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New Grading System and Treatment Guidelines for the Acute Ocular Manifestations of Stevens-Johnson Syndrome

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Purpose: To describe a new grading system and associated treatment guidelines for the acute ocular manifestations of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).

Design: Prospective case series.

Participants: Seventy-nine consecutive patients (158 eyes) evaluated and treated for acute ocular involvement in SJS or TEN during hospitalization.

Methods: Photographic and chart review of acute ocular findings, interventions received, and outcomes with regard to visual acuity, dry eye symptoms, and scarring sequelae at least 3 months after the acute illness.

Main Outcome Measures: Visual acuity, dry eye severity, and scarring of the ocular surface and eyelids were assessed after follow-up of at least 3 months.

Results: Cases graded as mild or moderate were managed medically. All had best-corrected visual acuity (BCVA) of 20/20, no dry eye symptoms, and no scarring sequelae. Cases graded as severe or extremely severe were treated with urgent amniotic membrane transplantation (AMT) in addition to medical management. Severe cases all had BCVA of 20/20 and mild or no dry eye problems. Five of 28 patients had mild tarsal conjunctival scarring. No other scarring sequelae occurred. Nine of the 10 extremely severe cases had BCVA of 20/20 (1 was 20/30). Three of 10 had moderate scarring of the tarsal conjunctiva and lid margins and also moderate dry eyes with severe photophobia. Seven of 10 had only mild or no dry eye symptoms and scarring sequelae.

Conclusions: This grading system facilitates decision making in the evaluation and management of the acute ocular manifestations of SJS and TEN. Mild and moderate cases have a low risk of significant scarring or visual sequelae and may be monitored and treated medically if not worsening. Severe and extremely severe cases should receive urgent AMT to decrease the risk of scarring and visual sequelae. *Ophthalmology 2016;■:1–6 © 2016 by the American Academy of Ophthalmology.*

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are acute epithelial blistering diseases that have variable involvement of the eyes. Cases with severe eye involvement can yield extensive, permanent damage to the ocular surface and eyelids. These patients may experience severe eye pain, photophobia, and visual disability. Multiple recent case reports and case series have suggested that cryopreserved amniotic membrane transplantation (AMT) to the eyes and eyelids early in the acute phase of the disease can decrease the destructive inflammation and limit the severity of damage to the eyes.[1–14] Although some published reports examining acute aspects of the disease have graded the severity of eye involvement, there is still no established grading system for the acute ophthalmic manifestations of SJS or TEN.[10,15] There is also minimal information in the literature to help determine which patients should receive AMT. This study presents a grading system for the ophthalmic findings in acute SJS and TEN based on the extent of epithelial sloughing on the eyelid margins, palpebral conjunctiva, and ocular surface. The system is designed to be clinically practical and to provide a framework for the evaluation of disease severity and treatment options.

Methods

Study Population

Photographs and clinical records of 158 eyes of 79 consecutive patients diagnosed with SJS or TEN were reviewed after approval by the Colorado Multiple Institutional Review Board. All patients were treated at the University of Colorado Hospital or the Children's Hospital of Colorado between June 2006 and July 2013. The extent and location of epithelial sloughing, as determined by fluorescein staining, was documented in each case. The treatments received were noted, and the visual outcomes and dry eye severity were documented for each case at least 3 months after the acute illness.

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Table 1. Ophthalmologic Grading Criteria and Treatment Recommendations for Acute Stevens-Johnson Syndrome

Staining Location and Treatment Recommendations	Severity of Eye Involvement			
	Mild	*Moderate*	*Severe**	*Extremely Severe*†
Lid margin	No stain	Stain <1/3 of lid margin length	Stain >1/3 of lid margin length on at least 1 lid	Stain >1/3 of lid margin length on more than 1 lid
Cornea	No stain	No stain	Any epithelial defect more than punctate staining	Any epithelial defect more than punctate staining
Conjunctiva (bulbar and palpebral)	Hyperemia, without stain	(+)Stain, <1 cm in greatest diameter	(+)Stain >1 cm	Multiple areas of stain >1 cm
Treatment recommendations	Medical	Medical & close observation	Medical & urgent AMT	Medical & urgent AMT (may require repeat AMT)

AMT = amniotic membrane transplantation.
*A case was considered severe if there was severe involvement of the lid margin, cornea, or conjunctiva. It was not required that all 3 areas have severe involvement simultaneously.
†Extremely severe cases had multiple areas of extensive fluorescein staining simultaneously.

Acute Phase Evaluations

Regardless of the extent of skin involvement, all patients received an ophthalmologic consultation within 1 day of hospital admission. At each evaluation, mucus and debris were rinsed from the eyes using sterile saline first. Fluorescein then was applied to the eyes, and the extent and location of fluorescein staining were recorded using both photographic and written descriptions. The longest axis of any areas of bulbar or tarsal conjunctival fluorescein staining, or both, was noted. The upper and lower fornices were inspected for staining in every case simply by retracting each lid and shining the cobalt blue light from a handheld direct ophthalmoscope into the fornix. Any corneal epithelial defects were measured and noted. When present, the extent of lid margin staining was described as involving less than one-third or more than one-third of each lid margin.

Acute Phase Grading

Based on the extent and location of epithelial sloughing, each patient's ocular involvement was given a severity grade (Table 1 and Fig 1).[16] The superior and inferior halves of the bulbar conjunctiva and the superior and inferior halves of the palpebral conjunctiva of each eye were considered as separate, discrete sections for the purposes of evaluation and grading. Mild cases had only conjunctival hyperemia with no epithelial sloughing in any areas of the ocular surface or lid margins. Moderate cases had no corneal sloughing beyond punctate keratopathy, but did have limited, discrete sloughing of the conjunctiva or lid margins. Any lid margin sloughing involved less than one-third of the length of the lid margin. Any areas of bulbar or palpebral conjunctival staining measured less than 1 cm in largest diameter (the areas of staining were significantly smaller than the areas without staining or epithelial sloughing). Severe cases had at least 1 of the following staining criteria: (1) a corneal epithelial defect beyond punctate keratopathy, (2) at least 1 lid margin with staining involving more than one-third of its length, and (3) any section of bulbar or palpebral conjunctiva with staining of more than 1 cm in largest diameter. To qualify as severe, only 1 of these 3 criteria had to be met, not all 3 at once. Extremely severe cases were those that simultaneously met the severe criteria on more than 1 lid margin and also on multiple sections of the bulbar and palpebral conjunctiva.

Acute Phase Interventions

All patients underwent daily ophthalmologic examinations as described above until it was clear that the ocular surface inflammation was subsiding with no further progression. Mild and moderate cases were treated medically with moxifloxacin 0.5% drops (Vigamox; Alcon, Fort Worth, TX) 4 times daily, cyclosporine 0.05% drops (Restasis; Allergan, Irvine, CA) twice daily, and dexamethasone 1% drops twice daily. Combination tobramycin 0.3% plus dexamethasone 0.1% ointment (TobraDex; Alcon) was applied to the lid margins twice to 4 times daily. No AMT was used in the mild or moderate cases.

The severe and extremely severe cases received the same topical medications as the mild and moderate cases. Additionally, all of the severe and extremely severe cases also underwent AMT within the first 10 days of the illness using techniques described previously.[5,8] All received sutured AMT to the lid margins and palpebral conjunctiva. The treatment of the surface of the globe varied, however, depending on the extent of bulbar conjunctival staining. Cases with severe bulbar conjunctival staining (areas >1 cm in diameter) involving both the superior and inferior halves of the conjunctiva received AMT sutured to the entire surface of the globe. In cases with less extensive bulbar conjunctival staining (no areas >1 cm in diameter), a ProKera was placed on the eye instead of suturing amniotic membrane to the globe. Because of the limited bulbar conjunctival sloughing, it was believed that a ProKera would be sufficient treatment for the surface of the eye, allowing for a more efficient procedure without compromising outcomes. Patients with extremely severe eye involvement frequently were treated with a second application of AMT 7 to 14 days after the initial application (60% of patients). Repeat AMT was performed when the original AMT had degraded, but the ocular surface still appeared significantly inflamed with extensive hyperemia and persistent fluorescein staining. Two of these patients underwent a third round of AMT during the acute phase.

Outcome Measures

All patients had at least 3 months of follow-up and were assessed for best-corrected visual acuity (BCVA), severity of dry eye symptoms, and extent of ocular surface and eyelid scarring. The BCVA included spectacle correction or any form of contact lens correction. The presence of dry eye symptoms was assessed using the short questionnaire for dry eye syndrome developed by Gulati et al.[17] Dry eye severity was graded as none, mild, moderate, or severe based on the interventions needed to control symptoms and the guidelines of the International Dry Eye Workshop.[18] Mild symptoms were controlled with artificial tear supplements only. Moderate symptoms were controlled with artificial tears