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Long-term follow up of oral mucosa autograft sutured to the sclera in severe symblepharon

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ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> Mucous graft Chemical burn Symblepharon	Purpose: To evaluate the clinical outcomes and complications of oral mucosa autograft (OMAU) sutured to the sclera to treat symblepharon after severe chemical or fireworks burn. Methods: Our surgical technique for OMAU sutured to the sclera is presented along with clinical data and outcomes of 7 symblepharon carriers. Our surgical technique was performed unilateral in all cases. An OMAU with a mean length of 3 cm and 2 cm wide was sutured to the bare sclera 1–3 mm behind the limbus. Amniotic membrane transplant was placed covering the rectus muscles and bare sclera proximal to the limbus. The fornix was secured into the skin with deepening bolster sutures. A temporary tarsorrhaphy was performed, and a symblepharon ring was placed on top of a bandage contact lens. Results: There were no cases of intraoperative complications. Three years postoperatively, all patients had perfect integration of the OMAU and there were no cases of symblepharon's recurrence. Two patients developed mild superior entropion and 2 patients developed mild strabismus (one esotropia and another exotropia). Conclusion and Importance: OMAU sutured to the sclera after symblepharon release caused by severe ocular burns, results in excellent cosmetic and anatomical outcomes with no recurrence.

1. Introduction

Symblepharon is defined as adhesions between the palpebral and the bulbar conjunctiva and can result from several conditions as conjunctival chronic inflammatory diseases (ocular cicatricial pemphigoid, Steven-Johnson), trauma, infections or burns (chemical or thermal). The adhesions can occur in small areas or obliterating the entire fornix, deforming the position of the lids, leading the eyelashes to touch the ocular surface. Despite the etiology, association has also been reported between symblepharon with ocular dryness and limbal stem cell deficiency (LSCD).¹

Although symblepharon is easily diagnosed, treatment remains challenging and currently, there is no standardized surgical treatment for symblepharon. Usually the treatment involves symblepharon lysis and a conjunctival autograft,^{1,2,3} oral mucosa autograft (OMAU),^{2,4–6} nasal mucosa autograft,^{7,8} OMAU associated or no to the skin graft,^{9,10} amniotic membrane transplant (AMT),^{3,11–14} keratolimbal allograft,¹⁵ ex vivo cultivated cadaveric limbal allograft,¹⁶ or combining different

techniques. Currently, there is no standardized surgical treatment for symblepharon.

The aim of the present study is to present our technique to treat severe symblepharon using OMAU sutured to the bare sclera, and evaluate the clinical outcomes and complications.

2. Materials and methods

This retrospective case series evaluated the outcomes and complications of a surgical technique for symblepharon using OMAU. The study was approved by the Institutional Review Board of the King Khaled Eye Specialist Hospital, Riyadh, Kingdom of Saudi Arabia; and adhered to the principles of the Declaration of Helsinki. Six eyes with mainly inferior symblepharon and one eye with superior symblepharon were included. All eyes were severe cases caused by chemical or fireworks burns and treated using a technique of symblepharon release and interposing OMAU sutured to the bare sclera. Only severe cases of chemical or fireworks burns were included. Data was retrieved from

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electronic medical records. Data was collected on patient demographics, laterality of the symblepharon, eye conditions, symblepharon etiology complications and outcome after surgery. Severity of the symblepharon was grading following the Kheirkhah scale³ and LSCD following the global consensus.¹⁷

2.1. Surgical technique

All eyes underwent the surgical procedure by one surgeon (HMO). Surgeries were performed under general anesthesia. The symblepharon was released from the affected areas starting from the limbus, using 6900 blade (Miniature Blade Round Tip, Surgistar, USA) and Westcott scissors. All adherences sites and tenon capsule were removed until reaching the fornix. The extraocular muscles were identified and exposed using 4-0 Silk to guarantee no damage, remaining surrounding fibrous tissue were removed. Then, the bare area requiring the graft was measured. The graft was prepared to be 20% larger than the recipient area to address possible contraction. The buccal donor area was the inferior lip. After surgical field was prepared with Povidone-iodine Topical Solution 10%, submucous Xylocaine 2% with adrenaline 1:200000 was injected to decrease bleeding and facilitate the dissection of the mucous from the subside tissues. A retractor clamp specially designed for the procedure was used for better exposure of the donor area. A full-thickness OMAU in an elliptical fashion distant 1 cm from the red portion of the inferior lip using a number 15 blade and scissors was excised. After removal, the donor area was sutured using 4-0 Vycril in uninterrupted sutures. Minor salivary glands and submucous fat were removed from the internal surface of the OMAU, then mild trimming was performed with scissors. OMAU was preserved in BSS until was grafted. AMT was placed over the bare sclera covering the rectus muscles, then was sutured using 9-0 Vycril in interrupted sutures. The OMAU with the epithelium face up was sutured to the bare sclera 1-3 mm behind the limbus with a mean length of 3×2 cm using uninterrupted Vycril 8-0 sutures. The deepest fornix was anchoring to the skin with Nylon 6-0 and bolsters. The gap between the OMAU and the deepest fornix was also sutured with 8-0 Vycril. AMT filled also the gap adjacent to the limbus, covering the cornea and secured with interrupted 9-0 Vycril. A bandage contact lens (BCL) was adapted over the cornea and a symblepharon ring was placed above all. A temporary tarsorrhaphy was performed on the lid margin with 6-0 nylon (see Surgical Video of patient 1, Supplemental Digital Content 1).

Supplementary video related to this article can be found at htt ps://doi.org/10.1016/j.ajoc.2021.101099

2.2. Postoperative medication and follow up

Neomycin/polymyxin/dexamethasone drops (Alcon, USA) tapering for 1 month, then Loteprednol etabonate drops (Bausch Lomb, USA) for 3 months on a tapered schedule were prescribed. Preoperative inflammation was also controlled during 3 months prior to surgery with Loteprednol etabonate drops. The tarsorrhaphy was removed 3–5 days after surgery. The symblepharon ring, BCL and bolsters were removed after 2 weeks. Slit lamp examination was performed at 7, 30, 90, 180 days, 1, 2 and 3 years postoperatively.

2.3. Outcomes

Surgery was considered as a complete success when the anatomical depth of the fornix was restored and no further surgery was required for symblepharon correction. Excellent integration was defined as restoration of a smooth ocular surface with no gaps between the surrounding conjunctiva and the OMAU.

3. Results

The patients were between 6 and 56 years old, six patients had

unilateral burns (4 chemical burns and 2 fireworks induced burns) and one patient sustained bilateral chemical burn. One patient did not have previous surgery (patient 6). Four patients had undergone symblepharon release with AMT. Two other patients had undergone 5 previous surgeries. Symblepharon severity was classified as IIIc 2+ in all cases except patient 2 (IIc 2+). Inferior fornix was affected in all patients except patient 7 who had a superior fornix injury. The caruncula was compromised in all of them except patient 1. The symblepharon reached 1–4 mm into the cornea in all patients, except patient 2. Almost all patients had 360° LSCD (Stage III) except patient 1 who had inferior LSCD between 4 and 8 o'clock hours (Stage IA). Table 1 shows the ocular characteristics and outcomes for each patient.

There were no intraoperative complications. All patients showed perfect integration of the OMAU and anatomical restoration of the depth of fornix with no recurrence of symblepharon out to 3 years postoperatively (Fig. 1). Two patients developed mild superior entropion unrelated to OMAU and another two had a mild motility restriction (one esotropia and one exotropia); all patients were corrected with good results. Patient 7 had persistent epithelial defect 3 months after OMAU with mild corneal melting that was properly managed with autologous serum 20%, doxycycline and lubricants.

In patient 7, 360° LSCD was corrected with conjunctival-limbal autograft (CLAU) (Fig. 2). Patient 2 had simple limbal epithelial transplantation (SLET) and penetrating keratoplasty (PK). Patient 4 had penetrating keratoplasty (PK) alone. Patients 1 and 3 did not require additional surgery for LSCD. At the time of writing, patients 5 is awaiting of autologous SLET and patient 6 for primary Boston keratoprosthesis.

4. Discussion

The goal in the symblepharon treatment is to release all the adhesions from the bulbar conjunctiva and replace the cicatricial tissue with donor tissue. We are proposing OMAU as the optimal tissue to replace the affected conjunctiva. OMAU is easy to harvest, with mild morbidity to the donor area and there is an ample source of the donor tissue for reconstruction of the ocular surface.¹⁸ Additionally, OMAU contains goblet cells that may improve the tear film by contributing mucin to the eye.¹⁰

Our patients had severe symblepharon after chemical or fireworks induced burns. Several surgical approaches for the reconstruction of the ocular surface in cicatricial disorders have been suggested with encouraging results. Historically, conjunctival autograft was frequently used to treat symblepharon with intense conjunctival scarring^{1,2} but a healthy conjunctiva is not always available.³ Although many of our patients had available conjunctiva in the fellow eye, we prefer the use of OMAU because it is easy to obtain and is available in relatively large amount. OMAU was first used to treat recurrent pterygium,^{19,20,21} and has been used before in symblepharon surgery to cover the bare sclera.^{2,4,5,22} OMAU has recently been "re-discovered" as reported in two case reports with short-term follow up.9,10 OMAU has also been used for fornix reconstruction with good outcomes^{3,6}; and it has been frequently used for socket reconstruction.²³ According to our personal experience, OMAU can work as a barrier to prevent keratinization's relapsing in chemical burn cases.

We harvested OMAU from the internal aspect of the inferior lip but it could also be harvested from the internal aspect of the cheek avoiding the Stenon's duct.² We recommend harvesting a graft larger than necessary to address mild shrinkage that occurs postoperatively. Although the donor area can heal by secondary intention, in our experience it is better to approach the borders with absorbable sutures in order to avoid pain during healing. Over the ocular surface, the epithelium grows fairly well and mixed with the conjunctiva epithelium recovers well the bare area created after the cicatricial tissue removal.

We removed submucous fat, minor salivary glands and performed mild trimming of the OMAU. To treat cases of symblepharon with a very dry ocular surface, as in some cases of Steven-Johnson, the combination

Table 1

Clinical characteristics, Surgical procedures and outcomes.

Eye No.	Age (y)	G	Cause	Eye	Pre- OP VA	Previous surgery, No.	Extension of symblepharon/LSCD	Severity grading	OMAU size (cm)	Outcome	EOM/POP Complication	Follow-up (months)
1	6	М	CB 2015	OS	F&F	SR + AMT 1x	3'0–9'0 (180°)/ 4'0–8'0 (90°)	IIIc 1+	2x1	CS/EI	Full/Mild nasal entropion SE	36
2	17	F	CB 2013	OS	HM	SR + AMT 1x	3′0–11′0 (240°))/ 360°	IIc 2+	3X1	CS/EI	Mild ET/none	42
3	14	М	F 2011	OD	20/ 400	SR + AMT 2x; ER; 2x; CLAU 1x;	1′0–11′0 (300°)/ 360°	IIIc 2+	3X2	CS/EI	Full/none	38
4	56	М	CB 2015	OS	HM	SR + AMT 1x	3′0–9′0 (180°)/360°	IIIc 2+	2X 2	CS/EI	Full/none	44
5	22	М	F 2014	OS	HM	SKG 2x; SCG 1x; SR + AMT 2x	3′0–11′0 (240°)/ 360°	IIIc 2+	3X1	CS/EI	Mild XT/Mild entropion SE	36
6	30	F	CB 2015	OU (OD)	HM	None	11′0–7′0 (240°)/ 360°	IIIc 2+	3X1	CS/EI	Full/none	36
7	18	Μ	CB 2014	OS	CF	SR + AMT 1x	7′0–5′0 (300°)/360°	IIIc 2+	3x2	CS/EI	Full/none	42

G: Gender. M: Male. F: Female. CB: Chemical burn. F: Fireworks. OD: Right eye. OS: Left eye: F&F: Fix and follow. HM: Hand motion. CF: Counter fingers. SR: Symblepharon release. AMT: Amniotic membrane transplantation. ER: Entropion repair. CLAU: Conjunctival-limbal autograft. SKG: Skin graft. SCG: Scleral graft. OMAU: Oral mucosa autograft. CS: Complete success. EI: Excellent integration. EOM: Extraocular motility. ET: Esotropia. XT: Exotropia. POP: Post-operative. SE: Superior eyelid.

of OMAU containing associated salivary glands can improve the dry condition of the ocular surface. $^{\rm 24}$

The OMAU can be harvested using mucotome, ^{4,21} or with a blade and trimming the posterior aspect with scissors as described in our technique.² Full-thickness OMAU can result in a beefy red appearance.²¹ However, reducing bulk and a pinky appearance can result in better cosmesis. Additionally, primary contraction is reduced with thinner grafts.^{2,21} Hence, we recommend mild trimming of the graft.

In the current series, all patients except one had undergone previous symblepharon release surgery and the OMAU surgery was performed at least 9 months after the last surgery. Inflammation was medically controlled for 3 months before and after the surgery. Areas of conjunctival shortening and symblepharon were dissected. Fibrous adhesions and Tenon capsule were all released and resected. This aspect of surgery is important because of the presence of myofibroblasts in these tissues,²⁵ and the control of preoperative and postoperative inflammation improves the postoperative outcomes.²⁶

Although AMT is an accepted approach to the surgical management of symblepharon, by itself, it is not strong enough to restore the ocular surface. To improve the results using AMT alone, Mitomycin C has been applied to the deepest fornix however, symblepharon recurrence has been reported in 6-40% of the patients.^{3,9,11,13,14,26}

The "gaps" were sealed to cover any bare sclera with OMAU, AMT and suturing the deepest fornix to the OMAU. A smooth ocular surface and sealing the gap between the Tenon capsule and the surrounding tissues can reduce recurrences, avoiding the use of mitomycin.²⁶ AMT supports epithelialization by promoting migration, adhesion, and differentiation of epithelial cells, and also suppresses the immune and inflammatory response.¹⁰

We suggest exposing the extraocular muscles as warranted. Exposing the extraocular muscles is important for better evaluation of the extension of the sclera that has to be covered. The OMAU sutured to the bare sclera, but respecting the extraocular muscles is a strong element for preventing new adhesions. Even though, fibrous tissue and Tenon capsule were resected and the muscles were released and covered with AMT, two patients developed mild strabismus with normal motility. Both patients had mild strabismus before OMAU surgery but recurrence of strabismus demonstrated that the cicatricial changes of the ocular surface could continue after the restoration of fornix depth. Wrapping of the muscles with AMT during the management of restrictive strabismus surgery improved the ocular motility,^{27,28} however at the long-term had a moderate strabismus success.²⁸ We observed the same behavior in 2 of our patients.

contact lens. The contact lens separates the symblepharon ring and cornea to avoid any trauma postoperatively. The symblepharon ring is mandatory at least for 15 days after surgery and in some cases may remain in place for 4–12 weeks.^{9,10,21} Postoperatively, topical antibiotics are mandatory until the epithelium covers the whole ocular surface, and topical steroids are required until inflammation had subsided which is usually 3 months.²⁶

The mild cicatricial entropion observed on two of our patients was due to focal contraction of the tarsal plate unrelated to the symblepharon surgery as the tarsal plate was untouched during the surgery. Entropion occurred in one patient (patient 5) who sustained a fireworks related trauma and had undergone five reconstructive surgeries. The younger patient (6 years old) with entropion had also undergone a previous reconstructive surgery. Entropion can be easily treated with appropriated technique but close observation is necessary to avoid new adhesions.

The origin of the epithelium covering the sclera between the limbus and the OMAU was not established but the fluorescein staining pattern suggested that the epithelium was conjunctival or mixed with oral epithelium (Fig. 2.3). Corneal melting after Ex vivo cultivated oral mucosa autograft (EVOMAU) has been described however, it was associated with persistent epithelial defect.²⁹ We also observed persistent epithelial defect in one patient after OMAU that was successfully managed with medical therapy (Fig. 2.3).

Regarding the LSCD, patient 7 was managed with CLAU with excellent anatomical outcome (Fig. 2.8). CLAU was performed 18 months after OMAU in order to ensure the inflammation was wellcontrolled after the surgery. Prior to performing any surgical procedure to correct LSCD, optimization of the ocular surface is essential. However, uninflamed ocular surface may require a long period of time, as the expression of high levels of HLA-DR have been detected 24 months after chemical burns.³⁰ Along the same line, Patient 2 underwent SLET 2 years after OMAU and PK 9 months after SLET. Patient 4 had PK alone 3 years after OMAU. Patient 5 is still awaiting of autologous SLET and patient 6 is pending of primary Boston keratoprosthesis insertion (bilateral LSCD). Two of our patients did not require additional surgery, patient 1 who had partial inferior LSCD with 270° healthy limbus; and patient 3 who undergone CLAU before OMAU, the corneal epithelium had good transparency despite mild LSCD over 360°. Oral mucosa epithelium after EVOMAU resulted in a stable ocular surface that improve postoperative vision, the same effect was observed in some of our patients.²

In our technique, a symblepharon ring is placed over the bandage

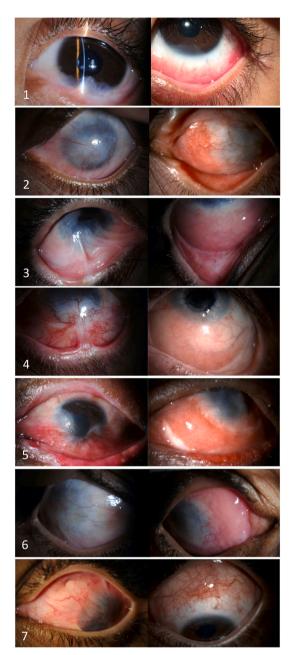


Fig. 1. Photographs of the seven eyes showing oral mucosa autograft (OMAU) sutured to the sclera in severe symblepharon. Left side: Preoperative photographs. Right side: Representative postoperative photographs showing the OMAU integration at different period of times. Patient 1: 24 months. Patient 2: 36 months. Patient 3: 20 months. Patient 4: 33 months. Patient 5: 31 months. Patient 6: 3 months. Patient 7: 26 months.

5. Conclusion

OMAU sutured to the bare sclera in symblepharon surgery to treat severe ocular burns can provide excellent cosmetic and anatomical outcome with no recurrence out to 2 years postoperatively. This old technique is safe and can be used for the treatment of severe symblepharon after unsuccessful surgeries or as a primary surgery in selected patients.

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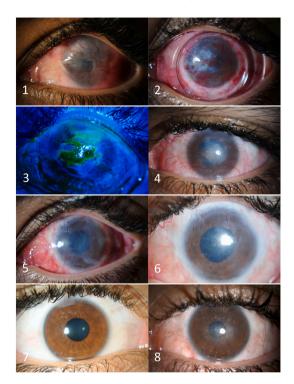


Fig. 2. Photographs of the patient 7 showing the Limbal Stem Cell Deficiency (LSCD) progression. 1. Preoperative. 2. 1 week after symblepharon release + OMAU with symblepharon ring. 3. Fluorescein staining 3 months after OMAU showed the oral epithelium growing over the superior cornea. 4. 18 months after OMAU. 5. 2 weeks after Conjunctival-limbal autograft (CLAU). 6. 1 month after CLAU. 7. 12 months after CLAU, the donor cornea (right eye) was transparent without LSCD. 8.24 months after CLAU showing clear cornea with mild stromal scarring.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Patient consent

This report does not contain any personal identifying information.

Declaration of competing interest

The authors have no financial disclosures.

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