Stevens-Johnson Syndrome and Corneal Ectasia: Management and a Case for Association

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• PURPOSE: To report the occurrence of corneal ectasia (ECT) in patients with history of Stevens-Johnson syndrome (SJS), and to make the case for an association between these 2 diagnoses. We also report the impact of prosthetic replacement of the ocular surface ecosystem (PROSE) treatment on visual acuity (VA) in these patients.

• DESIGN: Retrospective cohort study.

• METHODS: A manufacturing database of PROSE patients from 2002 to 2014 at Boston Foundation for Sight (BFS), a single-center clinical practice, was reviewed to identify patients with diagnoses of both SJS and ECT.

• RESULTS: Nine patients were identified with diagnoses of both SJS and ECT. In each case, review of the medical record revealed that diagnosis of SJS preceded that of ECT. The prevalence of ECT in this population exceeded that in the general population ($P < .0001$). Videokeratography was available for 13 eyes in 7 patients; using Krumeich's classification of keratoconus, 3 eyes were found to be at stage 1, 3 at stage 2, 1 at stage 3, and 6 at stage 4. Sixteen of 18 eyes underwent PROSE treatment. Of these 16 eyes, initial median VA was 20/200 (range, count fingers to 20/20; logMAR 1.0). Median VA after PROSE customization was 20/30 (range, 20/60–20/15; logMAR 0.1761, $P < .0025$).

• CONCLUSIONS: ECT occurs at a higher-than-expected rate in patients with a history of SJS. PROSE treatment improves VA in these patients. The basis of the association between SJS and ECT is considered, as well as the role of plausible contributory factors such as corneal microtrauma and matrix metalloproteinases. (Am J Ophthalmol 2016;169:276–281. © 2016 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).)

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STEVENS-JOHNSON SYNDROME (SJS) AND ITS MORE severe form, toxic epidermal necrolysis (TEN), are on a spectrum of immune-mediated, mucocutaneous diseases triggered by medications and, less commonly, infections.[1,2] SJS/TEN is typified by an acute febrile illness associated with prodromal target lesions, followed by skin detachment and involvement of at least 2 mucous membrane sites.[3] Ocular surface involvement occurs in 50%-78% of SJS/TEN cases and can result in significant long-term ocular sequelae, with 35% of survivors of SJS/TEN experiencing permanent vision loss.[4,5]

Long-term medical and surgical management of patients with severe ocular surface disease, as can occur after SJS/TEN, is complex. One form of nonsurgical management is the use of therapeutic contact lenses.[6–9] Clinicians may hesitate to consider therapeutic contact lenses in SJS/TEN patients because of assumptions that cicatricial conjunctival changes may be a barrier to achieving satisfactory fit. Additionally, these patients might be excluded as candidates because of ocular comorbidities such as aqueous tear deficiency and limbal stem cell deficiency that together would put patients in a high-risk category for epithelial breakdown and superinfection.

Prosthetic replacement of the ocular surface ecosystem (PROSE) is a treatment approach developed by Boston Foundation for Sight (BFS), Needham, Massachusetts, that uses a custom-designed and fitted, FDA-approved, rigid gas-permeable scleral lens prosthetic device to support ocular surface functions. The devices used in PROSE treatment vault the cornea and limbus and rest on sclera. They are filled with sterile saline at the time of application, worn on a daily-wear basis, and removed for sleep (Figure 1).[10,11] PROSE treatment is also used in the management of corneal ectasia (ECT),[11,12] a degenerative disorder that manifests as progressive corneal thinning and steepening. The resultant irregular astigmatism, myopia, and irregular corneal surface can lead to impaired vision and can require surgical intervention.[13] The most common of the corneal ectasias is keratoconus (KC). KC is also the most common condition requiring scleral lens wear.[12] Scleral lenses have been shown to improve visual acuity and comfort in patients with KC.[14] However, when scleral lenses and other treatment options fail, PROSE treatment has been shown to significantly improve vision and visual function,[8,11,15] which may delay and perhaps eliminate the need for surgical intervention with its inherent risks and unpredictability.

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FIGURE 1. Prosthetic replacement of the ocular surface ecosystem (PROSE) device filled with sterile saline prior to insertion.

TABLE 1. Clinical Classification of Patients With Stevens-Johnson Syndrome and Corneal Ectasia by Stage Using the Krumeich Classification of Keratoconus[a]

Stage[b]	Characteristics	Number of Eyes at Each Stage
1	Eccentric steepening Induced myopia and/or astigmatism of ≤5.00 D K-reading ≤48.00 D Vogt lines, typical topography	3
2	Induced myopia and/or astigmatism of 5.00 to ≤8.00 D K-reading ≤53.00 D Pachymetry ≥400 μm	3
3	Induced myopia and/or astigmatism of 8.00 to ≤10.00 D K-reading >53.00 D Pachymetry 200–400 μm	1
4	Refraction not measurable K-reading >55.00 D Central scars Pachymetry ≤200 μm	6

D = diopters.
Pachymetry is measured at the thinnest site of the cornea.
[a]Adapted from Krumeich et al.[16]
[b]Stage is determined if 1 of the characteristics applies.

In the course of a medical records review of patients with SJS/TEN, we noticed several patients who also had a diagnosis of ECT. This coincidence was striking, given the rarity of each condition. We present a review of 9 such cases here. Though the literature addresses corneal pathophysiology in SJS/TEN and ectatic disorders individually, to our knowledge, there are no reports of the prevalence, pathogenesis, and management of these entities as associated disorders.

METHODS

THIS STUDY WAS CONDUCTED ACCORDING TO THE DECLARation of Helsinki, was compliant with the Health Insurance Portability and Accountability Act (HIPAA), and was determined to be exempt from review by the New England Institutional Review Board. A manufacturing database of PROSE patients from January 1, 2002 to December 31, 2014 at BFS was searched to identify patients with diagnoses of both SJS/TEN and ECT. Referral to BFS occurred for management of poor or worsening visual function. All cases of ectasia were first diagnosed by the referring ophthalmologist and independently confirmed at BFS at the time of consultation. For this study, the diagnosis of ECT was confirmed by reviewing clinical examination notes and videokeratography. The Krumeich staged clinical classification of KC was used to stage the level of disease.[16] Though the accuracy of videokeratographic data in SJS/TEN is unknown, generation of central 3-mm simulated keratometry (sim K) values was designated as a reliable measurement of keratometry values for Krumeich classification. Other relevant data were extracted from the medical records, with visual acuity recorded in Snellen format and then converted to logarithm of the minimum angle of resolution (logMAR) for analysis. Statistical analysis was performed using the InStat statistical package by GraphPad Software, Inc (La Jolla, California, USA) with the level of statistical significance set at .05.

RESULTS

TWO HUNDRED FIFTY PATIENTS WITH A DIAGNOSIS OF SJS/TEN were identified in the BFS database of patients for whom prosthetic devices were manufactured between 2002 and 2014. Seventeen eyes in 9 of these patients had been coded with a secondary diagnosis of ECT. Review of referral letters, notes, and records revealed that in each of these 9 cases, the diagnosis of ECT was made after acute SJS/TEN, with a range of 1–33 years.