Correlation of Corneal Complications with Eyelid Cicatricial Pathologies in Patients with Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis Syndrome

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Purpose: To look at the correlation between many factors (time of hospitalization, floppy eyelid syndrome, trichiasis, open lacrimal puncta, symblepharon, and aqueous tear deficiency) and corneal complications in Stevens–Johnson syndrome (SJS).

Design: Observational cases series.

Patients: Clinical data were retrospectively reviewed from 38 patients (32.7±20.1 years old) with SJS (n = 11) and with toxic epidermal necrolysis (TENS) (n = 27) from January 2002 to August 2004. One case report with SJS was included to verify the presence of tarsal/lid margin ulceration at the acute stage.

Methods: The medical history was retrieved regarding presumed causative medications used within 15 days and the duration of hospitalization. Data of the latest photographic documentation and eye examination were compared and correlated in a masked fashion.

Main Outcome Measures: Floppy eyelid, trichiasis, lid margin keratinization, meibomian gland orifice metaplasia, symblepharon, tarsal scar, and corneal complications.

Results: Acute SJS/TENS was characterized by tarsal conjunctival ulceration. Keratinization of the eyelid margin with variable degrees of meibomian gland dysfunction was observed in all cases. Floppy eyelid, trichiasis, partially or totally opened lacrimal punctum, symblepharon, and aqueous tear deficiency were not significantly correlated with corneal complications. In contrast, there was a strong correlation between the severity of eyelid margin and tarsal pathology and the extent of corneal complications (Spearman *r*, 0.54; $P = 0.0005$). A multivariable regression analysis also showed that the extent of eyelid and tarsal pathology had a significant effect on corneal complications (coefficient, 0.84; $P = 0.006$).

Conclusions: Patients with acute SJS/TENS are characterized by severe inflammation and ulceration of the tarsal conjunctiva and lid margins. If left unattended, lid margin keratinization and tarsal scar, together with lipid tear deficiency, contribute to corneal complications because of blink-related microtrauma. Attempts to suppress inflammation and scarring by amniotic membrane transplantation at the acute stage and to prevent microtrauma at the chronic stage are vital to avoid sight-threatening complications. *Ophthalmology 2005;112: 904–912 © 2005 by the American Academy of Ophthalmology.*

Stevens–Johnson syndrome (SJS) is considered one of the most devastating ocular surface diseases that cause corneal damages and threaten vision. Power et al[1] retrospectively reviewed a total of 366 patients with erythema multiforme, SJS, and toxic epidermal necrolysis syndrome (TENS) during a period of 34 years and reported an incidence of 24% ocular complications, ranging from conjunctivitis to symblepharon and corneal ulceration. They speculated that the initial vesicular (blister) stage is followed by conjunctivitis, thus the illness severity is parallel to the skin change and correlated with subsequent symblepharon or ankyloblepharon. Because of the high mortality rates of 3% and 27% in SJS and TENS, respectively,[1] management of ocular involvement might have been compromised by directing much attention to maintaining the vital functions during the acute stage. Inadequate control of ocular surface inflammation might set in a vicious circle, leading to the chronic stage of scarring (cicatrix), which then contributes greatly to subsequent corneal complications.

Originally received: August 23, 2004.
Accepted: November 16, 2004. Manuscript no. 2004-43.

From the Ocular Surface Center, Miami, Florida.

Supported in part by an unrestricted grant from Ocular Surface Research and Education Foundation, Miami, Florida.

Dr Tseng and his family are more than 5% shareholders of TissueTech, Inc., which owns United States patent nos. 6 152 142 and 6 326 019 on the method of preparation and clinical uses of human amniotic membrane, which is currently distributed by Bio-Tissue, Inc.

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ISSN 0161-6420/05/$–see front matter
doi:10.1016/j.ophtha.2004.11.035

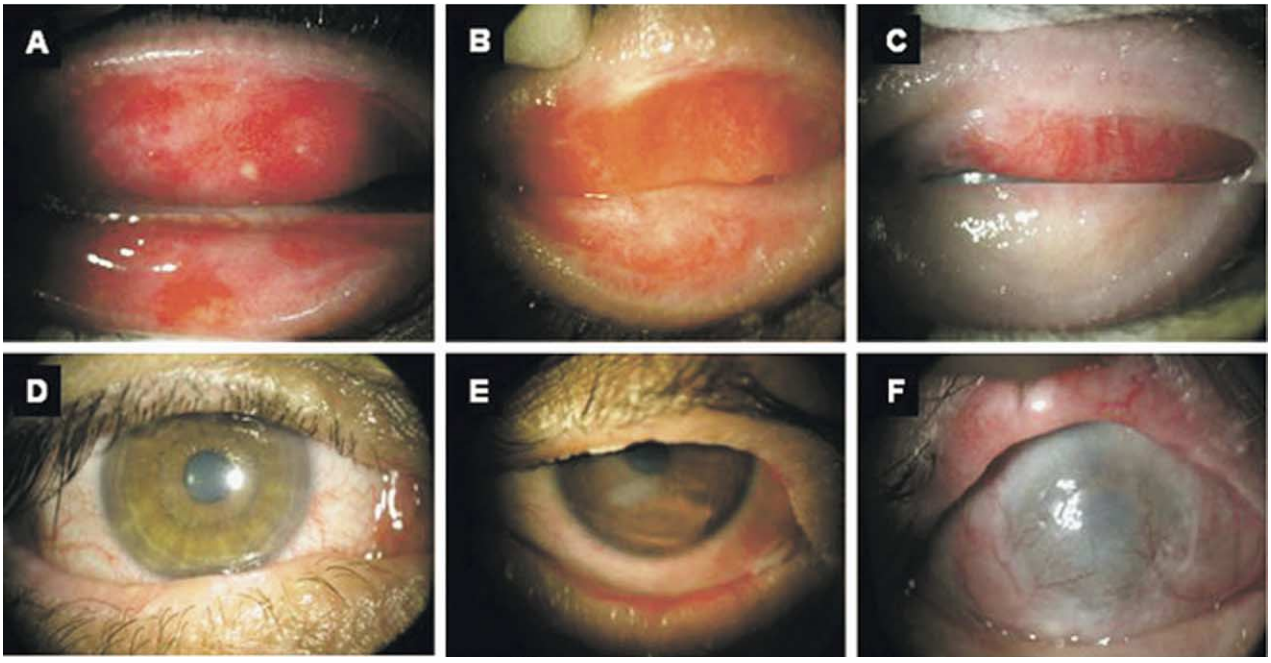


Figure 1. Representative grading of the severity of eyelid/tarsal cicatrix (**A–C**) and corneal complication (**D–F**). Both upper and lower tarsal conjunctiva and lids were shown for (**A**) grade 1, mild; (**B**) grade 2, moderate; and (**C**) grade 3, severe lid margin and tarsal scarring and keratinization. The cornea showed (**D**) grade 1, mild; (**E**) grade 2, moderate; and (**F**) grade 3, severe complications.

Amniotic membrane (AM) transplantation used as a temporary graft (or patch) during the acute stage of chemical and thermal burns can suppress inflammation and prevent subsequent scarring in the later stage.[2–4] Amniotic membrane has also been used as a temporary graft in 2 patients with acute SJS/TENS to suppress inflammation and facilitate wound healing that resulted in normal ocular surface, milder scar on tarsal conjunctiva, and a transparent cornea with minimal peripheral corneal neovascularization.[5]As shown in our case report, we also observed a similar success of AM transplantation in treating a child with acute SJS. During the course of management, we noted a striking finding: severe tarsal conjunctival ulceration in all 4 lids at the acute stage. Because such ulceration was successfully covered by AM, leading to the suppression of inflammation and scarring, we did not observe cicatrix-mediated lid margin, lash, and tarsal abnormalities in the later stage. As a result, the patients were asymptomatic and did not have any corneal complication.

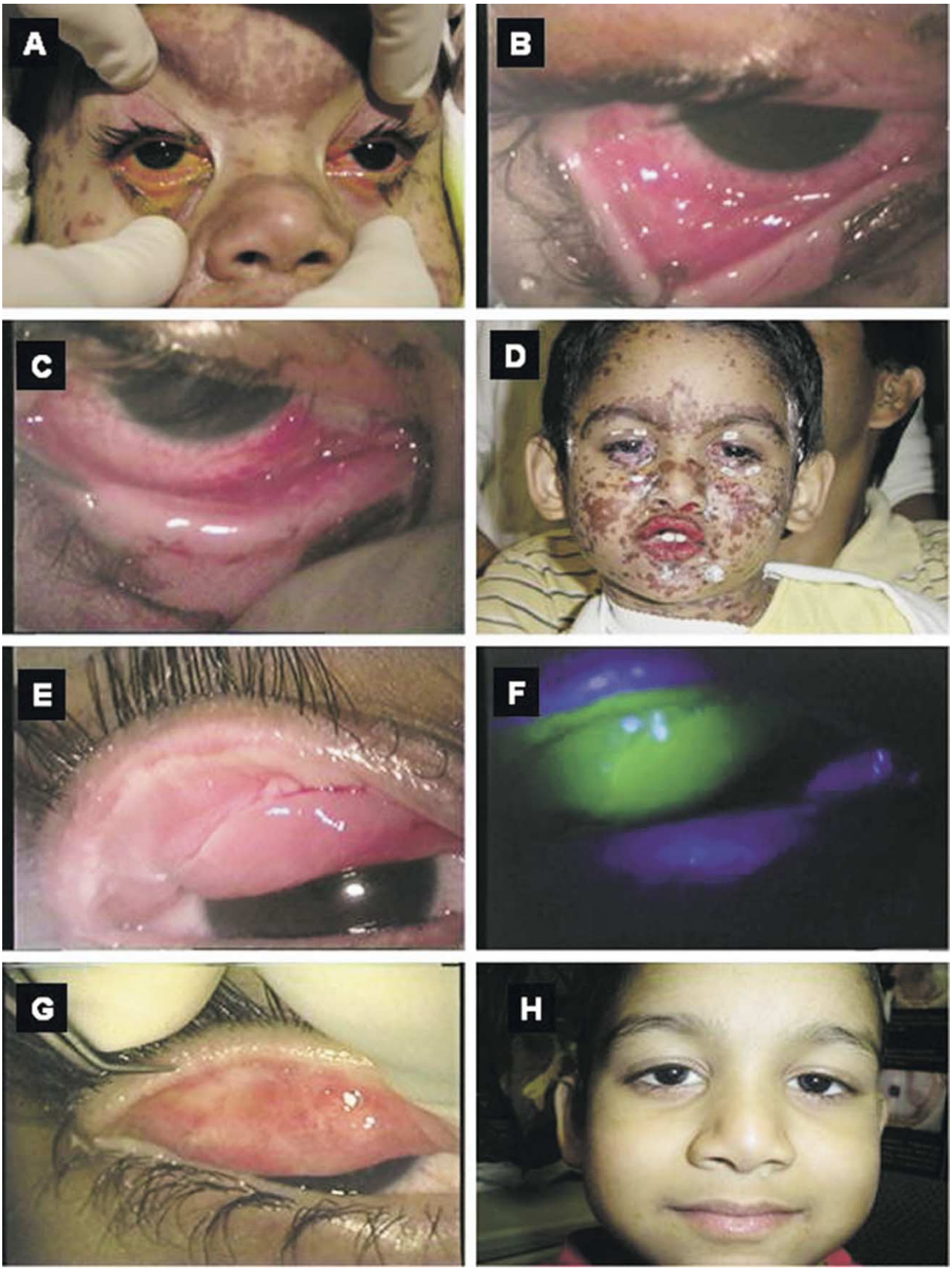
This observation prompted us to speculate that morbidities of corneal complications might be caused by cicatrix-mediated lid margin/tarsal pathologies in patients with SJS/TENS. To examine this hypothesis, we retrospectively reviewed clinical records and photographs of 38 patients with SJS/TENS and report herein the strong correlation between the severity of lid margin/tarsal pathologies and that of corneal complications. The significance of these findings is further discussed.

Patients and Methods

This study was approved by the Institutional Review Board of the Baptist Hospital of Miami and South Miami Hospital to retrospectively review the clinical data of patients with SJS or TENS seen at Ocular Surface Center, Miami, Florida, during the period from January 2002 to August 2004. We included patients with the diagnosis of SJS and TENS on the basis of the criteria previously summarized by Power et al.[1] We also included 1 additional patient with an acute attack of SJS hospitalized in the Pediatric Intensive Care Unit of Baptist Hospital of Miami.

Medical history was retrieved regarding presumed-causative medications used within 15 days from the onset of symptoms and the duration of hospitalization. Patients with any eyelid or ocular surface surgery were excluded from the study. Besides symptoms and visual acuity, external and slit-lamp examinations were performed to detect any abnormality in the ocular surface, lid margin, lashes, and the entire external adnexa. Special tear function tests were also performed. Aqueous tear secretion was determined by the average of the wetting length of 2 Schirmer strips performed at a 10-minute interval during fluorescein clearance test.[6] The extent of "floppy eyelid" was graded as 1+ when less one third of the tarsal conjunctiva, as 2+ when greater than one third but less than one half of the tarsal conjunctiva, and as 3+ when more than one half the tarsal conjunctiva was everted. Special attention was given to cicatricial complications involving different locations of the ocular surface (e.g., lids [entropion], puncta [auto-occlusion], lashes [trichiasis and districhiasis], lid margin [scar and keratinization], and meibomian gland orifice metaplasia, fornix [foreshortening, symblepharon, and ankyloblepharon], and bulbar conjunctiva [scarring with or without motility restriction]).

The severity of cicatrix-mediated lid margin/tarsal pathologies was graded as mild, moderate, and severe by reviewing in a masked fashion all photographs including those showing the everted upper eyelids. As shown in Figure 1, grade 1 (mild) showed sporadic lid margin keratinization that encompassed less than one third of the entire lid length with minimal subconjunctival scar (Fig 1A). Grade 2 (moderate) showed continuous lid margin keratinization that encompassed between one third and one half of the entire lid length and invaded up to 1 mm of the tarsal con-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junctiva, and subconjunctival scar that changed the tarsal contour without cicatricial entropion (Fig 1B). Grade 3 (severe) showed continuous lid margin keratinization that encompassed more than one half of the entire lid length and invaded more than 1 mm of the tarsal conjunctiva and prominent subconjunctival scar that caused cicatricial entropion (Fig 1C).

The severity of corneal complications was also graded as mild, moderate, and severe by examining in masked fashion the corneal photographs. Grade 1 (mild) showed a clear cornea with superficial punctate keratopathy (Fig 1D). Grade 2 (moderate) showed corneal haze localized at the periphery or peripheral neovascularization less than 3 continuous hours (Fig 1E). Grade 3 (severe) showed central corneal haze or scar or extensive neovascularization with more than 3 continuous hours that may or not reach the central cornea (Fig 1F).

Statistical Analysis

Two investigators (EME and DTSL) evaluated independently the photographs taken from the eyelids and corneas with a 90% agreement. The comparison between the severity of corneal complications with other variables such as hospitalization time, floppy eyelid syndrome, trichiasis, lacrimal punctum status, symblepharon, aqueous tear deficiency (ATD), and eyelid margin and tarsal pathology were performed by nonparametric correlation (Spearman *r*). To further confirm that the effect of eyelid margin and tarsal pathology on corneal complications has accounted for the effects of other variables mentioned previously, we performed a multivariable analysis regression using GraphPad InStat.[7] A P value of < 0.05 was considered statistically significant.

Case Report

Lid Margin and Tarsal Ulceration without Corneal Involvement and Successful Management by Amniotic Membrane Transplantation in Acute Stevens–Johnson Syndrome/Toxic Epidermal Necrolysis Syndrome

A 4-year-old boy, with a medical history of asthma and autism, had skin rashes of the face and neck develop the next day after taking ibuprofen to control fever. On the following day, both eyes were red, and blisters were noted in the mouth, resulting in eating difficulty. He was admitted to a pediatric intensive care unit with a presumptive diagnosis of SJS. The skin rashes affected 9% of the body in the ensuing 3 days of hospitalization. He kept both eyes closed and was treated with topical tobramycin and dexamethasone ointment twice a day. The bedside examination performed 5 days after the initial attack showed that both eyes were totally closed and covered by crust, and both eyelid skins were ulcerated; each eye, but the cornea, was not affected (Fig 2A). Examination under anesthesia performed 2 days later showed an additional finding that the tarsal conjunctiva on eversion was severely inflamed and ulcerated (Fig 2B). Cryopreserved AM obtained from Bio-Tissue (Miami, FL) was sutured to cover the entire ocular surface from lid margin to lid margin as a temporary graft (patch) (Fig 2C) with bolsters to the skin in the same manner as previously reported.[3] On the following day, the patient comfortably opened both eyes (Fig 2D). A second examination under anesthesia performed 9 days after surgery showed that AM dissolved from the entire ocular surface, ulcers on the skin and eyelid margin healed without scar, both bulbar conjunctivas were noninflamed, and both corneas were clear. On eyelid eversion, we noted that all tarsal conjunctival ulcers were covered by AM in both eyes (Fig 2E, F). Examination under anesthesia 3 months after AM transplantation showed that there was minimal scar in the lid margin and tarsal conjunctiva (Fig 2G). He remained asymptomatic and free of any corneal complication, and the ocular surface was noninflamed and stable for 12 months at the last follow-up visit (Fig. 2H).

Data Summary

From 53 patients with SJS/TENS, we excluded 15 who had received eyelid surgeries such as mucous membrane graft, hard palate graft, and eyelid fracture for entropion correction. The remaining 38 patients, 23 females and 15 males, had a mean age of 32.7 ± 20.1 years old (mean $\pm$ standard deviation). According to the diagnostic criterion provided by Power et al,[1] 27 patients were more severely inflicted with TENS, whereas 11 patients only had SJS. Except for 2 patients in whom the offending agent was not identifiable, the rest had SJS/TENS develop after administration of oral medications such as penicillin, sulfa, and ibuprofen (in a descending order of frequency). The mean hospitalization time was 3.9 ± 2 weeks. Other pertinent information can be found in Table 1.

Uncorrected visual acuity ranged from 20/20 to counting fingers. Keratinization of the eyelid margin with variable degrees of meibomian gland dysfunction, manifesting lipid tear deficiency (LTD), was observed in all cases. Floppy eyelid was observed in 20 (52.6%) cases; all except 4 cases were symmetric in both eyes and graded as 1 to 2+. Trichiasis was present in 27 (71%) cases. Fifteen (41%) cases had partially or totally occluded lacrimal puncta; among them 9 (60%) cases had auto-occlusion caused by the disease, whereas the remaining 6 (40%) cases were closed by cauterization. Obliteration of tear meniscus by symblepharon was observed in 27 (71%) cases. Twenty-one (55.2%) cases had severe ATD; among them 14 (66.6%) cases still had partially or totally opened lacrimal puncta. On the basis of the grading system illustrated in Figure 1, all cases, except for 4, had symmetric grading of the eyelid severity between the two eyes; 5 cases were classified as grade 1 (Fig 1A), 3 cases as grade 2 (Fig 1B), and the remaining 26 cases as grade 3 (Fig 1C). The grading of the corneal severity was symmetric between the two eyes in 33 cases and asymmetric in 5 cases. In the symmetric cases, 14 cases were graded as grade 1 (Fig 1D), and 19 cases were graded as grade 3 (Fig 1F), besides the visual acuity of all these symmetric cases were not affected during the hospitalization time, they developed corneal complications months and years after discharge from the hospital (range, 2 months–15 years). In the asymmetric cases, 2 cases had grade 1

Figure 2. A 4-year-old boy with acute Stevens–Johnson syndrome was unable to open his eyes. **A**, Both eyes were forced opened by hands to show ulcers involving the skin and eyelid margin and conjunctival injection. The cornea was not affected. **B**, Examination under anesthesia showed tarsal conjunctival inflammation. **C**, Amniotic membrane (AM) was applied to cover the entire ocular surface as a temporary graft. **D**, On the following day,the patient comfortably opened both eyes. **E, F**, A second examination under anesthesia performed 9 days after AM transplantation showed that the upper tarsal conjunctival ulcer was covered by AM. **G**, Examination under anesthesia 3 months after surgery showed minimal scarring in the lid margin and tarsal conjunctiva. **H**, Twelve months after surgery the patient remained asymptomatic, and the ocular surface was not inflamed.

Table 1. Demographic Data

Cases	Age/Gender	Diagnosis	Drugs	Time of Hospitalization (Wks)
1	5/M	SJS	Ibuprophen	2
2	4/F	SJS	Ibuprophen	1
3	50/M	TENS	Neviparine	3
4	63/F	SJS	PCN	2
5	45/M	TENS	SMX/TMP	2
6	48/F	TENS	Lamotrigine	4
7	61/F	SJS	Vancomycin	2
8	47/F	TENS	Lamotrigine	8
9	30/M	SJS	Gentamicin	3
10	9/F	TENS	SMX/TMP	3
11	2/M	TENS	Azithromycin	2
12	16/M	TENS	Amoxacillin	4
13	39/F	TENS	Lamotrigine	4
14	21/F	TENS	SMX/TMP	4
15	51/M	TENS	Azithromycin	3
16	40/M	TENS	SMX/TMP	8
17	9/M	TENS	Amoxacillin	4
18	50/M	TENS	Carbamazepin	4
19	8/F	SJS	PCN	8
20	37/F	SJS	PCN	3
21	14/F	TENS	Amoxaciline	4
22	8/M	TENS	PCN	3
23	6/F	SJS	Ibuprophen	2
24	8/M	TENS	NA	5
25	18/M	TENS	Diclofenac Sodium	4
26	33/F	TENS	Ibuprophen	8
27	35/F	TENS	Leflunamide	3
28	43/F	TENS	PCN	5
29	49/F	TENS	Diclofenac Sodium	3
30	80/F	SJS	SMX/TMP	1
31	48/M	TENS	Diphenylhydantoin	8
32	62/M	TENS	PCN	8
33	25/F	SJS	PCN	2
34	22/F	TENS	Difenilhydantoin	4
35	35/F	TENS	Difenilhydantoin	4
36	29/F	TENS	NA	6
37	36/F	SJS	SMX/TMP	3
38	58/F	TENS	Senna	4

F = Female; M = male; NA = not available; PCN = penicillin; SJS = Stevens–Johnson syndrome; SMX/TMP = trimethoprim sulfamethoxazole; TENS = Toxic epidermal necrolysis.

and grade 2 (Fig 1E), 2 cases had grade 2 and grade 3, and 1 case had grade 1 and grade 3 between the two eyes.

Correlation of Variables

Further statistical analyses showed that there was no correlation between the extent of corneal complications and any of the following variables: time of hospitalization (Spearman r, 0.2976; 95% confidence interval [CI], −0.05–0.55; $P = 0.08$), floppy eyelid syndrome (Spearman correlation r, 0.1030; 95% CI, −0.23–0.42; $P = 0.5$), trichiasis (Spearman r, −0.25; 95% CI, −0.14–0.48; $P = 0.2$), open lacrimal punctum (Spearman r, −0.02; 95% CI, −0.34–0.31; $P = 0.9$), symblepharon (Spearman correlation r, −0.10; 95% CI, −0.41–0.23; $P = 0.5$), and ATD (Spearman r, −0.10; 95% CI, −0.42–0.22; $P = 0.5$). In contrast, there was a strong correlation between the extent of corneal complications and the eyelid margin–tarsal severity (Spearman r, 0.54; 95% CI, 0.25–0.73; $P = 0.0005$). To confirm the effect that the eyelid margin–tarsal severity had taken account of the effects of other variables, we performed multivariable regression analysis and noted that, indeed, the extent of eyelid-tarsal severity had a significant effect on corneal complications ($P = 0.006$, Table 2).

Correlation of Upper Lid Margin and Tarsal Pathologies with Upper Corneal Complications

Because there was a strong correlation between the pathology of keratinization and scarring of the lid margin and the severity of corneal complications (Table 2), we thus speculated that mechanical friction generated by the upper lids should have caused more severe corneal scarring and vascularization of the upper cornea. Indeed, we have identified a total of 27 cases with such a strong topographic and spatial correlation. Figure 3 illustrates 3 such cases. The pannus of the upper cornea was associated with conjunctivalization in 13 cases (Fig 3A–D) and with severe squamous metaplasia in 14 cases (Fig 3E, F).

We further confirmed that the upper tarsus of all 38 patients with SJS showed scar formation resulting from prior ulceration. Figure 4 summarizes 4 such representative changes, revealing different extents of scarring associated with the lid margin keratinization and scarring. In the severest extent, such scarring caused cicatricial entropion, which, together with symblepharon, frequently resulted in exposure keratitis or ulceration because of incomplete or infrequent blinking. Furthermore, scarring in the

Table 2. Multivariable Regression Analysis

Variables	Coefficient	95% Confidence Intervals	P Values
Eyelid margin-tarsal severity Grading	0.77	0.35–1.85	0.006
Time of hospitalization	0.09	−0.04–0.23	0.08
Floppy eyelid syndrome	−0.23	−0.06–0.12	0.19
Trichiasis	0.46	−0.14–1.07	0.13
Open lacrimal punctum	−0.05	−0.22–0.10	0.48
Symblepharon	−0.21	−0.84–0.41	0.50
Aqueous tear deficiency	−0.21	−0.75–0.32	0.42

superior temporal fornix frequently resulted in ATD dry eye (data not shown).

Corneal Complications Observed during the Hospitalization Time

Five cases had acute corneal complications such as persistent epithelial defect (2 cases), corneal ulcers (2 cases), and corneal perforation (1 case). Interestingly, all these cases were asymmetric, and their visual acuities were compromised during hospitalization time; they also had TENS.

Discussion

For SJS/TENS, severe inflammation and ulceration, if allowed to be recalcitrant and chronic, led to scarring (cicatrix). Depending on the site of involvement, such cicatrix may result in ATD (obliterating lacrimal excretory ducts), LTD (obliterating meibomian orifices), fornix shortening, symblepharon, ankyloblepharon, punctal stenosis, trichiasis and entropion. On the bulbar conjunctiva, it may cause squamous metaplasia, ranging from goblet cell loss to frank keratinization.[8] On the limbus, it may lead to limbal stem cell deficiency.[9] On the cornea, it may result in scar and vascularization. Indeed, these 38 cases with chronic SJS/TENS manifested different extents of the aforementioned cicatricial complications. The central question we would like to address in this report is whether one or several of these cicatricial problems leads to corneal complications.

Although, any of the preceding cicatricial problems, if left unattended, can potentially lead to corneal complications, our analyses disclosed that the extent of corneal complications was most significantly correlated with lid margin/tarsal scarring (Table 2). On the one hand, the relationship between the two is purely correlative and not causative, because inflammation and ulceration can attack both the lid margin/tarsus and the cornea simultaneously at the acute stage. This interpretation was supported by the finding that a small proportion of 5 cases (13 %) had corneal complications develop during or immediately after hospitalization as a result of corneal ulcer or perforation. These 5 cases all had asymmetric involvement and TENS. On the other hand, it is more plausible that the relationship between the two is causative. This interpretation was supported by the finding that most of the 33 cases (87%) retained clear vision on discharge from the hospital as illustrated in our case report, in which ulceration was present in the tarsal conjunctiva, but not the cornea, at the acute stage (Fig 2). Furthermore, this interpretation was also supported by the finding that the upper cornea was preferentially involved and correlated well with upper lid margin/tarsal pathologies (Fig 3), and such a corneal pathology worsened with time (not shown). On the basis of this interpretation, chronic microtrauma will cause more corneal complications even if the cornea and the lids/tarsus are simultaneously involved in the acute stage.

Therefore, we speculate that lid margin/tarsal pathologies generate blink-related microtrauma, a concept recently summarized and reviewed by Cher et al,[10] to the corneal surface. It was also worth noting that all SJS/TENS manifested meibomian gland orifice metaplasia, which could lead to LTD aggravating blink-related microtrauma because of the lack of lubricity. By the use of the kinetic analysis of tear interference images, we detected the presence of blink-related microtrauma even in eyes without notable corneal complications (i.e., grade 1 [unpublished observation]), resembling the pattern seen in patients with LTD dry eye.[11] If the reserve of limbal epithelial stem cells is healthy, chronic microtrauma to the ocular surface may lead to hyperproliferation-induced squamous metaplasia,[12] generating the corneal pannus similar to superior limbic keratoconjunctivitis.[13] However, if the reserve is poor, chronic microtrauma may facilitate their population attrition, leading to limbal stem cell deficiency manifesting conjunctivalization. Indeed, we noted 13 cases had limbal stem cell deficiency develop, whereas 14 cases had squamous metaplasia develop. By use of impression cytology, we reported that both conjunctivalization and squamous metaplasia can occur in patients with SJS.[9] Collectively, these 2 pathologic changes in the cornea lead to a severe loss of vision. If we extrapolated the concept that we have learned from the study of SJS/TENS to other cicatricial diseases like trachoma and ocular cicatricial pemphigoid, we also speculate that corneal blindness is not directly caused by the disease itself but by a late event caused by blink-related microtrauma as a result of lid/tarsus cicatricial problems.

Although other cicatricial problems were not significantly correlated with corneal complications, they did contribute to corneal morbidity. For example, ATD dry eye was present in 21 cases; they were also found to have focal scarring in the superior temporal fornix (unpublished observation). Among them, we were surprised to note that 7 cases

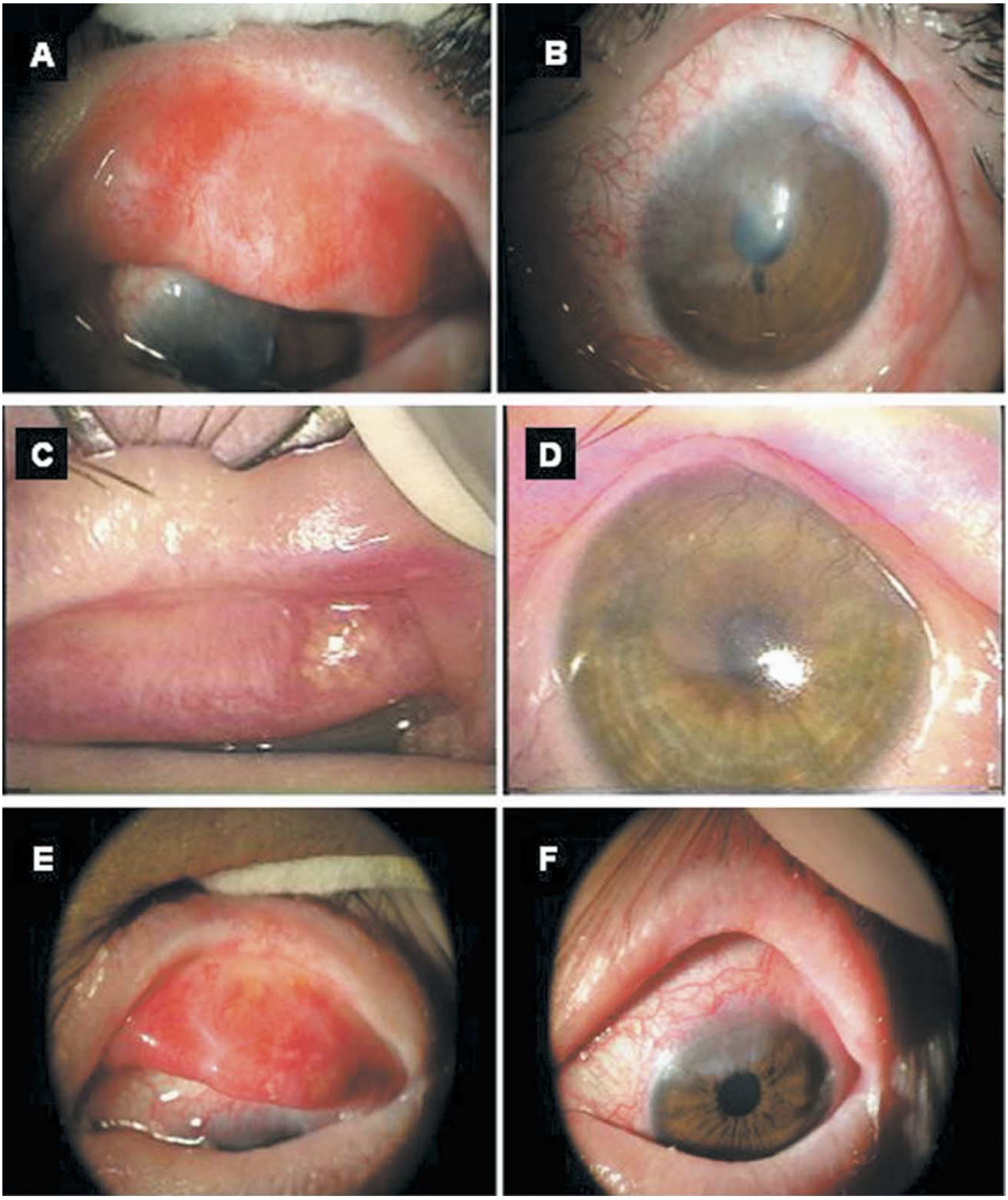

Figure 3. Correlation between eyelid margin/tarsal pathology and corneal complication. In these 2 representative cases, corneal pannus corresponding to focal limbal stem cell deficiency was correlated with the upper lid margin/tarsal pathologies in the same eye (**A, B** and **C, D**, respectively). In another representative case, corneal pannus corresponding to squamous metaplasia was correlated with the upper lid margin/tarsal pathologies in the same eye (**E, F**).

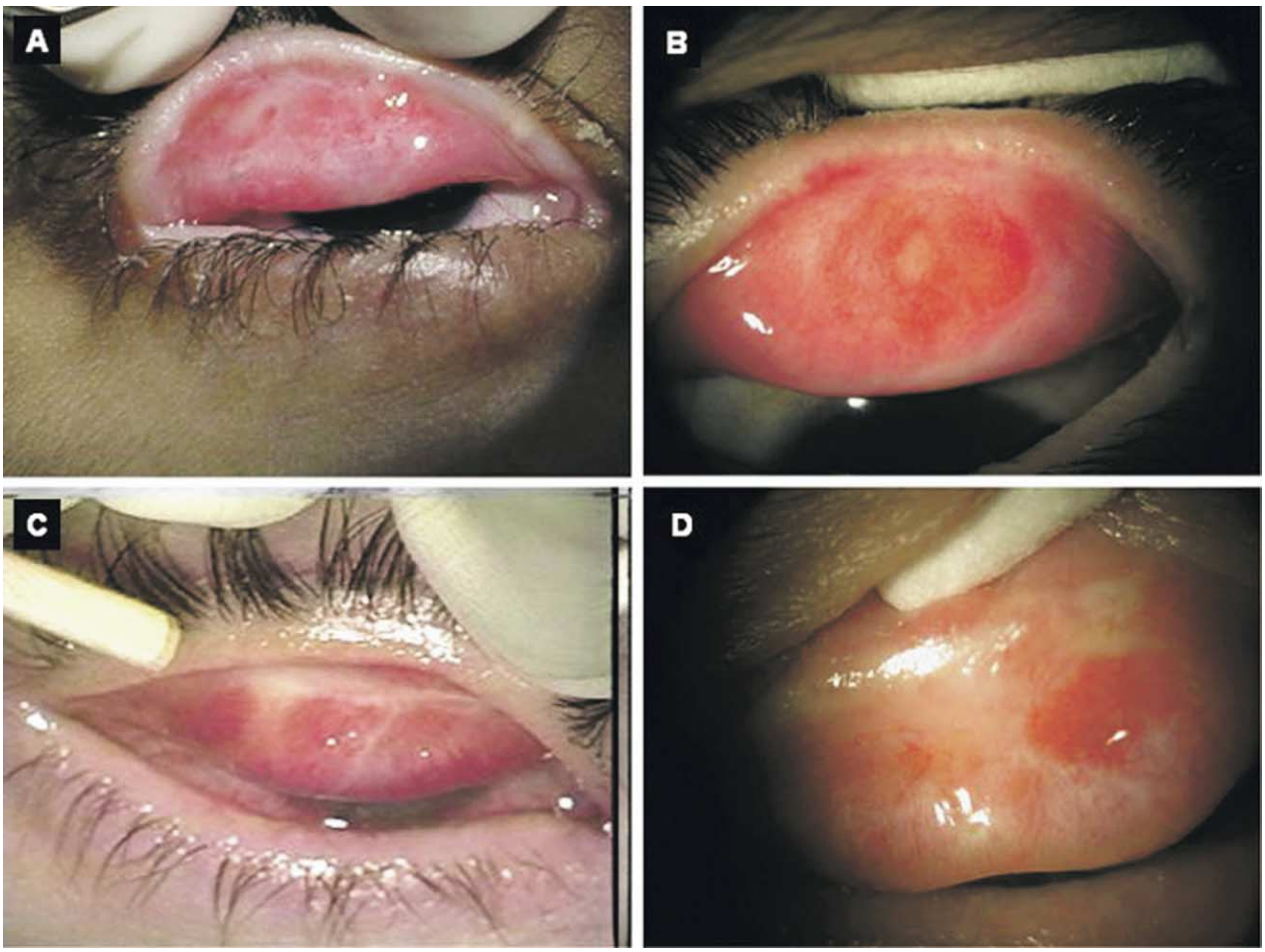

Figure 4. Representative cases with tarsal scar changes. In the chronic stages, tarsal conjunctival ulcers healed with different manifestations: mild subconjunctival scar (**A**), moderate bandlike scar with meibomian gland constipation (**B**), severe tarsal scar without entropion (**C**), and severe broad-band scar with contraction of tarsal plate and cicatricial entropion (**D**).

(33.3%) still had open puncta, indicating inadequate, if not improper, management. It has been recognized that ATD is a high risk factor adversely affecting the surgical outcome of keratolimbal allograft in patients with SJS/TENS.[14] It should also be noted that severe cicatricial complications of the lid margin and the tarsus might also result in entropion and deficiency in lid closure and blinking, collectively leading to exposure keratitis and aggravating the corneal complications. It is no wonder that surgeries to correct these cicatricial problems are mandatory to achieve subsequent successful ocular surface reconstruction by limbal stem cell transplantation (for a recent review, see 15).

Our study further demonstrated that the lid margin/tarsal scarring pathologies noted at the chronic stage were most likely caused by inflammation and ulceration at the acute stage. This notion was supported by the case report with acute SJS (Fig 2) and further supported by the finding that there were variable extents of lid margin and tarsal scarring in all 38 cases (Fig 4). During the acute attack, patients with SJS or TENS are severely ill, and the initial management is understandably directed to the life support. Because both eyes tend to be closed, as shown in the case report, caretakers may not suspect serious eye involvement. Besides severe conjunctival inflammation, the other hallmark of acute SJS/TENS is tarsal ulceration. We were intrigued by the finding that 52.6 % of patients also manifested notable floppy eyelids. Future studies are needed to determine whether floppy eyelids are preexisting and may promote the development of conjunctival inflammation and/or tarsal ulceration in patients with SJS/TENS.

Amniotic membrane transplantation has been shown to be effective in suppressing inflammation (for review see Ref. 16). Consistent with what has been reported by John et al,[5] transplantation of AM as a temporary patch was effective in suppressing inflammation and promoting healing of tarsal ulceration in 1 case with acute SJS/TENS (Fig 2). Therefore, it is advisable that AM transplantation be considered as an important measure to suppress inflammation and to promote healing during the acute stage of SJS/TENS, so as to prevent the formation of cicatricial complications at the chronic stage. Measures such as bandage contact lenses and scleral lenses[17–19] to prevent blink-related microtrauma and surgeries, such as mucous membrane graft to correct the lid margin and tarsal

pathologies, are critical to prevent the loss of vision caused by corneal complications.

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