to 6/15 after a decade. In conclusion, after maximum medical therapy, a carefully planned serial surgeries of cultivated oral mucosal epithelial transplantation (COMET) and PK has proven beneficial for this patient with advanced limbal stem cell deficiency (LSCD).

INTRODUCTION

Ocular chemical injuries account for 11.5-22.1% of ocular traumas resulting in a substantial number of industrial-related ocular disabilities.[1] They cause serious ocular injuries due to their devastating effects which include persistent epithelial defects, corneal melting and scarring, limbal stem cell deficiency (LSCD), and secondary glaucoma. Chemical injuries cause destruction of cells, denaturation of tissues, and release of inflammatory mediators and proteolytic enzymes. The goals of therapy after such injuries include removal of the damaging agents, normalising the ocular surface pH, re-establishing corneal clarity, and preventing glaucoma.[2]

Besides the cornea, chemical injury can damage limbal stem cells and conjunctiva which are essential for corneal epithelial regeneration and maintaining the integrity of the ocular surface. Deficiencies in the above integrity manifest as epithelial defects, chronic inflammation, keratitis, vascularisation and fibrosis, all of which may ultimately result in blindness.

We report a case of a man who was blinded for more than 10 years by an extensive ocular chemical injury. He was treated with developing techniques and eventually his vision was satisfactorily recovered.

CASE REPORT

A 53-year-old man was referred to the eye clinic of Hospital Kuala Lumpur in July 2003 from a district hospital, three months after an industrial accident where a tank filled with alkaline soda exploded and splashed onto him and injuring both his eyes. He received immediate standard treatment and was admitted at the district hospital. When his burn injuries improved, he was referred to our tertiary centre for further management. On presentation at our facility, he had sustained 50% total body surface chemical burns and his vision was hand movement OD and counting fingers OS. Slit lamp examination revealed bilateral grade IV Roper-Hall[3] chemical injuries (Table I) with large corneal epithelial defects, diffuse corneal opacities, and 360° limbal-corneal vascularisation with severe limbal ischaemia. The patient had also developed secondary glaucoma and a fibrovascular cataractous lens in his right eye.

Despite maximum medical treatment, his right eye deteriorated to absolute blindness and subsequently became phthisical (Figure 1). His left eye had multiple recurring epithelial defects with a dense stromal scar covering two third of the cornea, inferior stromal thinning, 360° pannus with superficial corneal vascularisation, and his visual acuity remained at counting fingers (Figure 2A). At time, surgical intervention was not considered due to limited resources for epithelial transplantation and marked LSCD to sustain a corneal graft. The patient was followed-up regularly every four months to optimise his ocular surface condition. Ten years after the initial accident, with developing technology and newer facilities, a buccal mucosa biopsy was performed for trial of cell growth on de-epithelialised human amniotic membrane, which was then sent to the microbiology laboratory. When there was promising epithelial growth on the first culture, a second buccal mucosa specimen was obtained, washed with antibiotics, cut into smaller pieces and cultivated on a de-epithelialised amniotic membrane in an incubator for four weeks. When the culture was ready, the patient underwent left eye cultivated oral mucosal epithelial transplantation (COMET), along with an amniotic membrane transplantation (AMT). He was kept on tapering dose of topical dexamethasone 0.1% and antibiotic, preservative-free artificial tears, oral Doxycycline and oral Vitamin C for almost a year. The eye exhibited good uptake and response to the epithelial transplant, with reduced corneal vascularisation and healthier epithelial surface (Figure 2B). Ten months later, when there were no signs of stem cell failure, the patient had a left eye subconjunctival Ranibizumab 0.5 mg injection, followed by penetrating keratoplasty (PK) with cataract extraction and intraocular lens implantation (Figure 2C). Post corneal transplant, he

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Table I: Roper-Hall3 classification of severity of ocular surface burns

Grade	Conjunctiva/ Limbus	Corneal involvement	Prognosis
I	No limbal ischemia	Epithelial damage	Good
II	<1/3 limbal ischemia Iris details visible	Corneal haze	Good
II	1/3 to ½ limbal ischemia Stromal haze Iris details obscured	Total epithelial loss	Guarded
IV	>½ limbal ischemia Iris and pupil obscured	Cornea opaque	Poor

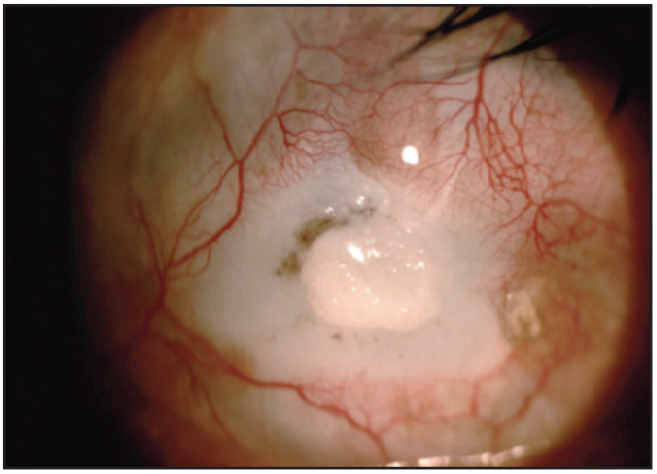

Fig. 1: Right eye phthisis bulbi.

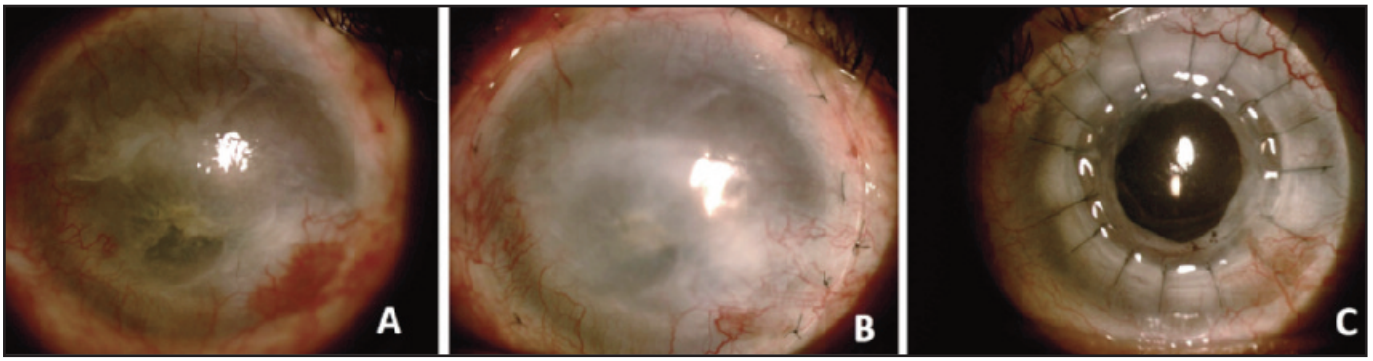

Fig. 2: A. Left eye prior to surgery with recurrent epithelial defect, 360o superficial corneal vascularisation, and diffuse corneal scarring. B. Left eye post COMET and AMT surgery with resolved epithelial defect, reduced superficial corneal vascularisation and dense corneal scaring. C. Left eye post penetrating keratoplasty and cataract extraction with IOL implant.

was on tapering dose of oral prednisolone over three months and kept on oral tacrolimus 1g daily for one year. One year postoperatively, for the first time after a decade, the patient obtained a best corrected visual acuity of 6/15 OS with N6 at near and no signs of graft rejection or failure.

DISCUSSION

Alkaline agents are lipophilic and cause saponification of fatty acids of cell membranes, therefore penetrating tissue deeper and rapidly compared to acidic agents. When a chemical injury destroys the limbal stem cells, the eye will react with conjunctivalisation, vascularisation, chronic inflammation, recurrent epithelial defects, and loss of corneal transparency.[4] Alkali substances can penetrate into the anterior chamber causing inflammation, cataract formation, and damage to the trabecular meshwork inducing glaucoma. In cases with recurrent epithelial defect, methods of treatment other than immediate corneal transplantation, include epithelial transplantation. There are many modalities of epithelial transplants, including conjunctival-limbal autografts, conjunctival-limbal allografts and kerato-limbal allografts which are conventional surgeries.[2] These methods were not applied in this case because there was

insufficient viable limbal cells salvageable from the other damaged eye and cadaveric allograft was not practise in our centre. Therefore, newer alternative method such as COMET on an amniotic membrane carrier was a better option. The advantage of ex-vivo cultivation over conventional methods is that only a small sample biopsy is needed. The cultivated membrane is larger and therefore maximising the surface coverage. AMT is an effective adjunctive treatment to support epithelial healing and restore ocular surface integrity with potential to improve vision.[1] PK after COMET is a proven successful procedure which can be used to restore visual function in cases of total LSCD associated with severe stromal opacity due to chemical burns. Limitation of this procedure is the requirement to delay surgical intervention in an inflamed eye. Patient was required to be on a long duration of topical and oral immunosuppression prior and post-operatively to improve surgical success rate.[5]

Severe ocular surface chemical injuries are a challenge to treat because the course of healing varies with duration, often taking months and in this patient years. To our knowledge, successful treatment with COMET and PK is rarely reported in Malaysia. We believe such method is useful in dense stromal scar with advanced LSCD, but further studies are warranted.

CONCLUSION

Ocular chemical injuries are uncommon. Treatment of ocular chemical injury needs to be meticulous. In this case, a timely series of ocular surgeries including COMET with AMT, PK and medical optimisation proved beneficial for this patient who was legally blind for more than a decade after sustaining severe ocular surface injury with advanced LSCD.

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