Stevens-Johnson Syndrome: The Hopeful Truth
Gloria Chow OD, Danielle Iacono OD, Susan P. Schuettenberg OD, FAAO

Abstract

A case report detailing the clinical findings, treatment options and prognosis of a forty-one year old African American female suffering from severe dry eye secondary to Stevens-Johnson Syndrome are discussed and explored.

Case History

A forty-one year old African American female presents with a chief complaint of dryness, pain and photosensitivity worse in the right eye than left eye. Her ocular and medical history is significant for severe ocular dryness secondary to Stevens-Johnson Syndrome diagnosed in 2008 following an adverse reaction to Dilantin. Prior to presenting to the clinic, this patient was treated on Restasis BID OU for one year, autologous tears, and lubricating drops and ointments without success or improvement in symptoms.

As a direct result of Stevens-Johnson Syndrome, this patient has experienced a significant increase in weight since 2008, depression and pigmented macules of the face and neck. Her medical history is also remarkable for occasional sinus congestion and asthma which is controlled on albuterol. In addition, she also uses a preserved formulation of Refresh Tears dosing every 10 minutes or more for ocular dryness. She is allergic to Dilantin and sulfa drugs.

Pertinent Findings

- Clinical:
  - Keratinization of the upper and lower lid margins OU
  - Madarosis of the lid and eyebrows OU
  - Meibomian orifice scarring OU
  - Conjunctival injection OD>OS
  - Depleted tear lake OD>OS
  - Neovascular fan extending from temporal limbus through visual axis, involving approximately 60% of cornea OD
  - Stromal scarring OU- not within visual axis
  - Severe pannus corneal SPK OD>OS
  - Immediate TBUT with areas of +&- staining OU
  - BCVA OD 20/70 OS 20/25

- Physical:
  - Pigmented macules of irregular size and shape covering face and neck
Histopathology studies of the skin (diagnosed elsewhere)
  - Necrotic keratinocytes characterized by an infiltrate with few cells, predominating macrophages and dendritic cells with a strong immunoreactivity for tumor necrosis factor (TNF-alpha) – (1) (4)

**Differential Diagnosis**
- **Primary:** Severe Dry Eye 2' to Stevens-Johnson Syndrome (SJS)
  - Frequency of ocular involvement in patients with SJS: 69%-81% (1)
- **Others:**
  - Toxic Epidermal Necrolysis (TEN): also on the same spectrum of acute vesiculobullous disorders; however it is differentiated from SJS based on skin involvement: SJS involves less than 10% total body surface area while TEN involves greater than 30% of epidermal detachment. (3)
    - SJS and TEN are characterized by widespread macules or flat atypical target lesions usually located on the trunk or head.
    - Histopathology: necrotic pattern characterized by infiltrate with fewer cells (2)
    - Etiology: drug related in almost all cases
    - Frequently involves eye 50%-67% of time, and does not recur (2)
  - Erythema Multiforme Majus (EMM): characterized by localized typical targets or raised atypical targets located predominantly on the extremities
    - Histopathology: inflammatory pattern with high density cell infiltrate rich in T-lymphocytes
    - Etiology: usually viral in origin (Herpes)
    - does frequently recur but does not usually involve the eye
  - Chemical burn
  - Sjogrens Syndrome
  - Atopic Keratoconjunctivitis
  - Trachoma

**Diagnosis and discussion**
- Elaborate on condition

Stevens-Johnson Syndrome is a rare disease and part of a spectrum of acute systemic vesiculobullous disorders. Incidence is about 6 per million persons a year and often results from an adverse complication to a medication, most commonly antibiotics, NSAIDs and in this case, an anticonvulsant, Dilantin. The mortality rate of this condition is relatively high ranging from 1%-5%. Because it results in an extensive sloughing of the skin and mucosal surface, the conjunctiva and oropharynx represents the most frequently involved of the membranous tissues.

Ocular manifestation of this condition is usually described and categorized by its acute and chronic stages. Though no clear consensus has been reached on the exact time period delineating the two, traditionally the first 2-6 weeks following the onset of symptoms have been recognized as the acute stage (1). A severity grading
scale was first proposed by Power et al which instituted a mild, moderate, and severe grading system of ocular findings during the acute stage correlated with the ocular prognosis at the conclusion of the acute stage (1). Furthermore, Di Pascuale et al proposed a scaling system for use during the chronic stage to describe eyelid involvement and found a high correlation between the severity of scarring and keratinization of the mucosal surfaces of the eye lid with the severity of corneal vascularization and scarring. (1). Later, Sotozono et al established an additional system describing severity of common conjunctival and corneal complications using a 0-3 numerical scale system similar to that of Di Pascuale.

Because ocular surface damage from SJS can often result in a chronic life long battle with pain, blindness, ocular motility problems, and severe dryness, proper treatment is critical during the acute phase of the condition in order to most successfully reduce the risk of chronic ocular complications. Such complications include, but are not limited to ulceration and perforation of the cornea, corneal and conjunctival scarring, obstruction of the openings to excretory ductules of the lacrimal gland secondary to scarring within the fornix, symbelpharon and ankyloblepharon formation, ectropion, entropion, trichiasis, distichiasis, meibomian gland orifice metaplasia, punctual scarring, keratinization of the mucosal surfaces, limbal stem cell deficiency, and eye infections secondary to ocular barrier compromise.

Unfortunately in the case of this patient, the acute stage of her disorder occurred in 2008 and has since past. She now presents with symptoms of severe discomfort and pain which have been escalating since that time. Though supportive and palliative therapy have been instituted within the few years immediately following her diagnosis, aggressive therapy does not appear to have been implemented during the acute phase of her condition. Treatment for patients with chronic ocular symptoms resulting from SJS have been largely unsuccessful compared to patients who received acute treatment with amniotic membrane grafts within the first 2-6 weeks of disease onset.

Because keratinization of the lid margin, scarring of the meibomian glands, and severely decreased aqueous outflow due to obstruction or lacrimal gland damage has occurred, a normal tear film will not only be difficult to restore and maintain, but also hard to distribute evenly across the ocular surface, not to mention the pain it may involve in doing so. In the face of an unstable tear film, scarred mucosal lid surfaces and likely limbal stem cell deficiency, a corneal transplant and conjunctival limbal allografts will be invariably hard to maintain and studies have found to be largely unsuccessful during chronic stages of this disease.

Potential avenues this patient might explore in the future include scleral lenses which will help effectively create a barrier between the palpebral conjunctiva and bulbar conjunctiva and cornea. This treatment would aid to decrease the sensation of pain from the continuous micro-trauma caused by friction from the scarred mucosal surface of the eyelid on the cornea. In addition, a scleral lens also provides
an aqueous reservoir to help further increase comfort and decrease corneal desiccation as a result of severe dryness (8). Reduction of contact between the palpebral conjunctiva and bulbar conjunctiva will also minimize risk of symblepharon formation. Vision will also be improved due to the introduction of a more regular refractive surface. Potential complications of this treatment strategy involves a heightened risk of infection to an already compromised corneal surface with the introduction of a contact lens. In the event corneal compromise is a concern, a topical fluoroquinolone may be used prior to lens insertion and after lens removal (7).

An oral mucosal graft with amniotic membrane transplantation may also be considered. It proved to be successful in a small case study by Liu et al with 7 eyes (1 of which had SJS) with total stem cell deficiency. All 7 eyes had severe symptoms of severe vision loss, photophobia and pain which was resolved with oral mucosal graft treatment (5).

Furthermore, topical bevacizumab may also serve as a worthwhile treatment option to reduce ocular surface neovascularization in the patient's right eye. This was demonstrated to be a potentially viable consideration for SJS patients with corneal vascularization by Harvey et al. (6)

Treatment and Management

- In the end, the patient was referred to a dry eye specialist for continued care and exploration of more advance treatment options.
- During the interim period, frequent use of non-preserved artificial tears and non-preserved lubricating ointment was recommended every 15 minutes or more.
- Use of sunglasses was advised for indoors and outdoors to help decrease symptoms of photosensitivity and enhance comfort.
- Continuous lubrication was stressed.

Potential treatment options for ocular manifestations of SJS

- use of amniotic membrane (inner most layer of the placenta) during acute stages
  - The use of amniotic membrane is believed to be effective for several reasons:
    - it creates a physical barrier between inflamed, denuded mucosal membranes thereby minimizing adhesions
    - it has an anti-inflammatory effect
    - and anti-fibrotic effects
    - it appears to aid in the re-epithelialization process by possibly providing a scaffold for the migration of epithelial cells (3)
- systemic pulse corticosteroid therapy and topical corticosteroid application (3)
- systemic immunoglobulin (IVIG) and cyclosporine A(CsA) (1)
• amniotic membrane and intensive short-term topical corticosteroid (3)- study involving 16 eyes affected by SJS or TEN by Shammas et al
  o Treated with amniotic membrane and: FML 0.1% ointment q1-2hrs and tapered as soon as skin and mucosal lesions began healing (~1-2 weeks); bacitracin ointment, Vigamox, and Restasis QID
  o Result: BCVA 20/40 or better with intact ocular surface and good ocular comfort
• Prokera (sutureless) with coverage of only the cornea and most of the bulbar conjunctiva
  o less successful at preventing ocular surface abnormalities vs sutured amniotic membrane grafts
• Scleral contact lenses
• PKP- increased risk of failure in eyes with limbal stem cell deficiency (1)
• Conjunctival limbal autograft
• Keratolimbal allograft- complications of graft rejection and loss of donor epithelial cells
• Boston keratoprosthesis, less successful than
• Osteo-odonto-keratoprosthesis more successful in late SJS
  o Limited centers offering this trmnt (1)
• Moisture chamber goggles
• Maskin Procedure
  o Potential treatment option for patients with scarred meibomian gland orifices, but intact glands
• Lateral/Total tarsorrhaphy- after all other treatment options are exhausted

Conclusion
• Clinical pearls, take away points
  o Importance of aggressive treatment during acute stage
  o Highest success of restoring good function of lids, ocular surface and vision has been with sutured amniotic membrane grafts during the acute stage of disease onset.
o Optometric roles in patient management and co-management is invaluable and may involve the following supportive and palliative treatments depending on severity of symptoms:
  ➢ Preservative free tear replacement solutions and ointments
  ➢ Removal of pseudomembranes
  ➢ Lysis of symbelpharon
  ➢ Debridement of loose epithelim
  ➢ Topical antibiotics to prevent secondary infections
  ➢ Topical corticosteroids to prevent scar formation
  ➢ Cycloplegic drops to relieve pain, photophobia and ciliary spasm
  ➢ Bandage contact lenses to help maintain integrity of corneal epithelium (use extreme caution)
  ➢ Scleral lens fit
  ➢ Fitting and recommending moisture chamber goggles
  ➢ Referral to specialty care for advanced disease
Patient education

Bibliography