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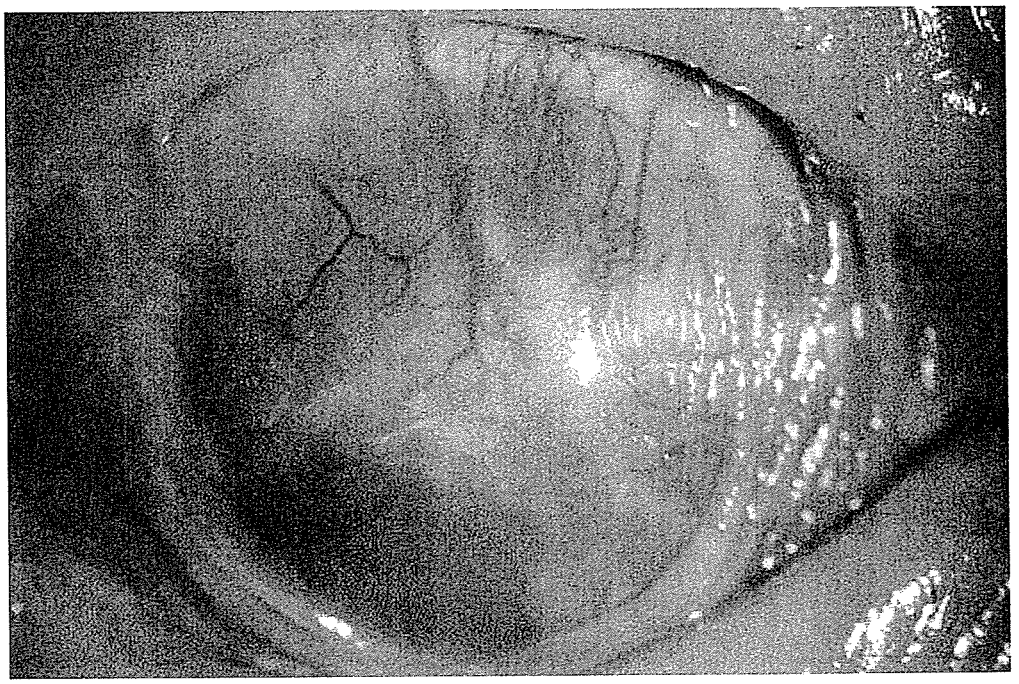
Figure1

A.



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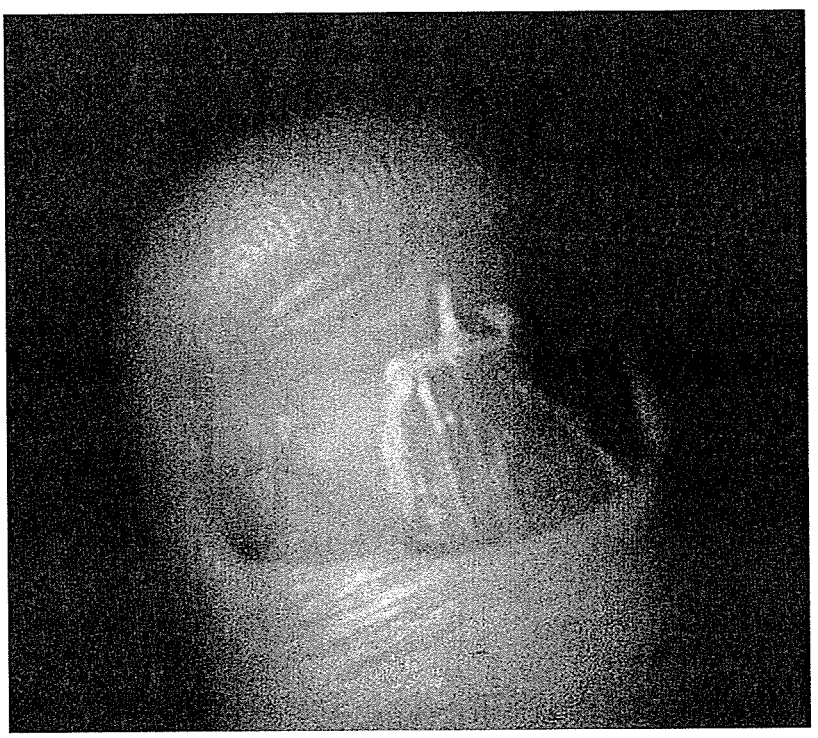
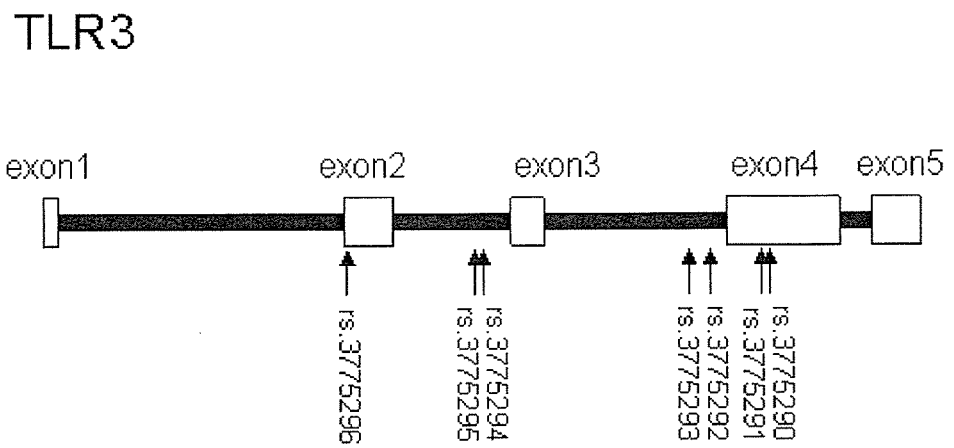


Figure2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A NEW GRADING SYSTEM FOR THE EVALUATION OF CHRONIC OCULAR MANIFESTATIONS IN PATIENTS WITH STEVENS-JOHNSON SYNDROME

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Running head: A new way to grade ocular manifestations in Stevens-Johnson syndrome

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ABSTRACT

Purpose: To evaluate and grade the extent and severity of chronic ocular manifestations in Stevens-Johnson syndrome (SJS).
Design: Prospective, multicenter case series.
Participants: We enrolled 73 patients (138 eyes) with SJS seen between April 2003 and March 2005 at 3 tertiary referral centers.
Methods: Patients with a confirmed history of SJS and chronic ocular complications that persisted for at least 1 year from the onset of SJS were included. Their detailed medical history and ophthalmic examination results were recorded on an itemized data-collection form. Complications were categorized as corneal-, conjunctival-, and eyelid complications and 13 components were evaluated and graded on a scale from 0 to 3 according to their severity.
Main Outcome Measures: These were broadly classified as corneal- (superficial punctate keratopathy, epithelial defect, loss of the palisades of Vogt, conjunctivalization, neovascularization, opacification, keratinization), conjunctival- (hyperemia, symblepharon formation), and eyelid complications (trichiasis, mucocutaneous junction involvement, meibomian gland involvement, punctal damage).
Results: The most severely affected complication components were loss of the palisades of Vogt (114 eyes, 82.6%) and meibomian gland involvement (102 eyes, 73.9%). Visual acuity in 74 of the 138 eyes (53.6 %) was worse than 20/200. The severity of corneal-, conjunctival-, and eyelid complications was significantly correlated with visual loss. All 13 complications were significantly correlated with LogMAR visual acuity; the correlation coefficient (R) ranged from 0.359 to 0.810 ($p<0.0001$); for corneal epithelial defects R was 0.169 ($p=0.0473$). Eyes with a higher total score for the 3 complication categories had poorer vision ($R= 0.806$, $p<0.0001$). Multivariable regression analysis showed that corneal neovascularization, opacification, keratinization, and cataracts significantly affected logMAR ($p<0.0001$, $p<0.0001$, $p=0.0142$, $p=0.0375$, respectively)
Conclusions: We describe a new method for grading the extent and severity of ocular involvement in patients with SJS and demonstrate that the severity of ocular involvement was significantly correlated with the final visual outcome. This new grading system provides a more objective method for evaluating SJS patients and may be adapted for use in other cicatricial ocular surface diseases.

INTRODUCTION

Stevens-Johnson syndrome (SJS) is an acute, self-limiting disease of the skin and mucous membranes that predisposes patients to life-threatening complications such as sepsis, respiratory dysfunction, and multiorgan failure. In the acute stage, more than 50% of patients experience ocular complications ranging from minimal (e.g., mild conjunctival hyperemia) to very severe (e.g., corneal melting and perforation).[1-4] Inflammation and epithelial erosion of the ocular surface often persist beyond the acute stage and the resolution of skin eruptions, leading to ocular complications and scarring in the chronic stage. Severe ocular surface disease arising from SJS encompasses a spectrum of ocular manifestations and complications that is often associated with significant visual morbidity. Visual impairment and ocular discomfort continue throughout life and patients usually require long-term medication for disease control.

Over the past 40 years, it has been widely accepted that erythema multiforme (EM), SJS, and toxic epidermal necrolysis (TEN) are part of a single "EM spectrum".[5-7] However, as no clear diagnostic criteria have been established, reaching a definitive diagnosis can be difficult. Roujeau et al.,[6] who performed a retrospective analysis of the type and distribution of skin lesions and the extent of epidermal detachment, concluded that EM major (EMM) and SJS were two separate clinical entities that differed with respect to histopathologic changes and etiology. A large international case-control study, called the Severe Cutaneous Adverse Reaction (SCAR) study, prospectively evaluated the validity of this clinical distinction; its results strongly supported the hypothesis that EMM is different from SJS and TEN, and that SJS and TEN are severity variants of a single entity.[5] The classification was based on the clinical appearance and pathology of skin lesions present in the "acute stage". However, patients often present to ophthalmologists in the late stage of the disease with chronic cicatricial complications, after resolution of the dermatological changes, and it can be difficult to elicit the original clinical manifestations used to distinguish between EMM and SJS/TEN from patients seen many years after disease-onset. Therefore, from the ophthalmologist's perspective, ocular surface diseases arising from EM, SJS, or TEN are often collectively regarded as SJS.

Corneal transplantation in SJS patients with severe ocular surface disease is associated with a poor prognosis. Persistent epithelial defects occurring after penetrating- or lamellar keratoplasty often progress to corneal melting and perforation. Transplanted limbal stem cells or keratoepithelioplasty in these chronically inflamed eyes often elicit graft rejection and loss of donor epithelial cells, resulting in progressive conjunctivalization, scarring, and visual loss.[8,9] Over the past decade, new ocular surface reconstructive procedures such as amniotic membrane- and cultivated epithelial transplantation yielded promising results for the treatment of SJS.[10,11] However, despite its potentially devastating nature and the increasing indications for ocular reconstructive surgery, there is currently no standardized method for evaluating the spectrum of ocular manifestations and the severity of ocular complications in this blinding disease.

The aim of this study was to elucidate the profile of chronic ocular manifestations in SJS patients, and to develop an objective method for grading the extent and severity of ocular complications in patients with cicatricial ocular surface diseases. Three large tertiary referral ophthalmic centers participated in this multicenter study; to our knowledge, it represents the largest series of SJS patients with ophthalmic complications studied to date. As it provides a common platform for the discussion and

management of these patients, this study has important clinical implications for the diagnosis, treatment, and the prediction of visual outcomes in patients with SJS.

PATIENTS AND METHODS

Patients

The 3 ophthalmic centers that participated in this multicenter study are Kyoto Prefectural University of Medicine, Keio University, and Tokyo Medical Center. All patients with chronic ocular complications from SJS who were referred to these centers between April 2003 to March 2005 were prospectively evaluated in this study. Patients with a confirmed history of SJS and chronic ocular complications that persisted for at least 1 year from the onset of SJS were included. The diagnosis of SJS was based on a confirmed history of the acute onset of high fever, serious mucocutaneous illness with skin eruptions, and involvement of at least 2 mucosal sites including the ocular surface. Eyes with a past history of ocular surface surgery were excluded from this study. The study was approved by the Ethics Committee and Institutional Review Boards of each institute; the guidelines of the Declaration of Helsinki in Biomedical Research Involving Human Subjects were followed, and written informed consent was obtained from each patient.

The symptomatology, physical findings, detailed ophthalmic examination results, and ocular complications were recorded on an itemized data-collection form. The detailed ophthalmic examination included an assessment of visual acuity, tonometry, slit-lamp examination, fluorescein staining, and anterior-segment photography. A careful drug history was also taken by the attending physician. A drug was considered a possible etiologic agent if it had been taken shortly before the onset of symptoms, i.e. within 2 weeks of disease onset. If the reaction showed signs of regression during the continued administration of the drug, a causal relationship was considered unlikely.

Classification and grading of ocular involvement

We considered 13 components of 3 categories of ocular complications to be important in the assessment of the 138 eyes; each component was graded on a scale from 0 - 3 depending on the severity of involvement. The complications were broadly classified as corneal complications comprised of superficial punctate keratopathy, epithelial defect, loss of the palisades of Vogt, conjunctivalization, neovascularization, opacification, and keratinization components, conjunctival complications with hyperemia and symblepharon formation as the components, and eyelid complications consisting of trichiasis, mucocutaneous junction involvement, meibomian gland involvement, and punctal damage as the evaluated components. The following classification and grading system were used to evaluate the nature of the ocular complications in these patients:

Corneal complications

1. Severity of superficial punctate keratopathy (SPK). We used fluorescein staining and a simplified method of Miyata et al.[12] to grade SPK based on the area and density of the lesions. The area was graded as A0 when there was no punctate staining and as A1, A2, or A3 when the area occupied less than one-third, one-third to two-thirds, or more than two-thirds of the cornea, respectively. Density was graded as D0 when there was no punctate staining and as D1, D2, or D3 when density was sparse, moderate,

or high and the lesions overlapped, respectively. While Miyata *et al.*[12] used the sum of the grades assigned to the area and density to obtain the final grade for the eye, we simplified their grading system and assigned scores of 0 - 3: A1D1 was scored as 0; A1D2 or A2D1 as 1; A1D3, A2D2, or A3D1 as 2, and A2D3, A3D2, or A3D3 as 3.

2. *Corneal epithelial defect.* The extent of corneal epithelial defect was scored from 0 - 3, where 0 = no epithelial defect, 1 = epithelial defect involving less than one-quarter of the corneal surface, 2 = defect involving one-quarter to half-, and 3 = defect involving more than half of the corneal surface.

3. *Loss of the palisades of Vogt.* The extent of the loss of the limbal palisades of Vogt (POV) was graded from 0 - 3, where 0 = presence of the entire POV, 1 = loss of less than half of the entire circumference of POV, 2 = loss of more than half of the entire circumference of POV, and 3 = total loss of POV.

4. *Conjunctivalization.* The extent of conjunctivalization was graded clinically from 0 - 3 as follows: 0 = absence of conjunctivalization, 1 = conjunctivalization involving less than one-quarter of the corneal surface, 2 = conjunctivalization involving one-quarter to half-, and 3 = conjunctivalization involving more than half of the corneal surface (Fig. 1).

5. *Corneal neovascularization.* The extent of corneal neovascularization was scored from 0 - 3, where 0 = no neovascularization, 1 = neovascularization confined to the corneal periphery, 2 = neovascularization extending up to the pupil margin, and 3 = neovascularization extending beyond the pupil margin into the central cornea (Fig. 1). In eyes where significant opacification or extensive symblepharon formation made it difficult to evaluate corneal neovascularization a score of 3 was assigned.

6. *Corneal opacification.* The severity of corneal opacification was graded from 0 - 3, where 0 = clear cornea with iris details clearly visualized, 1 = partial obscuration of the iris details, 2 = iris details poorly seen with pupil margin just visible, and 3 = complete obscuration of iris and pupil details (Fig. 1).

7. *Corneal keratinization.* The extent of keratinization was graded from 0 - 3, where 0 = no corneal keratinization, 1 = keratinization involving less than one-quarter of the corneal surface, 2 = keratinization involving one-quarter to half-, and 3 = keratinization involving more than half of the corneal surface (Fig. 1).

Conjunctival complications

8. *Conjunctival hyperemia.* Conjunctival hyperemia was graded from 0 - 3 based on the following clinical features: 0 = absence of hyperemia, 1 = mild- (mild or sectoral engorgement of the conjunctival vessels), 2 = moderate- (diffuse engorgement of the conjunctival vessels), and 3 = severe hyperemia (significant engorgement of the conjunctival vessels).

9. *Symblepharon formation.* The extent of symblepharon formation was scored from 0 - 3, where 0 = no symblepharon, 1 = symblepharon formation involving only the conjunctival surface, 2 = symblepharon formation involving less than half-, and 3 = symblepharon formation involving more than half of the corneal surface (Fig. 1).

Eyelid complications

10. *Trichiasis.* The extent of trichiasis for the total area of the upper and lower eyelids combined was scored as 0 - 3, where 0 = no trichiasis, 1 = trichiasis involving less than one-quarter of the lid margin, 2 = trichiasis involving one-quarter to half-, and

3 = trichiasis involving more than half of the lid margin.

11. Mucocutaneous junction involvement. The severity of mucocutaneous junction involvement was scored from 0 - 3, where 0 = normal mucocutaneous junction and 1, 2, and 3 are mild-, moderate-, and severe irregularity of the mucocutaneous junction (Fig. 2). Fluorescein staining of the conjunctiva was helpful to evaluate the involvement of the mucocutaneous junction. Normal mucocutaneous junction showed the linear staining at the end of the conjunctiva, and either mild-, moderate-, or severe irregularity of this line was observed in the eyes with mucocutaneous junction involvement. In eyes where significant keratinization of the lid margin or extensive symblepharon formation made it difficult to evaluate mucocutaneous junction involvement, a score of 3 was assigned.

12. Meibomian gland involvement. The severity of meibomian gland involvement was determined clinically by the nature of the meibomian gland secretion expressed manually at the center of the upper lid, and scored from 0 - 3, where 0 = clear oily fluid expressed, 1 = yellowish-white oily fluid expressed, 2 = thick cheesy material expressed, and 3 = inability to express any fluid from the meibomian glands.

13. Punctal involvement. Punctal damage and occlusion were graded from 0 - 3, where 0 =normal patent puncta, 1 = iatrogenic punctal occlusion (e.g., punctal plugs or suture), 2 = either superior or inferior puncta occluded by scarring, and 3 = both superior and inferior puncta occluded by scarring.

Overall total score

Each eye was evaluated and graded by at least 2 trained corneal specialists. When the scores varied from one corneal specialist to another, the scores were averaged or determined after a discussion. The results were then added together to give an overall score from 0 to 39, with 39 representing the most severely affected eyes.

Visual acuity

We categorized the 138 eyes from the 73 patients according to their visual acuity. In group 1 (n=28 eyes) visual acuity was 20/20 or better, in group 2 (n=36 eyes) it was worse than 20/20 and up to and including 20/200, in group 3 (n=32 eyes) it was worse than 20/200 and up to and including 20/2000, and in group 4 (n=42 eyes) it was worse than 20/2000.

Eye complications independent of ocular surface disorders

Cataract, glaucoma, retinal diseases, or other eye diseases independent of ocular surface disorders were also evaluated and their presence, absence, or the inability to diagnosis due to ocular surface abnormality was recorded.

Statistical analysis

Spearman correlation coefficients (two-tailed) were used to evaluate whether the scores of the 13 components were correlated with logarithm of the minimum angle of resolution (LogMAR) visual acuity. The correlation between the total score and logMAR and the correlations between the subtotal scores of 3 problem categories and the total score were also evaluated. Using a logistic regression model, the scores for each of the 13 components in eyes with better visual acuity (20/200 or better; i.e., groups 1 and 2) were compared with the scores obtained for eyes with poorer visual

acuity (worse than 20/200; i.e., groups 3 and 4). The statistical model for predicting logMAR visual acuity was calculated using a linear model with stepwise variable selection (multivariable regression analysis). In multivariable regression analysis, cataract and glaucoma were graded as follows: with cataract, 1; without cataract or lens invisible, 0; with glaucoma, 1; and without glaucoma or unable to diagnosis glaucoma, 0. All statistical tests were conducted at a 5% level of significance.

RESULTS

A total of 138 eyes of 73 patients from the 3 institutions were included in this study. There were 33 males and 40 females. Their age ranged from 10 to 83 years (47.9 ± 18.5, mean ± SD). At disease onset, the patients' age ranged from 2 to 69 years (mean 28.4 ± 18.2 years), and the duration of the illness prior to seeking consultation at our centers ranged from 1 to 54 years (18.8 ± 15.5). Drugs were the most commonly associated etiologic factor in 47 patients (64.4%). Because 14 of these patients used 2 or 3 types of drugs simultaneously it was difficult to identify the drug(s) implicated in disease-onset, therefore, we considered all their drugs causative. The causative drugs were antibiotics in 21 patients, cold remedies in 18, non-steroidal anti-inflammatory drugs (NSAIDs) in 10, anticonvulsants in 6, and other in 4 patients. The precise history regarding the use of drugs was unclear in 20 patients because of the long interval between disease-onset and this study.

Corneal complications

A detailed summary of the 7 evaluated components comprising corneal complications is shown in Table 1. Among the 138 eyes examined, 114 (82.6%) manifested a total loss of POV (grade 3). Moderate to severe (grade 2 or 3) corneal SPK was present in 93 eyes (67.4%), neovascularization in 83 (60.1%), and conjunctivalization in 82 (59.4%).

Conjunctival and eyelid complications

Among the 6 evaluated components that comprise conjunctival and eyelid complications, the meibomian glands were most frequently and most severely involved; 102 of the 138 eyes (73.9%) manifested grade 3 meibomian gland involvement (Table 2). The scores for punctal damage and mucocutaneous involvement were also high; grade 2 or 3 punctal damage was assigned to 93 eyes (67.4%), and grade 2 or 3 mucocutaneous involvement to 71 eyes (51.4%).

Eye complications independent of ocular surface disorders

Cataract was observed in 11 eyes out of 138 eyes. Glaucoma was diagnosed in 4 eyes, none of which had central loss of visual fields. There were no other eye complications independent of ocular surface disorders.

Visual acuity

The number of eyes in each of the 4 groups was fairly evenly distributed (Table 3). Of the 138 eyes examined, 74 (53.6%) had visual acuity worse than 20/200 (group 3, n=32; group 4, n=42). Only 28 eyes (20.3%) had visual acuity equal to or better than 20/20.

Correlation between visual acuity and grade of complications

When we compared eyes with better (20/200 or better) and worse (worse than 20/200) visual acuity with respect to the scores obtained for each of the 13 components, we found that with the exception of epithelial defect, the scores differed significantly (Table 4).

We estimated the correlation coefficient between the visual acuity of the 138 eyes and the severity grade, scored from 0 - 3, of each of the 13 evaluated components in the 3 categories of complications. We found that all 13 components were significantly correlated with logMAR; the correlation coefficient (R) ranged from 0.359 to 0.810 ($p<0.0001$); for corneal epithelial defects R was 0.169 ($p=0.0473$) (Table 5). Of all the scores, corneal neovascularization, opacification, and conjunctivalization were most highly correlated with poor vision ($R= 0.810$, $p<0.0001$; $R= 0.784$, $p<0.0001$; and $R= 0.726$, $p<0.0001$, respectively).

The statistical model for predicting logMAR was calculated using a linear model with stepwise variable selection as follows: logMAR = -0.2573 + cataract* 0.4153 + POV* 0.2814 + SPK* 0.08551 + epithelial defect* 0.3018 + neovascularization* 0.3471 + opacification* 0.3202 + keratinization* 0.1347. This multivariable regression analysis showed that corneal neovascularization, opacification, keratinization, and cataract had a significant effect on logMAR (Table 6). The predicted logMAR was significantly correlated with the actual logMAR visual acuity measured ($R=0.960$, $p<0.0001$).

Overall total score

The mean overall total score for the 13 components was 19.3 ± 9.5 (range 0 to 35). As shown in Tables 3 and 4 and Fig. 2, eyes with a higher total score had poorer vision. The averaged scores for the 4 visual acuity groups were: group 1, 5.86 (range 0-19), group 2, 16.64 (range 2-28), group 3, 23.31 (range 15-33), and group 4, 27.45 (range 18-35). Pearson's analysis clearly demonstrated that the total score was significantly correlated with logMAR visual acuity ($R=0.806$, $p<0.0001$) (Fig. 3). The subtotal scores of 3 problem categories correlated with the overall total score (Fig. 4).

DISCUSSION

Severe ocular surface disease arising from SJS or TEN is associated with significant visual morbidity.[1-4] The evaluation of ocular complications in these patients is extremely important as ocular involvement often represents the only long-term complication of SJS. There is currently no established method for evaluating the spectrum of ocular manifestations arising from these diseases. In this study, we detailed the characteristic ocular complications in the chronic stage of SJS, and developed a grading system to assess more objectively the extent and severity of 13 components of these ocular complications. To the best of our knowledge, this is the first study that specifically attempted to improve and standardize the evaluation of ocular complications in SJS.

As we set out to develop a grading system that could be used easily by ophthalmologists, we identified complications that were important and could be easily evaluated by simple slit lamp examination. After several pilot studies, we eventually settled on 13 components of 3 categories of complications that we considered important for the assessment of severe or cicatricial ocular surface disorders. We used a simple

method for grading the severity of these complications, the components were assigned scores that reflected whether involvement was mild, moderate, or severe. This grading system was judged easy and convenient at the 3 participating ophthalmology centers that evaluated 138 eyes from 73 SJS patients. The results obtained at the 3 centers were consistent and comparable. Ours is one of few prospective studies on the ocular complications of SJS, and each patient was carefully evaluated by at least 2 ophthalmologists. To the best of our knowledge, this is the largest study reported to date.

The initial ocular pathologic process in SJS, inflammation and necrosis of the conjunctiva, is often accompanied by the destruction of goblet cells.[4,13,14] The production of mucin by these cells is vital for maintaining an adequate tear film essential for corneal clarity. Dry eye secondary to goblet cell destruction is the most common long-term ocular complication in patients with various ocular surface diseases.[4,13,14] Cicatricial lid- and conjunctival complications include symblepharon formation, forniceal shortening, keratinization, lid malposition (e.g., entropion), and misdirected eyelashes (trichiasis).[4,13,15-22] Limbal stem cell destruction, evidenced by loss of the POV, may also occur at disease onset and be accompanied by severe inflammation. The combination of these complications may result in recurrent corneal erosion, ulceration, vascularization, stromal scarring, conjunctivalization of the corneal surface, and progressive corneal melting and perforation.[4,13,15-22]

In our study, drugs were the most commonly identified etiologic factor; in 47 patients (64.4%) antibiotics (n=21 patients) cold remedies (n=18 patients), or NSAIDs (n=10) were the causative agents. These findings are consistent with previous reports.[15,16,19,23]

Of all the complications, severe (grade 3) meibomian gland involvement and loss of the POV (102 and 114 eyes, respectively) were the most common ocular complications of SJS. We found that the total score for each eye was significantly correlated with its visual acuity; consistently, eyes with higher overall scores had poorer vision. We categorized the complications as those involving predominantly the cornea, the conjunctiva, and the eyelid. As expected, corneal complications were most likely to have a detrimental effect on vision. In particular, corneal neovascularization and opacification were highly correlated with post-treatment visual acuity in the chronic stage. Conjunctivalization, a sequela of limbal stem cell deficiency, was also correlated with poor vision in our series.

In our study, there was a high rate of lid complications in chronic SJS. Of the eyelid complications, meibomian gland involvement was moderate or severe (grade 2 or 3) in 111 of the 138 eyes (80.4%). We found that eyes without apparent corneal complications also manifested cicatricial eyelid changes. As such, the meibomian glands appear to be susceptible to the injury following SJS. As the meibomian glands play a critical role in the stabilisation of the tear film, this is likely to contribute to the disruption of the tear film and severe dry eye condition experienced in patients in the chronic stage of SJS.

The use of a standardized method for grading the extent and severity of ocular complications in SJS patients offers significant advantages. The grading system introduced here can be used in the initial evaluation and the follow-up and monitoring of ocular complications in SJS patients. As documented here, the lid margin is a commonly affected site in the disease process. However, because attention often focuses

on the ocular surface, changes in the lid margin may be overlooked. Our grading system ensures that important ocular complications are detected by corneal specialists as well as non-specialized ophthalmologists.

Ocular surface reconstructive procedures such as limbal- and cultivated epithelial stem cell transplantation have been used to treat severe ocular manifestations in SJS patients.[8-11,24] However, as many of the reported studies are non-randomized case series without control arms and as there is currently no standardized method for grading ocular complications in SJS patients in the acute and chronic stage, it is difficult to compare the treatment outcomes of these studies. Our grading system also provides a standardized method for evaluating patients prior to corneal and ocular surface transplantation procedures. The use of an objective method of grading the severity of the patient's preoperative condition may ultimately help in prognosticating the long-term clinical outcome of these eyes following surgery.

This is the first study that describes a method for classifying and grading the severity of ocular involvement in SJS patients. Our findings have important clinical implications and facilitate the objective evaluation of patients with ocular complications from of SJS. The method presented here may be adapted for use in patients with cicatricial ocular surface diseases arising from other causes such as ocular cicatricial pemphigoid and chemical injury. It also provides a common platform for the discussion and management of patients with ocular surface disorders and may be useful for predicting treatment outcomes. Our method also enables ophthalmologists to monitor more objectively the progression of complications during the follow-up of these patients.

Table 1. Summary of corneal complications

Complications	Grade 0	Grade 1	Grade 2	Grade 3
	No. (%)	No. (%)	No. (%)	No. (%)
Superficial punctuate keratopathy (SPK)	22(15.9)	23(16.7)	18(13.0)	75(54.3)
Epithelial defect	135(97.8)	2(1.4)	1(0.7)	0(0)
The loss of palisades of Vogt (POV)	21(15.2)	3(2.1)	0(0)	114(82.6)
Conjunctivalization	41(29.7)	15(10.9)	10(7.2)	72(52.2)
Neovascularization	35(25.4)	20(14.5)	22(15.9)	61(44.2)
Opacification	43(31.2)	41(29.7)	28(20.3)	26(18.8)
Keratinization	105(76.1)	10(7.2)	5(3.6)	18(13.0)

N=138

Table 2. Summary of conjunctival and eyelid complications

Complications	Grade 0	Grade 1	Grade 2	Grade 3
	No. (%)	No. (%)	No. (%)	No. (%)
Conjunctival complications				
Hyperemia	46(33.3)	61(44.2)	15(10.9)	16(11.6)
Symblepharon formation	40(29.0)	54(39.1)	21(15.2)	23(16.7)
Eyelid complications				
Trichiasis	42(30.4)	41(29.7)	44(31.9)	11(8.0)
Mucocutaneous junction involvement	16(11.6)	51(37.0)	34(24.6)	37(26.8)
Meibomian gland involvement	13(9.4)	14(10.1)	9(6.5)	102(73.9)
Punctal damage	36(26.1)	9(6.5)	15(10.9)	78(56.5)

N=138

Table 3. Ocular complications and visual acuity of SJS patients

	Visual acuity			
Complications	Group 1 VA equal or better than 20/20 Average grade	Group 2 VA 20/20 to 20/200 Average grade	Group 3 VA 20/200 to 20/2000 Average grade	Group 4 VA worse than 20/2000 Average grade
No. of eyes	28	36	32	42
Corneal complications				
SPK	0.82	1.92	2.40	2.78
Epithelial defect	0	0	0.03	0.07
The loss of POV	0.82	2.78	3.00	3.00
Conjunctivalization	0.11	1.36	2.59	2.76
Neovascularization	0.25	1.11	2.38	2.90
Opacification	0.11	0.61	1.66	2.31
Keratinization	0.04	0.11	0.50	1.26
Conjunctival complications				
Hyperemia	0.36	0.89	1.19	1.40
Symblepharon formation	0.18	0.97	1.19	2.07
Eyelid complications				
Trichiasis	0.57	1.08	1.38	1.50
Mucocutaneous junction involvement	0.79	1.56	1.91	2.10
Meibomian gland involvement	1.32	2.50	2.69	2.90
Punctal damage	0.50	1.78	2.65	2.58
Total score	5.86	16.64	23.31	27.45

Table 4. Comparison between ocular complications and visual acuity

Complications	VA of 20/200 or better - average grade	VA worse than 20/200 - average grade	P value
No. of eyes	64	74	
Corneal complications			
SPK	1.44	2.62	<0.0001
Epithelial defect	0	0.05	0.1208
The loss of POV	1.92	3.00	<0.0001
Conjunctivalization	0.81	2.69	<0.0001
Neovascularization	0.73	2.68	<0.0001
Opacification	0.39	2.03	<0.0001
Keratinization	0.08	0.93	<0.0001
Conjunctival complications			
Hyperemia	0.66	1.31	<0.0001
Symblepharon formation	0.63	1.69	<0.0001
Eyelid complications			
Trichiasis	0.86	1.45	0.0002
Mucocutaneous junction involvement	1.23	2.01	<0.0001
Meibomian gland involvement	2.02	2.81	<0.0001
Punctal damage	1.26	2.61	<0.0001
Total score	11.86	25.66	

Table 5. Correlation analyses between 13 complications and logMAR visual acuity

Complications	Coefficient	P value
Neovascularization	0.810	<0.0001
Opacification	0.784	<0.0001
Conjunctivalization	0.726	<0.0001
Symblepharon formation	0.649	<0.0001
SPK	0.601	<0.0001
The loss of POV	0.550	<0.0001
Punctal damage	0.518	<0.0001
Mucocutaneous junction involvement	0.488	<0.0001
Keratinization	0.477	<0.0001
Meibomian gland involvement	0.453	<0.0001
Hyperemia	0.383	<0.0001
Trichiasis	0.359	<0.0001
Epithelial defect	0.169	0.0473

Table 6. Multivariable regression analysis

Variables	Coefficient	95% Confidence Intervals	P values
Intercept	-0.2573	-0.5449-0.0303	0.0786
Neovascularization	0.3471	0.2113-0.4849	<.0001
Opacification	0.3203	0.1734-0.4672	<.0001
Keratinization	0.1347	0.0281-0.2413	0.0142
Cataract	0.4153	0.0249-0.8057	0.0375
The loss of POV	0.2814	-0.0784-0.6412	0.1228
SPK	0.0855	-0.0296-0.2006	0.1423
Epithelial defect	0.3018	-0.1057-0.7093	0.1434

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