Intraoperative Mitomycin C and Amniotic Membrane Transplantation for Fornix Reconstruction in Severe Cicatricial Ocular Surface Diseases

Scheffer C. G. Tseng, MD, PhD, Mario A. Di Pascuale, MD, Daniel Tzong-Shyue Liu, MD,
Ying Ying Gao, MD, Alireza Baradaran-Rafii, MD

Purpose: To investigate whether intraoperative application of mitomycin C may enhance the success of amniotic membrane transplantation in symblepharon lysis and fornix reconstruction in severe cicatricial ocular surface diseases.

Design: Noncomparative interventional case series.

Participants: Sixteen patients (8 female, 8 male; 18 eyes) with a mean age of 41 ± 23.4 years (range, 3–79) and suffering from severe chemical/thermal burns (7 eyes), multiple recurrent pterygia and pseudopterygia (5 eyes), Stevens–Johnson syndrome (4 eyes), and ocular cicatricial pemphigoid (2 eyes) were consecutively enrolled. All except for 2 eyes had had prior surgical attempts of surgical reconstruction, including 6 eyes with a mucous membrane graft (MMG), but still presented with symblepharon and persistent ocular surface inflammation.

Intervention: After excision of subconjunctival fibrovascular tissues, 0.04% mitomycin C was applied for 5 minutes in the deep fornix before amniotic membrane transplantation.

Main Outcome Measures: Deeper fornix, noninflamed ocular surface, and full motility.

Results: The mean epithelial healing time was 4.2 ± 1.9 weeks. During the follow-up of 14.16 ± 5.2 months, all eyes showed a marked reduction of conjunctival inflammation, a deep fornix, and a continuous tear meniscus. Of 12 eyes with motility restriction, 2 eyes with multiple recurrent pterygia and 1 eye with severe thermal burn showed recurrence of partial motility restriction 2 months after surgery. The vision of 9 eyes was successfully restored by an additional keratolimbal allograft with subsequent penetrating keratoplasty (6 eyes).

Conclusion: Intraoperative application of mitomycin C is an effective means to reduce chronic and deep-seated conjunctival inflammation, and helps amniotic membrane restore a deep fornix after symblepharon lysis, even in eyes that had a failed MMG. Restoration of deep fornix and tear meniscus is an important prerequisite to achieve successful reconstruction by subsequent limbal stem cell transplantation. *Ophthalmology 2005;112: 896–903 © 2005 by the American Academy of Ophthalmology.*

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Extensive scar formation (cicatrix) of the conjunctiva can be found in a number of severe cicatricial ocular surface diseases such as multirecurrent pterygia, chemical/thermal burns, Stevens–Johnson syndrome (SJS), and ocular cica-

tricial pemphigoid (OCP). When cicatrix obliterates the fornix, especially at the 12-o'clock and 6-o'clock positions, it destabilizes the tear film by disrupting the formation of an adequate tear meniscus. Furthermore, fornix foreshortening and symblepharon may also interfere with eyelid blinking and closure and induce inturning lashes, together further threatening ocular surface health. In some instances, severe cicatrix in the rectal muscle may restrict ocular motility, resulting in strabismus and annoying diplopia. There is a great need to develop an effective strategy of restoring a deeper fornix in these eyes, especially before ocular surface reconstruction (for a recent review, see Espana et al[1]).

Previously, we reported that amniotic membrane transplantation (AMT) as an alternative to a conjunctival autograft achieves a complete success in 12 of 17 eyes by restoring a deep fornix after symblepharon lysis.[2] However, 5 eyes with partial success or failure were found to have the aforementioned severe cicatricial diseases that exhibit relentless inflammation. This finding is similar to what had

been reported in recurrent pterygia, where AMT alone may not halt the slowly progressive return of fibrovascular tissue in the failure cases.[3] That was why we decided to investigate whether intraoperative application of mitomycin C (MMC) may enhance the success of AMT during fornix reconstruction by suppressing inflammation and controlling scarring in 18 eyes of 16 patients with severe cicatricial diseases.

Patients and Methods

This study was approved by the institutional review board of Baptist Hospital of Miami/South Miami Hospital, Inc. Informed consent was obtained in a total of 16 patients (18 eyes) seen at the Ocular Surface Center during the period of 2002 to 2004. Except for 2 patients, all others had had prior surgical attempts to reconstruct the fornix but still presented with conjunctival inflammation despite maximal medical therapies. They all manifested cicatricial complications that had caused an unstable tear film, mechanical friction to the ocular surface, or a combination of both. Twelve eyes were also associated with motility restriction caused by multirecurrent pterygia (n = 5), thermal burns (n = 1), chemical burns (n = 3), and SJS (n = 3). Their clinical data concerning demographic information, preoperative diagnosis, symblepharon location, and prior surgical procedures are summarized in online-only Table 1 (available at http://www.ophsource.org/periodicals/ophtha). Surgical outcomes, including preoperative and postoperative visual acuities (VAs), duration of epithelialization, and follow-up periods, are summarized in online-only Table 2 (available at http://www.ophsource.org/periodicals/ophtha). The extent of cicatrix was graded according to the visibility of deep episcleral vessels, as described by Tan et al.[4] The extent of conjunctival inflammation was graded by the intensity of vascular injection from 0 to 3. Grade 0 was normal, without injection; grade 1 was mild, with superficial injection only; grade 2 was moderate, with additional deep injection; and grade 3 was severe, with intense deep injection.

All patients were followed up at the first postoperative day, weekly until epithelialization, monthly or bimonthly for the first half year, and quarterly for the remaining time.

Surgical Technique

Under general anesthesia, all eyes received fornix reconstruction by symblepharon lysis, intraoperative application of MMC, and AMT performed by a single surgeon (SCGT). The surgical procedure was similar to what has been reported, with some modifications.[2] After standard preparation and draping, several drops of 1:1000 epinephrine were applied to the ocular surface several times in the beginning and during the surgical procedure to control hemostasis without extensive cauterization. For the eye with severe symblepharon obliterating the fornix to the extent that the speculum was not able to be inserted, one 4-0 black silk suture was placed at the lid margin through the tarsal plate of each lid as a traction (Fig 1A). Those eyes in which symblepharon was not as severe were opened with a lid speculum. Once the eye was opened, the conjunctiva was incised from the perilimbal region between the normal conjunctiva and the beginning of the cicatrix. If the cicatrix was focal, such an incision was made for <180°, and relaxing incisions were then made at the border of the cicatrix toward the fornix. If the cicatrix was 360°, a complete peritomy was performed, followed by 4 such relaxing incisions at each quadrant. 7-0 Vicryl sutures (ETHICON, Inc., Somerville, NJ) were affixed at the superior or inferior limbal sclera as traction of the globe, so

that the cicatrix could be better exposed. Meticulous dissection by scissors was then done to separate and remove all of the subconjunctival fibrovascular tissue in each bulbar conjunctiva up to the fornix in each quadrant (Fig 1B).

After the globe was rotated by the 7-0 traction suture and the removal of cicatrix, the incised conjunctival edge was invariably and naturally recessed to the deep fornix or the tarsus. A dry Weckcel sponge (Edward Weck & Co., Inc., Research Triangle Park, NC) was then cut into thin slices from the slant edge, and all slices were soaked in 0.04% MMC solution. Each well-soaked sponge was inserted into the deep fornix for 5 minutes (Fig 1C, D); the exact duration depended on the extent of fibrovascular tissue growth and inflammation. At the end of application, all sponges were counted and removed, and the fornix was rinsed with 20 to 40 ml of balanced salt solution. For eyes that needed 360° of fornix reconstruction, the above MMC application was best carried out in 2 separate sessions (i.e., treating the superior and inferior fornix separately). By doing so, the sponge was inserted to the deep fornix, covered by the recessed conjunctiva, and the bare sclera was kept dry by pulling the 7-0 traction suture and by occasional drying of the denuded bulbar sclera with a dry sponge so that no fluid was leaking from the inserted sponge.

Amniotic membrane, obtained from Bio-Tissue, Inc. (Miami, FL), was thawed, peeled off the filter paper, and laid down on the bare sclera with the stromal side facing down. If the symblepharon was focal and fornix shortening was limited, the membrane was secured to recessed conjunctiva or a mucous membrane graft (MMG) by an interrupted 8-0 or 9-0 Vicryl suture and attached to the deep fornix by interrupted 10-0 nylon sutures with episcleral bites. If the symblepharon was diffuse and fornix shortening involved nearly the entire fornix, the membrane was secured to the recessed conjunctiva by a running 8-0 or 9-0 Vicryl suture (Fig 1E), and the composite graft was pushed to the deep fornix by a muscle hook and anchored there by passing one double-armed 4-0 black silk suture per quadrant through the full thickness of the lid and securing it to the skin with a bolster made of silicone tubing or white sponge (Fig 1F). The remaining amniotic membrane was then flattened and secured on the bare sclera by interrupted 10-0 nylon sutures with long episcleral bites (Fig 1G, H).

Postoperative medications were similar to those used for routine cataract surgeries with topical steroid and antibiotics, the latter discontinued when epithelialization was completed, and the former tapered off when the conjunctival inflammation disappeared. The conjunctival epithelial healing was determined by fluorescein staining.

Outcome Measurements

The outcome of success was defined as restoration of a stable-depth fornix and being free of scar, inflammation, and motility restriction during a minimum follow-up of 6 months. Photographs taken before and after surgery were read by an independent observer (YYG) who was not aware of the clinical information and that reported herein. Partial success was defined as focal recurrence of scar tissue without inflammation, whereas failure was defined as the return of inflamed and scarred tissue in the area of surgery and the fornix being deeper than preoperatively at the last follow-up.

Results

As shown in online-only Table 1 (available at http://www.ophsource.org/periodicals/ophtha), there were 8 females and 8 males, with a mean age of 41±23.4 years (range, 3–79). Their diagnoses included severe chemical/thermal burns (7 eyes), mul-
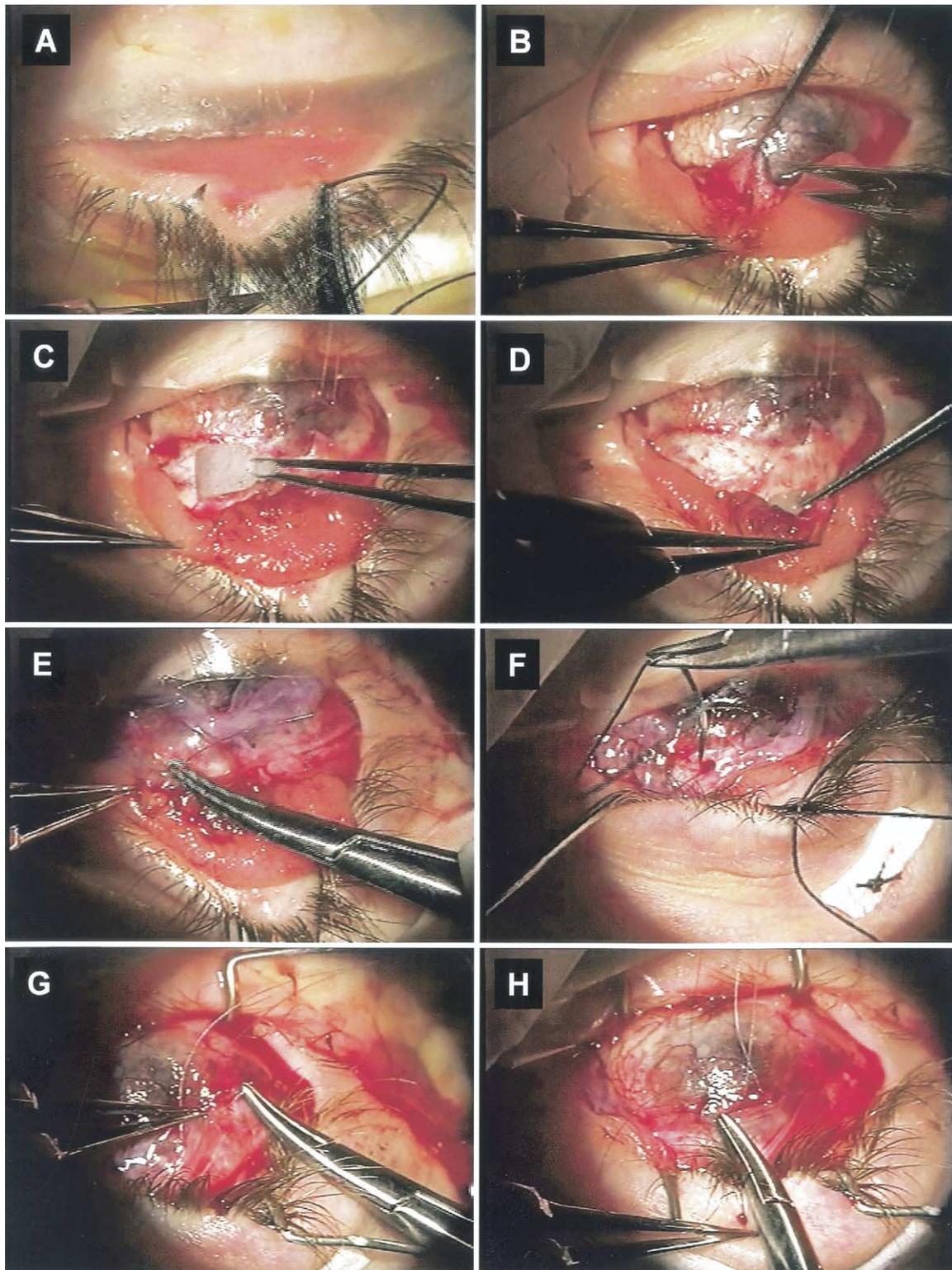
Figure 1. Key surgical steps. **A**, Because severe symblepharon precluded the insertion of the speculum, one 4-0 black silk suture was placed at the lid margin through the tarsal plate as a traction. **B**, After peritomy, a thorough dissection of subconjunctival fibrovascular tissue was performed. **C, D**, A Weckcell sponge soaked with 0.04% mitomycin C was inserted into the deep fornix for 5 minutes and subsequently removed. **E**, Amniotic membrane was attached to the recessed conjunctival edge by an 8-0 Vicryl running suture. **F**, Amniotic membrane was then pushed to the deep fornix by a muscle hook and anchored there by passing one double-armed 4-0 black silk suture through the full thickness of the lid and securing it to the skin with a bolster made of sponge or tubing. **G, H**, Amniotic membrane was then flattened and secured onto the bare sclera by interrupted 10-0 nylon sutures with long episcleral bites, 2 per quadrant.
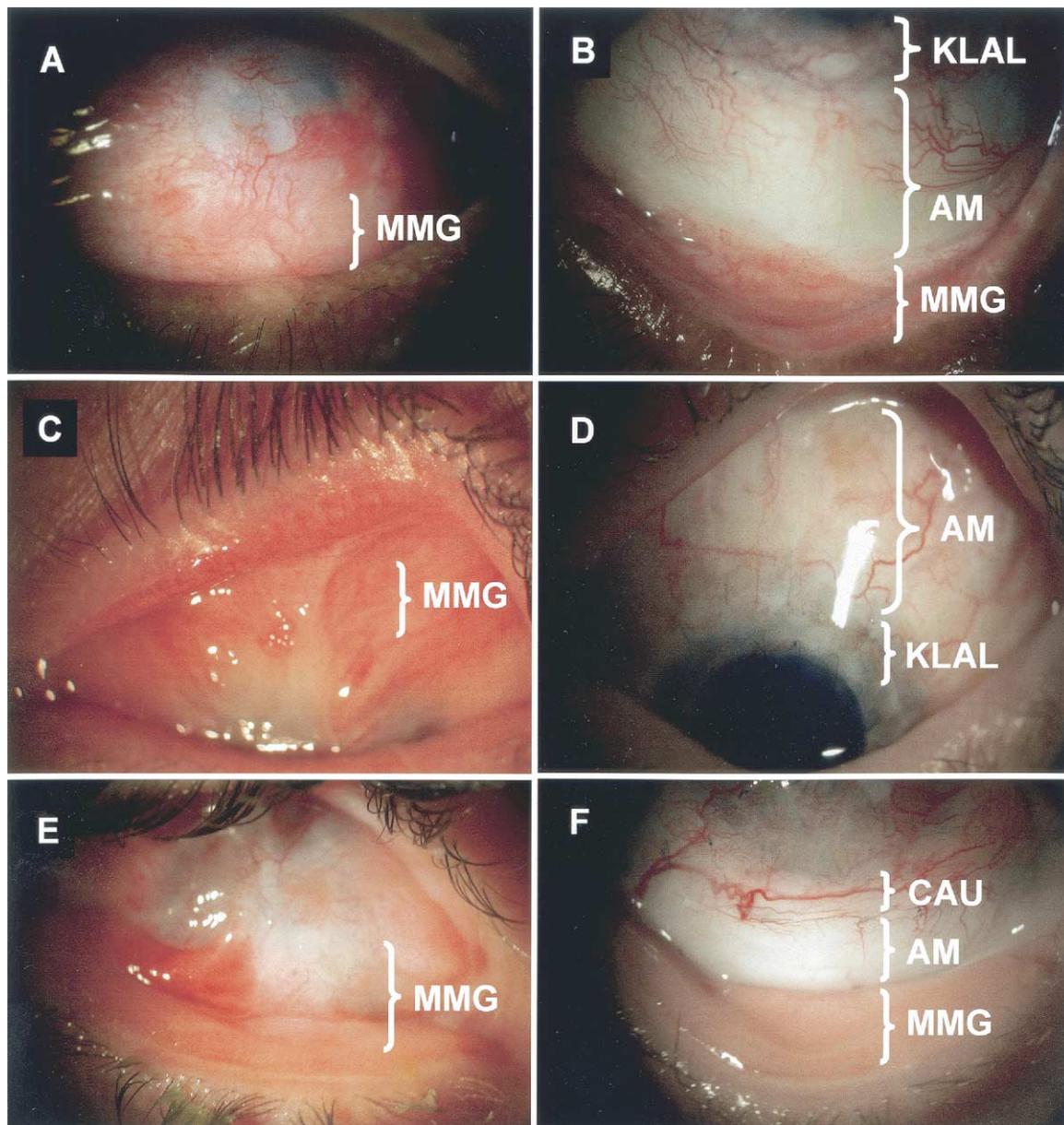
Figure 2. Before (left) and after (right) fornix reconstruction in 3 representative cases of chemical burn and prior mucosal membrane graft (MMG) failure. **A**, Case 6, manifesting total obliteration of the lower fornix, conjunctival injection, and total limbal stem cell deficiency. **B**, Case 6, showing a quiet deep fornix free of inflammation and scarring. **C**, Case 10, manifesting an inflamed symblepharon made of an MMG that obliterated the upper fornix. **D**, Case 10, showing a deep fornix without inflammation. **E**, Case 9, manifesting severe symblepharon, ectropion, and a dry MMG. **F**, Case 9, showing a deep fornix and wet ocular surface. AM = amniotic membrane; CAU = conjunctival autograft; KLAL = keratolimbal allograft transplantation.

tiple recurrent pterygia (5 eyes), SJS with toxic epidermal necrolysis (4 eyes), and OCP (2 eyes). Before surgery, all eyes presented with persistent conjunctival inflammation grade 3 and severe symblepharon leading to partial or total obliteration of the fornix and a deep scar with a fleshy appearance, graded as T3 (as described by Tan et al[4]). Twelve eyes manifested motility restriction caused by multirecurrent pterygia and pseudopterygia (n = 5), thermal burns (n = 1), chemical burns (n = 3), and SJS (n = 3).

Before enrollment into the study, all except 2 eyes had received several surgical procedures to restore the fornix obliterated by symblepharon. These included repairs of eyelid ectropion or entropion, a conjunctival autograft (10 eyes), a conjunctival limbal autograft (CLAU) (3 eyes), a living-related conjunctival limbal allograft (1 eye), AMT (7 eyes), multiple excisions of recurrent pterygia (for an average of >6 times per eye), and an MMG (5 eyes) (see Fig 2 for cases of prior MMG failures). Despite these surgeries, all eyes still had an obliterated fornix and absence of meniscus formation. For more details, see online-only Table 1 (available at http://www.ophsource.org/periodicals/ophtha).

Surgical outcome is summarized in online-only Table 2 (available at http://www.ophsource.org/periodicals/ophtha). The epithelial defect on the amniotic membrane–covered area healed within 4.2±2.3 weeks. The amniotic membrane remained in place and did not dissolve during follow-up. For a mean follow-up period of 14.1±5.2 months (range, 8–22), 15 of 18 (83.3%) eyes were successfully reconstructed with a deeper fornix, and the most
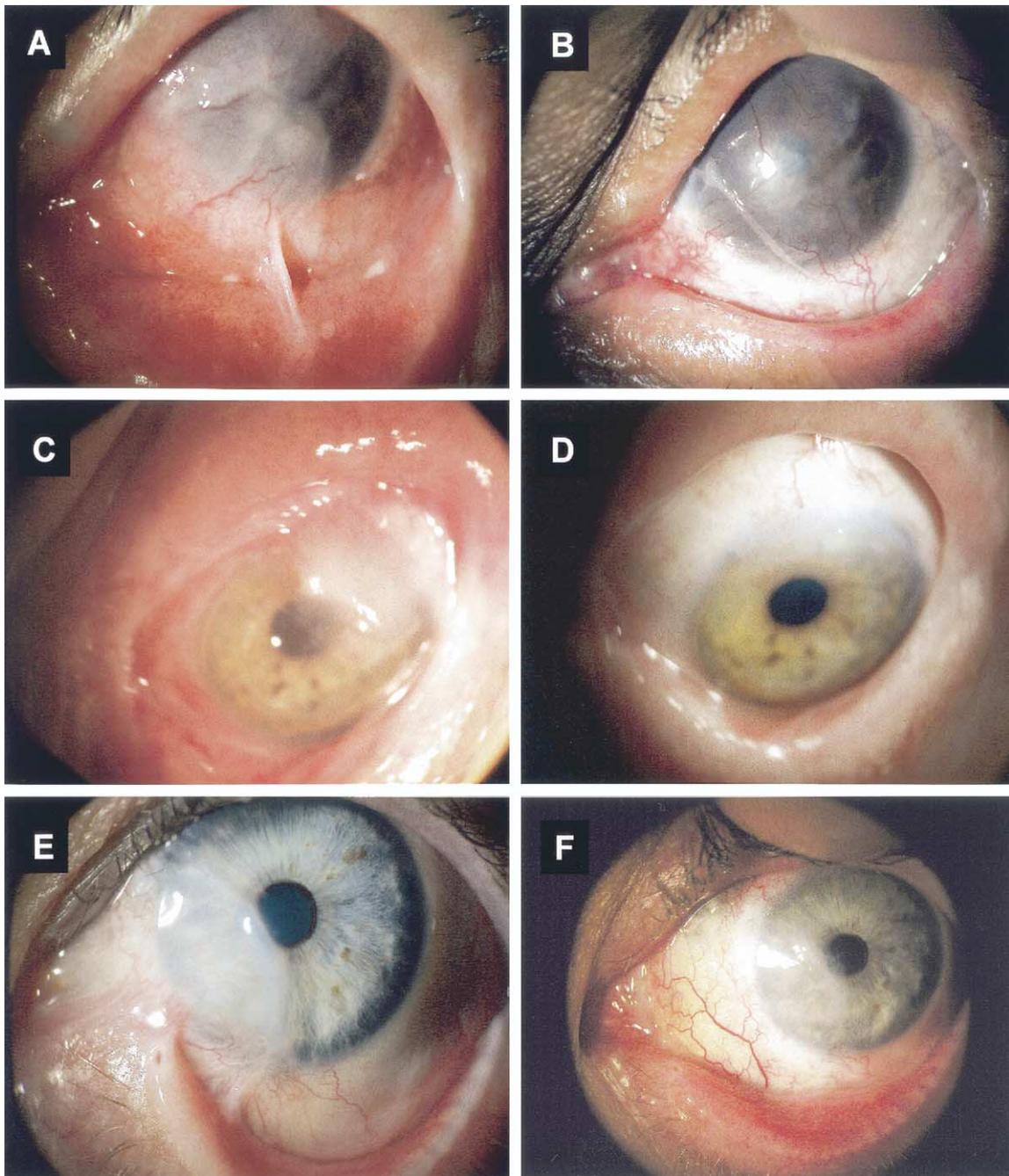
Figure 3. Representative cases of Stevens–Johnson syndrome/toxic epidermal necrolysis (**A, B**), ocular cicatricial pemphigoid (**C, D**), and multirecurrent pterygia (**E, F**). **A,** Case 2, manifesting a symblepharon and severe inflammation. **B,** Case 2, showing a deep fornix free of scarring and inflammation. **C,** Case 4, manifesting severe symblepharon, pannus, and severe inflammation. **D,** Case 4, showing a deep upper fornix and clear cornea without inflammation. **E,** Case 15, with multirecurrent pterygia despite 7 prior removals and manifesting a dense fibrovascular tissue invading the nasal cornea and obliterating the inferonasal fornix. **F,** Case 15, showing a deep fornix free of fibrovascular tissue and inflammation and a clear cornea.

notable finding was marked reduction of conjunctival inflammation in all eyes, from grade 3 before surgery to grade 0 after surgery (Figs 2, 3). In all eyes, the reconstructed fornix was deeper and free of inflammation (Figs 2, 3). All covering surfaces were graded as T1, except for cases 11, 13, and 14, which had grade T2, characterized as focal adhesion formed between the skin and the nasal bulbar conjunctiva (Fig 4A, C, E). These 3 cases were thus classified as partial successes, and they developed mild motility

restriction 2 months after surgery. Two of the 4 eyes with multiple recurrent pterygia required additional removal of subconjunctival tissue and the same repeat procedure to achieve no recurrence at the last visit (see example in Fig 4). Visual acuity improved after surgery in 12 eyes, 1 with ectropion surgical correction, 6 with keratolimbal allograft transplantation (see a recent review[1]) followed by penetrating keratoplasty (PK), 1 with CLAU, and 4 without any additional surgery. Visual acuity remained stable in 4
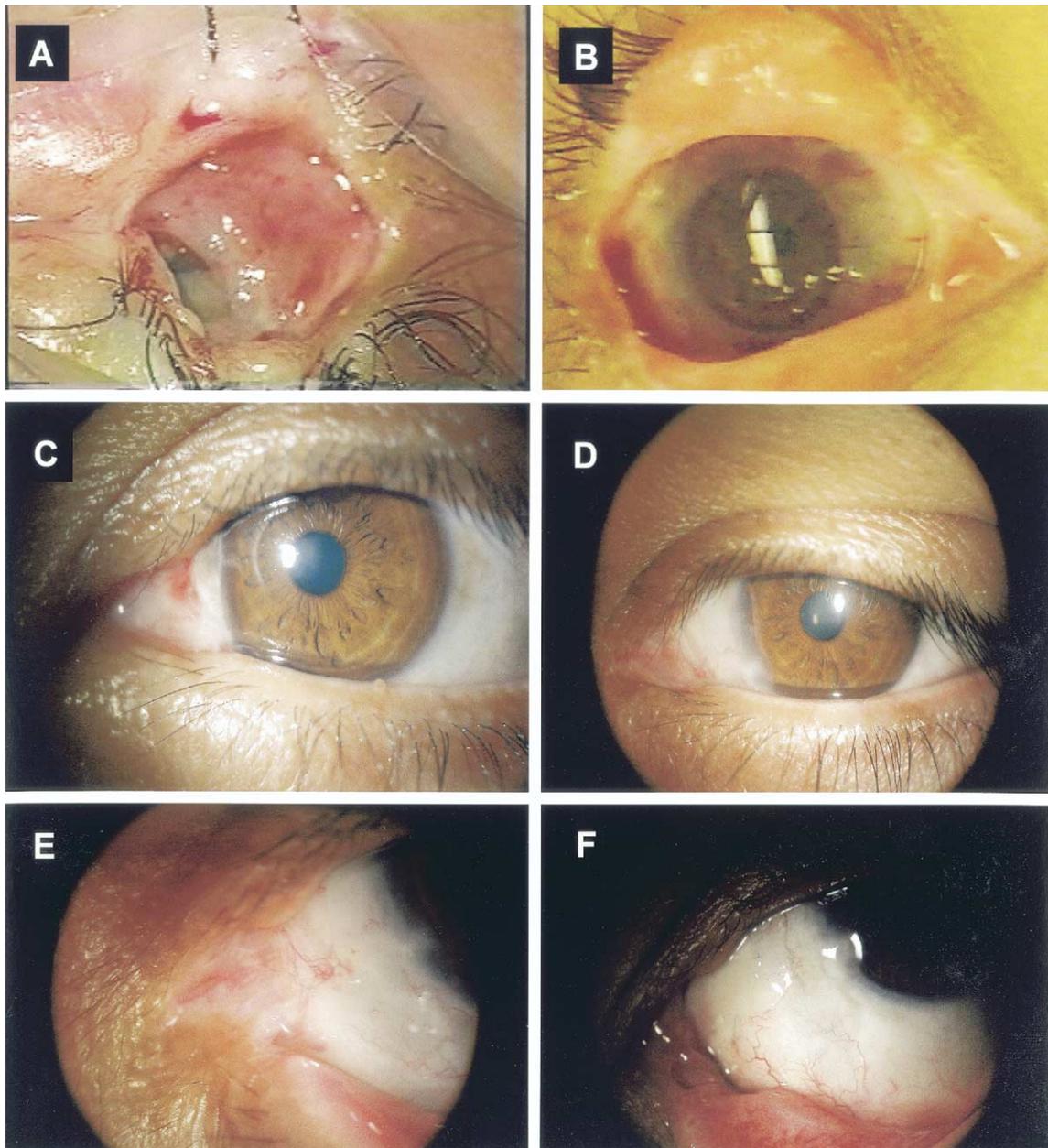
Figure 4. Patients with motility restriction after mitomycin C and amniotic membrane transplantation. **A**, Case 11, a thermal burn caused by fireworks, showing ankyloblepharon that covered 90% of the ocular surface. **B**, Case 11, showing a clear cornea with a deep fornix but still motility restriction after reconstruction with an additional conjunctival limbal autograft from the other eye and cornea transplantation. **C**, Case 13, with multirecurrent pterygia after 9 prior removals, showing dense inflamed fibrovascular tissue invading up to the cornea associated with motility restriction. **D, E**, Case 13, showing focal adhesion at the nasal conjunctiva limiting motility restriction 3 months later; however, the fibrovascular tissue did not reach the cornea. **F**, Case 13, showing a deep fornix free of scar and inflammation, with the ocular motility considerably improved after the second attempt.

eyes and deteriorated in 1 eye with multiple recurrent pterygia as a result of progressive macular edema (case 12). No complications related to application of MMC, such as delayed epithelial wound healing, epithelial defect, scleral thinning, or scleral ulceration, were noted during the entire postoperative follow-up period.

Discussion

In this study, we report that intraoperative application of MMC with AMT achieves successful fornix reconstruction in a total of 18 eyes with severe cicatricial diseases manifesting symblepharon and fornix obliteration. Among them, 12 eyes also had motility restriction. The severity of cicatricial process could be judged by the nature of these diseases being SJS/toxic epidermal necrolysis, chemical burns, and OCP, which, as shown in our previous report, tend to result in partial success or failure when AMT alone is used for fornix reconstruction.[2] Furthermore, despite the fact that nearly all these 16 eyes had undergone several surgical attempts (online-only Table 1 [available at http://www.ophsource.org/periodicals/ophtha];

Fig 2A, C, E), they still presented an obliterated fornix and absence of meniscus formation because the fibrovascular tissue in the symblepharon extended to the limbus. Thus, we postulate that persistent inflammation contributed to the prior surgical failures in these patients.

For pterygia, Solomon et al[3] have recognized that it is important to remove thoroughly such subconjunctival fibrovascular tissue, including the semilunar fold, before AMT to achieve a low recurrence rate in both primary and recurrent pterygia. Experimentally, it has been shown that subconjunctival body fibroblasts adopt the invasive phenotype of pterygium head fibroblasts with overexpression of metalloproteinase types 1 and 3 after stimulation by inflammatory cytokines.[5,6] Furthermore, our recent study of 5 exenterated eyes also revealed bundles of myofibroblasts located in the midst of the adipose tissue behind the orbital septum and contiguous with such a fibrovascular tissue.[7] Because the inflamed tissue extends deep into the fornix, it is not possible to eradicate completely the subconjucitval fibrovascular tissue by surgery in these cicatricial diseases, including pterygia. For OCP, it has been recognized that surgical procedures frequently aggravate conjunctival inflammation, potentially worsening the disease. That was why intraoperative application of MMC, an alkylating agent that dose dependently and time dependently inhibits fibroblast proliferation (for a review, see Crooke and Bradner[8]), was included as an important adjunctive measure. Clinically, intraoperative application of MMC has been successfully used to prevent pterygial recurrence,[9,10] and subconjunctival injection of MMC is effective in controlling the inflammatory activity and progression of OCP.[11]

We chose intraoperative application of 0.04% MMC for 5 minutes based on a low recurrence rate in primary and recurrent pterygia and few complications noted in a prospective study.[9] Unlike pterygia, for which intraoperative MMC was applied to the bare sclera,[9] we applied it directly underneath the conjunctiva in the fornix and nasal caruncle where the fibrovascular tissue originates. Because no control was included in our study, the clinical efficacy of intraoperative MMC is not proven definitively. Nevertheless, it has been reported that all 12 eyes, except 2 (excluding multiple recurrent pterygia), still developed severe symblepharon and an obliterated fornix despite several prior surgeries, including an MMG (5 eyes) and AMT (3 eyes). In 4 eyes with multiple recurrent pterygia, several procedures had also been tried before this study, including a conjunctival autograft (4 eyes), CLAU (3 eyes), AMT (2 eyes), and MMC (2 eyes); none received all these procedures at the same time. In this study, our sample size (n = 4), although more than what has been reported,[12] remained too small to conclude that MMC plays an important role in arresting the recurrence. Nevertheless, it is tempting to speculate that a combination of MMC and AMT is effective in suppressing conjunctival inflammation in all 18 eyes. Even in 2 eyes with multiple recurrent pterygia, repeated surgery with MMC and AMT had significantly improved the outcome (Fig 4). We have not noted such complications as delayed epithelial healing, epithelial defect, and corneal and scleral melting, previously reported with a topical[13,14] or single intraoperative use of MMC.[15,16] Although these complica-

tions may occur weeks to months later after application, Solomon et al[17] reported that a single intraoperative application of MMC is not associated with reduction of scleral thickness even 6 years after pterygium surgery. Therefore, we still caution that all patients treated with intraoperative MMC require a close long-term follow-up, and that a multicenter randomized clinical trial is necessary to validate the efficacy of intraoperative uses of MMC.

These cicatricial ocular surface diseases are frequently complicated with limbal stem cell deficiency,[18] and transplantation of autologous or allogeneic limbal epithelial stem cells is necessary for restoration of vision.[19] Several studies have recognized that dry eye,[20] keratinization,[21] and chronic conjunctival inflammation[22,23] are risk factors threatening the success of transplantation of allogeneic limbal stem cells because they increase the attrition of transplanted limbal stem cells and invite allograft rejection despite continuous oral cyclosporine administration. Experimentally, we have also noted that chronic limbal inflammation threatens the success of autologous limbal conjunctival autografts.[24] Therefore, we advocate that a noninflamed ocular surface with a deep fornix be restored and that an adequate tear meniscus be reformed to attain a stable tear film before corneal surface reconstruction can be successfully contemplated with limbal stem cell transplantation.[1,19] In this study, we indeed noted that VA improved after keratolimbal allograft transplantation followed by PK in 6 eyes, and after CLAU in 1 eye. A long-term study is under way to confirm this viewpoint. For multirecurrent pterygia with motility restriction, a recent report of 2 cases showed that a combined approach of intraoperative MMC, AMT, and CLAU is successful in preventing recurrence and restoring ocular motility.[12] In the present study, we used a conjunctival autograft without including the limbus to achieve the same success in 2 cases. Future studies are needed to develop a preoperative screening test or to arrive at a set of clinical profiles so that we may identify those patients more susceptible to developing progressive and recalcitrant inflammation and cicatricial complications. By doing so, we may then deploy intraoperative application of MMC to augment the success in symblepharon lysis and fornix reconstruction.

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Table 1. Summary of Clinical Data

Case	Age/Gender	Eye	Diagnosis	Symblepharon Location	Past Ocular Surgeries	
					For Fornix	*Not for Fornix*
1	8 F	R	SJS/TEN	Lower and upper	MMG	Lid evertion
2	40 M	L	SJS/TEN	Lower and upper	CAU	
3	33 F	OU	SJS/TEN	Lower and upper		
4	69 F	L	OCP	Upper	AMT/Lr-CLAL, R eye	
5	79 M	L	OCP/POAG/multiple surgeries	Lower		Trabeculectomy, glaucoma shunt
6	47 M	L	Chemical burn	Lower	MMG	KLAL, glaucoma shunt
7	66 M	R	Chemical burn	Lower		
		L	Chemical burn	Upper	AMT, tarsorrhaphy	
8	54 F	L	Chemical burn	Lower and nasal	CAU	Retinal reattachment surgery
9	26 F	R	Chemical burn	Lower and upper	MMG, CLAU and AMT	
10	40 M	L	Chemical burn	Lower and upper	MMG, AMT and CAU	
11	5 F	R	Thermal burn	Lower and upper	CAU	
12	71 M	L	Multiple recurrent pterygia with motility restriction (4 times)	Lower and nasal	Bare sclera, CAU, CLAU, AMT, eyelid surgery	
13	33 F	L	Multiple recurrent pterygia with motility restriction (9 times)	Lower and upper	Bare sclera, CAU, CLAU and MMC	
14	34 F	L	Multiple recurrent pterygia with motility restriction (3 times)	Upper and nasal	Bare sclera and CAU	
15	48 M	L	Multiple recurrent pterygia with motility restriction (7 times)	Lower and upper	Bare sclera, CAU, CLAU, MMC and AMT	
16	3 M	L	Multiples recurrent pseudopterygia with motility restriction (2 times)	Lower	CAU and AMT	

AMT = amniotic membrane transplantation; CAU = conjunctival autograft; CLAU = conjunctival limbal autograft; F = female; KLAL = keratolimbal allograft; Lr-CLAL = living related conjunctival limbal allograft; M = male; MMC = intraoperative application of mitomycin C; MMG = mucosal membrane graft; OCP = ocular cicatricial pemphigoid; OU = both eyes; POAG = primary open angle glaucoma; SJS/TEN = Stevens–Johnson syndrome/toxic epidermal necrolysis.

Table 2. Surgical Outcome

Case	Visual Acuity Preoperatively	Visual Acuity Postoperatively	Follow-up (mos)	Surgical Outcome	Additional Surgeries and Comments		Time Healing (wks)
					With Fornix Reconstruction	*After Fornix Reconstruction*	
1	LP	LP (amblyopia)	16	Success		KLAL	8
2	CF	20/400	8	Success		KLAL and PK	4
3	CF	20/200	8	Success		KLAL and PK	4
	HM	20/400	8	Success		KLAL and PK	4
4	20/100	20/50	22	Success			8
5	20/80	20/70	22	Success		Ectropion surgery	8
6	HM	20/300	19	Success	KLAL	KLAL and PK	2
7	20/300	20/60	9	Success		KLAL and PK	1
	LP	HM	9	Success			4
8	HM	HM (RD)	19	Success			8
9	LP	HM	18	Success			4
10	LP	20/200	17	Success	KLAL	KLAL and PK	4
11	LP	HM	16	Partial success	CAU	MMG, CLAU and PK	5
12	20/25	20/30 (macular edema)	19	Success			2
13	20/20	20/20	12	Partial success	CAU	MMC and AMT	3
14	20/20	20/20	16	Partial success		CAU, MMC and AMT	4
15	20/50	20/20	8	Success	CAU		1
16	NA	20/80	9	Success		CLAU	3

AMT = amniotic membrane transplantation; CF = counting fingers; CAU = conjunctival autograft; CLAU = conjunctival limbal autograft; HM = hand movements; KLAL = keratolimbal allograft; LP = light perception; MMC = mitomycin C; MMG = mucosal membrane graft; NA = not available; PK = penetrating keratoplasty; RD = retinal detachment.