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Original Research Article

Outcome of posterior lamellar replacement with oral mucous membrane graft in lid margin sequalae of Steven Johnson syndrome

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ABSTRACT

Purpose: to address common lid margin sequalae presented in steven Johnson syndrome and to assess the outcome of posterior lamellar replacement with oral mucous membrane graft.

Materials and Methods: This single center longitudinal study was conducted in Ispahani Islamia Eye Institute and Hospital. 56 diagnosed cases of Steven Johnson syndrome with lid margin sequalae during the period of July 2020 to June 2023 were included in the study. Patients with ocular cicatrizing pemphigoid and chemical burn were excluded from the study. Demographic profile, presenting lid margin sequalae, outcome of surgery and complication after intervention and its management were properly evaluated and recorded.

Results: A total of 98 eyelids (upper and lower) in 56 patients were evaluated. The Mean age was 38.33 ± 15.22 years (range 6 – 70 years). 21 patients were male and 35 were female (male: female=1:1.66). 14 patients had unilateral defect and 42 patients have bilateral defect. Most common lid margin sequalae was lid margin keratinization (85.71%), distichiasis (62.5%), trichiasis (21.42%) and entropion (8.92%). All lid margin defect were successfully corrected by posterior lamellar replacement with oral mucous membrane graft. During 6 months post-operative follow up, significant symptomatic relief from epiphora, foreign body sensation, pain and photophobia were achieved in all patients. There was remarkable reduction of conjunctival inflammation (88.63%) and persistent corneal epithelial defect (71.42%). Mean visual acuity was significantly improved. Common complications of the surgery were misdirected lashes (7.14%), dislodgement of graft (2.04%%), and recurrent entropion (2.04%). All complication was successfully managed through appropriate second procedure.

Conclusion: Posterior lamellar resection with an oral mucous membrane graft for modifying lid margin defects in Steven-Johnson syndrome shows promising results.

1. Introduction

The mucocutaneous junction of the margin plays an important role in preserving the environment of the ocular surface.[1] Disturbance of this important anatomical landmark leads to lid-margin anomalies, which have a prominent effect on the delicate balance of the ocular surface environment. This occurs in conditions like ocular cicatricile pemphigoid (OCP), chemical injury, and trachoma, most commonly following Stevens-Johnson syndrome.

Stevens-Johnson syndrome (SJS) is an immunologic inflammatory disease that primarily targets the skin and the mucosal surfaces.[2,3] In acute phase of SJS; there

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are conjunctival ulcerations, membrane formation, and sloughing of surface epithelium along with lid margin defect.[4] In chronic phases, there are sequelae like dry eyes, conjunctival scarring, limbal epithelial stem cell defect, and lid margin keratinization (LMK).[5]

In lid margin keratinization, the non-keratinized stratified squamous epithelium of palpebral conjunctiva becomes keratinized over time. It is due to the posterior migration of the mucocutaneous junction of the lid margin.[6] Keratinization means the deposition of whitish keratin over the lid margin and palpebral conjunctiva. Lid margin keratinization causes chronic epitheliopathy for which lid margin epithelium integrity is lost, and this ultimately results in lid margin sequelae like entropion, trichiasis, distichiasis and loss of normal architecture of the ocular surface, causing recurrent inflammation, corneal vascularization, formation of symblepharon, and scarring of the cornea which eventually can lead to blindness.[7,8]

The treatment of cicatricial changes of the eyelid is a complex task, primarily due to the progressive and recurring nature of Stevens-Johnson syndrome. Mucous membrane grafting (MMG) in the lid margin is an established treatment that effectively resolves the pathology and restores the posterior lid margin to normal function.[1] This surgical procedure replaces the keratinized lid margin and adjacent scarred tarsal conjunctival epithelium with healthy oral mucosa, significantly reducing lid margin sequelae and improving the ocular surface environment.

Many studies have shown the beneficial effects of mucous membrane grafting (MMG) on ocular surface health. After MMG, the level of pro-inflammatory cytokines on the ocular surface is reduced, while anti-inflammatory cytokines are enhanced.[9] This procedure can significantly alter the natural course of the disease, showing positive effects in improving ocular surface health. Ultimately, it preserves and even improves vision in affected eyes.[10,11] This efficient procedure is widely accepted by oculoplastic surgeons and ocular surface surgeons dealing with Steven Johnson syndrome cases. Here, we attempt to find out the common lid margin sequalae presented in Steven Johnson syndrome and to assess the outcome of posterior lamellar replacement with oral mucous membrane graft.

2. Materials and Methods

This single centre longitudinal study was performed at Ispahani Islamia Eye Institute and Hospital in Dhaka, Bangladesh from the time interval of July 2020 to June 2023. We included all patients who were clinically presented with lid margin defect suffering from Steven Johnson syndrome and underwent posterior lamellar resection with oral mucous membrane graft. The demographic and clinical profile included age, gender, ocular presentation, eyelid margin defect, preoperative and postoperative visual acuity, ocular surface condition, date of surgery and follow-up details recorded. Data on lid margin correction outcome, symptomatic relief, conjunctival inflammation and corneal epithelial defect reduction, visual acuity improvement, and complications were collected. Anatomical success was outlined if the lid margin defect was completely corrected. Functional success was defined by relief from irritation, photophobia, reduction of ocular surface inflammation and corneal epithelial defect, and improvement in visual acuity. Complications like graft dislodgement, entropion recurrence, and misdirected lashes were observed, and appropriate corrective approaches were taken. Ethical clearance was obtained on 30 August 2020 according to the Institute Policy, and the data collection was started from the 01 July 2020. The study followed the principles of the Declaration of Helsinki.

2.1. Surgical procedure

A small group of skilled oculoplastic surgeons performed the surgery under general anaesthesia. After everting the eyelid, a grey line incision horizontally separates the anterior and posterior lamella throughout the entire eyelid margin. Excision of the keratinized posterior eyelid margin and dissection in the subconjunctival plane was performed to remove scarred conjunctiva. Electrocautery was performed on the exposed roots of trichiasis lashes. Distichiasis was addressed by excising the tarsal strip carrying the distichiasis lash follicles. The size of the defect on the edge of the eyelid was measured horizontally and vertically.

The donor mucous membrane graft was harvested from the oral mucosa. The surgical site was exposed, and a No. 15 blade was used to outline the graft incision. The harvested graft is 30% larger than the lid margin defect, and the graft dissection was performed using Westcott scissors. Haemostasis was achieved using bipolar cautery. The exposed area of the oral cavity was then covered with an amniotic membrane graft, which was secured using fibrin glue and interrupted stitches with 6-0 Vicryl sutures. The graft was prepared by trimming any residual adherent fat. Subsequently, the graft was affixed to the host bed using fibrin glue and continuous 7-0 Vicryl sutures.

3. Results

A total of 98 eyelids (upper and lower) of 56 patients were included in the study. Demographic (Table 1) and clinical data of the patients are presented in the following tables.

The patients' ages ranged from 6 to 70. The male-female ratio was 1:1.66. Seventy-five per cent of the patients had bilateral disease, while 25% had one eye involved.

The most common lid margin defect (Table 2) in Steven Johnson syndrome was lid margin keratinization followed by distichiasis, trichiasis, and entropion. All 98 eyes underwent posterior lamellar resection with oral

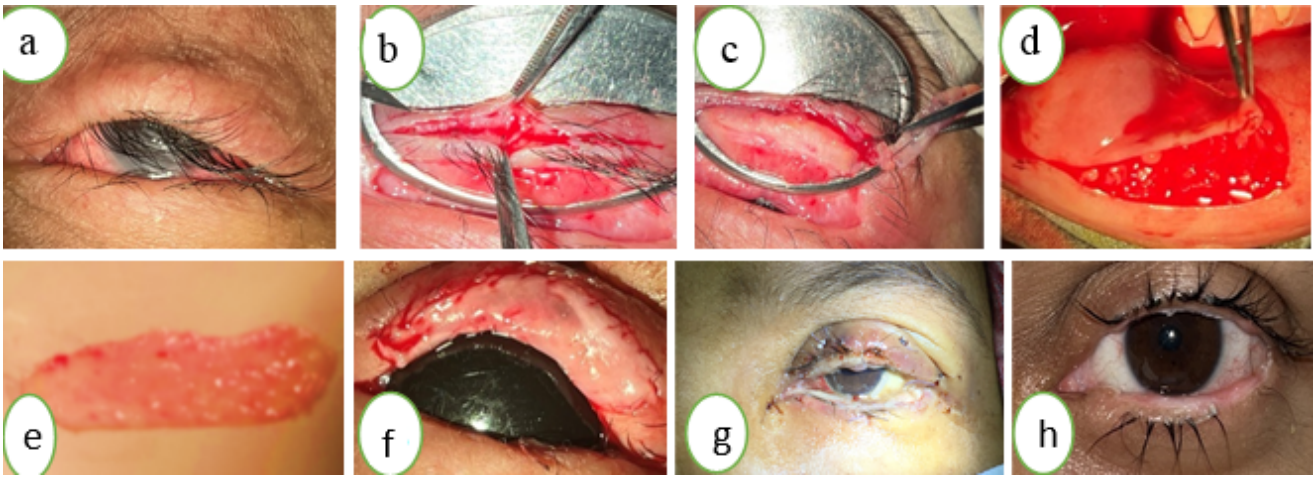

Figure 1: (**a):** Displays the preoperative condition of the left upper eyelid, while; (**b):** to 8 illustrate the steps of the surgical techniques involved. The steps include incision at the grey line along the full length of the eyelid margin (**b**); Excision of the scarred tarsal conjunctiva (**c**): Harvesting of mucous membrane from the oral mucosa (**d**), Trimming of the mucous membrane graft (**e**): Adherence and fixation of the mucous membrane to the host bed for covering the posterior lamellar defect (**f**): Everting sutures (**g**): and the outcome of the eyelid margin after six months of the surgery (**h**).

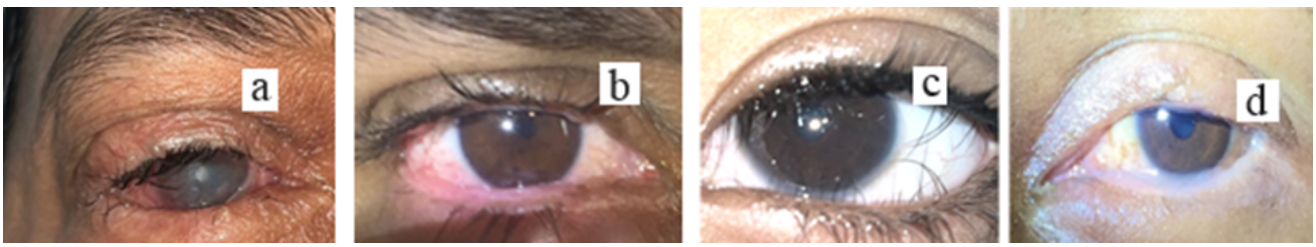

Figure 2: a and **c:** Displays the preoperative photographs and **b** and **d:** Shows the post operative outcome.

Table 1: Demographic profile and laterality of patients (n = 56)

Variable	Value	P value
Age, mean ± SD (years)	38.33 ± 15.22 years	<0.0001
Gender		<0.061
	Male: 21	
	Female: 35	
Laterality		<0.0001
	Unilateral: 14	
	Bilateral: 42	

P<0.01 = statistically significant

Table 2: Lid margin sequalae

Lid margin defect	Number (n)	Percentage (%)
Lid margin keratinization	84	85.71
Distichiasis	61	62.50
Trichiasis	21	21.42
Entropion	09	08.92

Table 3: Comparison of pre and post-operative outcome

Clinical feature	Pre-operative	1^{st} POD	14^{th} POD	After 1 month	After 3 months	After 6 months	P value
Lid margin defect	100%	14%	12%	11%	0%	0%	$7.1* 10^{-6}$
Conjunctival inflammation	88%	75%	63%	20%	12%	10%	0.01
Corneal epithelial defect	42%	42%	40%	18%	14%	12%	0.06
Visual acuity log MAR (Mean± SD)	0.85 ± 0.25	0.85 ± 0.25	0.70 ± 0.31	0.57± 0.30	0.5± 0.27	0.52 ± 0.37	<.0001

P<0.01 = statistically significant

Table 4: Post-operative complication

Post-operative complication	Number (n)	Percentage (%)
Misdirected lashes	7	7.14
Dislodgement of graft	2	2.04
Recurrence of entropion	2	2.04

mucous membrane graft to address lid margin defects, which commonly cause irritation, foreign body sensation, epiphora, and photophobia. All patients were assessed for symptom relief, anatomical success, and functional success on the 1st postoperative day (POD), the 14th POD, one-month post-op, three months post-op, and six months post-op. Nearly all patients (98%) experienced symptom relief within six months. Assessing anatomical success and functional outcome involves:

1. Correcting the lid margin defect.
2. Reducing conjunctival surface inflammation and corneal epithelial defect.
3. Improving visual acuity.

The lid margin defect had completely healed (Table 3) within six months. Conjunctival inflammation (Figure 2 a+b) was significantly reduced by 88.63%. The corneal epithelial defect (Figure 2c & d) was healed in 71.42% of the eyes, as observed by fluorescein staining. Patients with persistent epithelial defects were referred to the cornea subspecialty for further evaluation and treatment. Mean visual acuity showed significant improvement. The donor eyelid site had excellent healing in all patients.

Postoperative complications (Table 4) were found in a minority of patients and were treated successfully through an appropriate approach. Misdirected lashes were treated with electrocautery. Dislodged grafts were refixed the next day and sutured in places. Recurrent entropion was treated later on by tarsal fracture rotation.

4. Discussion

The posterior lid margin plays a significant role in maintaining the smoothness of the ocular surface. Various diseases, particularly Steven Johnson syndrome, can impact the integrity of the lid margin. It has been reported that lid changes occur in 31.8% to 71% of patients with Steven Johnson syndrome. These significant lid margin changes include lid margin keratinization, trichiasis, distichiasis, and cicatricial entropion. These changes can lead to pain, sensitivity to light, epithelial defects, limbal stem cell deficit, and corneal perforation. Lid margin keratinization in SJS is the most significant cause of continued conjunctival inflammation, corneal epithelial defects, and the worsening of the ocular surface environment. [1]

Ocular sequelae were associated with the severity of ocular involvement during the acute phase. Early ophthalmic evaluation and regular follow-up are beneficial as ocular involvement is the primary long-term complication in Steven Johnson syndrome, and Toxic epidermal necrolysis patients. [12]

Posterior lamellar resection followed by mucous membrane grafting of the lid margin is the well-recognized management for lid margin defect in Steven Johnson syndrome. This provides a smooth ocular surface and reduces chronic irritation and inflammation. It also aids in protecting limbal stem cells, preserving the cornea's clarity, reducing corneal vascularization, and enhancing visual acuity. [1]

In our study, 56 patients were selected, with an age range of 6 to 70 years and a mean age of 38.33 ± 15.22 years. The male-to-female ratio was 1:1.66. A study conducted by Shree N et al. reported a mean patient age of 42.5 years (standard deviation, SD-17.67) and a male-to-female ratio of 1:1.71, [8] which is closely related to our study.

The most common lid margin defect observed in this study is keratinization (85.71%), followed by distichiasis (62.5%), trichiasis (21.42%), and entropion (8.92%). Another study by Sodhi PK et al. found that the most common eyelid changes were cicatricile entropion and lid margin keratinization in 100% of cases, followed by trichiasis in 50%. [4] These findings differ slightly from

our study, which could be attributed to differences in the selection of patients.

The defects at the edge of the eyelid irritate, and there is a sensation of having a foreign material in the eye, excessive tearing, and sensitivity to light in the affected eye. All the patients received treatment for their lid margin defect through posterior lamellar resection, and the posterior lamella was substituted with a graft taken from oral mucosa. Various techniques have been studied in the literature for addressing lid margin defects in chronic SJS. Grafts such as oral mucous membrane, nasal turbinate, banked sclera, and hard palate have been used to extend the posterior lamella and create a smooth surface that won't irritate the ocular surface. However, MMG from oral mucosa is easier to obtain and is better tolerated by patients. Gurumurthy et al. demonstrated that the factors responsible for eye surface problems in Steven Johnson syndrome, including those related to fibrosis, inflammation, and reduced cell death, are significantly reduced after posterior lamellar graft with MMG.[9] Tarsal V-wedge resection is a highly effective alternative to more complex techniques for managing upper eyelid cicatricile entropion.[13]

All our patients were reviewed on the 1st postoperative day, the 14th postoperative day, after one month, three months, and six months. Anatomical outcome was achieved in 100% of cases. Conjunctival inflammation was reduced in 88.63% of cases, and corneal epithelial defect was healed in 71.42%. Mean visual acuity significantly improved. Iyer et al. found that MMG reduces chronic blink-related injury to the cornea and conjunctival congestion, restores patient comfort and improves visual acuity in Steven Johnson syndrome.[14] A more invasive technique like Hard palate mucosa grafts are alternative option for the replacement for tarsus and conjunctiva in eyelid reconstruction.[15]Anterior lamellar recession along with blepharoplasty, and supra tarsal fixation technique is a safe and effective for managing the upper lid cicatricial entropion without lagophthalmos.[16] In their study, Shree N et al. showed anatomical success of 96% and good functional success of 77%.[8] Sadia Sultana et al. also found a reduction of conjunctival inflammation, resolution of the corneal epithelial defect, and improvement of visual acuity after the procedure in her study.[17] These results are consistent with our study. Fu Y et al. recommended increasing the graft size to prevent shrinkage after surgery. We also opted for a graft 30% larger than the actual defect.[18]

The literature reports various perioperative complications during mucous membrane grafting, including bleeding from the donor site and intraoperative buttonholing. None of our patients experienced any perioperative complications, and only a small number of patients in our study experienced postoperative complications.

Misdirected lashes were found in 7.14% of cases and were treated with electrocautery. Grafts became dislodged in 2 patients but were repositioned the next day and secured with a suture. Entropion recurred in 2 patients, requiring correction by tarsal fracture rotation. In a study by Osaki et al., postoperative complications included a recurrence of lid margin keratinization, which necessitated a repeat MMG procedure. Other postoperative complications, such as graft displacement and necrosis, were also observed.[7]We have some limitations, including a single-centre study. A multi-centre study with a larger sample size and a shorter follow-up period may verify the outcome.

5. Conclusion

In conclusion, posterior lamellar resection with an oral mucous membrane graft for modifying lid margin defects in Steven-Johnson syndrome shows promising results.

6. Conflict of Interest

None.

7. Source of Funding

None.

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