Managing Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Kimberly C. Sippel, MD

Proactive ophthalmic management is important during the acute phase of the disease to reduce the risk of long-term complications.

Because Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) involve both systemic and ocular manifestations, treatment of these conditions requires a multifaceted approach. While systemic treatment is certainly the top priority, proper ophthalmic management during the acute phase of the disease is also critical to reduce the risk of potentially blinding ocular sequelae. In particular, a new treatment approach using amniotic membrane holds promise for improving long-term outcomes. Because SJS and TEN are both associated with serious ocular consequences, including conjunctival scarring and other complications, patients who present to the ophthalmic practice after the acute episode often exhibit profound dryness and end-stage corneal scarring (Figure 1). In these cases, patients may require fairly involved treatments, potentially including scleral contact lenses, limbal stem cell allografts, or keratoprosthesis.

Scleral Contact Lenses Are Gaining in Popularity—With Good Reason

Christine W. Sindt, OD, FAAO

New technology has breathed new life into scleral contact lenses, and they are now making it possible for patients with a variety of conditions to experience comfort as well as good vision. The bonus is that, compared to standard GP lenses, they are relatively easy to fit on complicated eyes.

Available since the late 19th century, scleral contact lenses are hardly new. Until the development of current rigid gas permeable (GP) materials, however, scleral lenses languished and were used only as a solution of last resort. Now, however, they are enjoying a resurgence, thanks to better, more oxygen-permeable materials, more sophisticated manufacturing technology, and a growing understanding of their capabilities and patient benefits.

Contact lens fitters have long been frustrated with eyes that either can't be fit with, or patients who aren't comfortable in, traditional GP lenses. Scleral lenses solve both those problems. In so doing they are finding applications in conditions that include keratoconus, high astigmatism, trauma, dry eye disease, neurotrophic keratitis, persistent epithelial defects, and penetrating keratoplasty.

Fitting scleral lenses differs considerably from fitting...
The pharmaceutical regimen

- During the acute phase
  - Topical corticosteroids
  - Antibiotics in patients who develop corneal epithelial defects

- After the acute phase
  - Topical cyclosporine

Ocular Consequences

The membranous or pseudomembranous conjunctivitis associated with SJS and TEN can cause conjunctival scarring which may damage goblet cells, accessory lacrimal gland tissue, and the meibomian gland ducts. As a result, SJS and TEN patients often develop profound ocular dryness. The cicatrizng conjunctivitis process also often results in trichiasis and keratinized lid margins which, in combination with a desiccated ocular surface, result in chronic mechanical trauma of the cornea.

Furthermore, the cicatrizng conjunctivitis can also damage limbal stem cells, resulting in limbal stem cell deficiency. Ultimately, this damage can result in chronic or persistent corneal epithelial defects, corneal neovascularization, scarring, and corneal perforations—potentially leading to blindness.

Treatment during the Acute Phase

Because the causes of SJS and TEN remain poorly understood, physicians currently have no way to identify at-risk patients or to prevent the disease from occurring. Nor is it possible to arrest the disease process during the acute phase.

Considering to be a spectrum of disease, the main difference between SJS and TEN is the degree of skin involvement, with SJS usually involving skin lesions over less than 20% of the body surface area, and TEN patients exhibiting more widespread sloughing of the epidermis, often over 50% of the skin surface (Figure 2). Both conditions exhibit similar ocular manifestations in the acute stage, ranging from mild conjunctivitis to a membranous or pseudomembranous conjunctivitis, with varying degrees of corneal epithelial defect formation. The acute phase of the disease tends to resolve within a few weeks, and survivors often have few long-term systemic complications. However, survivors are often left with lifelong and blinding ophthalmic problems.

While both SJS and TEN are devastating—and, in the case of TEN, life threatening—both are also fortunately quite rare. The incidence of SJS is only 1.1 to 7.1 cases per million person-years, and the incidence of TEN is even lower: 0.4 to 1.3 cases per million person-years.
Use of Amniotic Membrane in the Acute Phase of SJS and TEN

While both SJS and TEN can be quite serious during the acute phase, patients who survive tend to do quite well afterwards, at least systemically. However, when ophthalmic complications occur, they can persist long after other issues have resolved.

To minimize ocular complications, a method of using amniotic membrane to protect the eye has been developed, and case reports suggest that it can significantly improve outcomes. Amniotic membrane may help to reduce inflammation during the acute phase, and by preventing raw and inflamed tissues from adhering, amniotic membrane also helps to minimize the scarring that causes many of the ocular sequelae of SJS and TEN.

The technique involves covering the entire surface of the eye with amniotic membrane. First the eyelashes are removed (if necessary), and a sheet of amniotic membrane is sutured to the outside of the lid margin with a nonabsorbable suture. The amniotic membrane is then pushed down into the fornices with a muscle hook and secured with a suture through the eyelid. This process is repeated for both the upper and lower eyelids. Next, a sheet of amniotic membrane is applied to the bulbar conjunctiva and the cornea. This sheet is also secured with a nonabsorbable suture, after which a large diameter bandage contact lens or symblepharon ring may be applied to the eye. While this procedure is typically performed in an operating room setting, in a critically ill patient who cannot be brought to the operating room, the amniotic membrane may also be sutured to the lids at the bedside.

The net effect can be quite impressive (Figure 1 A-D).

Reference

Patients tend to develop symblepharons, these membranes may need to be lysed to prevent permanent adhesions.

In addition to these largely supportive measures, a technique for using amniotic membrane during the acute phase of SJS and TEN has recently been developed and holds promise for improving long-term outcomes (see box). So far, case reports suggest that this technique can significantly reduce the risk of ocular complications, but controlled studies are needed to confirm these findings.

Given the importance of preventative ophthalmic treatments, involvement of an ophthalmologist during the acute phase of the disease can significantly improve patients' long-term outcomes. When considering amniotic membrane treatment or other therapies, however, ophthalmologists need to keep in mind that SJS and TEN patients are invariably treated in a hospital setting, often in a burn unit. Ophthalmologists will therefore need to coordinate with the physician who is managing the patient's systemic treatment, and ophthalmic treatments may need to be performed at the bedside if the patient's condition prevents transfer to an operating room.

Treatment after the Acute Phase

Ideally, ophthalmic treatment should be initiated during the acute phase to reduce the risk of long-term ocular consequences, but sometimes patients do not receive care until after the acute phase has ended. When this situation occurs, several therapies can be employed to improve patients' vision and ocular comfort, although these methods may not be able to fully restore function that has been lost.

In most patients, dry eye therapies are necessary to provide ocular surface lubrication. In addition to
REVIEW SUMMARY: Based on full prescribing information, revised January 2006.

INDICATIONS AND USAGE
Zydelig is indicated for steroid-responsive inflammatory sarcoidosis conditions for which a corticosteroid (corticosteroids) and an immunosuppressive agent (corticosteroids) is indicated and where the patient has achieved control with these agents alone. Immunosuppressive agents are indicated for the treatment of sarcoidosis when the use of corticosteroids is not feasible or when the patient has not achieved control with corticosteroids alone.

CONTRAINDICATIONS
Zydelig is contraindicated in patients with a history of lymphoma, including non-Hodgkin lymphoma, or a history of lymphoid malignancy.

WARNINGS
Skin/Allergic Reactions
Skin reactions, including Stevens-Johnson syndrome, toxic epidermal necrolysis, and systemic involvement, have been reported in patients treated with Zydelig. Symptoms include rash, fever, and malaise. Life-threatening reactions, including death, can occur. Patients should be monitored closely for signs of skin reactions, and treatment should be discontinued if skin reactions develop.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis: The carcinogenic potential of Zydelig has not been evaluated in humans or animals. However, increased liver injury has been seen in animals treated with Zydelig. Patients should be monitored for changes in liver function tests.

Mutagenesis: The mutagenic potential of Zydelig has not been evaluated in humans or animals.

Impairment of Fertility: The effect of Zydelig on fertility has not been evaluated in humans or animals.

PREGNANCY
There are no adequate and well-controlled studies in pregnant women. Use of Zydelig during pregnancy should be avoided as it may cause fetal harm.

NURSING MOTHERS
It is unknown whether Zydelig is excreted in human milk. It is recommended that the mother should not nurse while taking Zydelig.

Pediatric Use: The safety and effectiveness of Zydelig in children have not been established.

Geriatric Use: No age-related differences in safety and effectiveness have been observed in elderly patients.

ADVERSE REACTIONS
Adverse reactions that have occurred with zidovudine/steroid combination drugs which can be attributed to the streptococcal component, the anti-infective component, or the combination.

Zydelig is a white to off-white powder. Each 24 mg capsule contains 1 mg of zidovudine and 2 mg of prednisone. It is supplied in bottles of 100 capsules. Each capsule contains 1 mg of zidovudine and 2 mg of prednisone. The capsules are made of gelatin and are imprinted with "Zydelig" and "24 mg/2 mg". The capsules are not scored.

FIGURE 2 Skin lesions in acute Stevens-Johnson syndrome typically cover less than 20% of the body surface area.

THE BOTTOM LINE
The involvement of an ophthalmologist during the acute phase of SJS and TEN can ensure appropriate treatment and help minimize some of the devastating ocular consequences of these conditions. In particular, a new treatment approach using anti-mitotic membrane holds promise for improving long-term outcomes. In cases in which the acute phase of the disease has seriously damaged the ocular surface, subsequent treatment must address the consequences of severe ocular surface damage, lid abnormalities, resultant mechanical trauma, and limbial stem cell deficiency.

Other therapies that may help to restore vision include the use of a bandage contact lens (if the patient has a severe corneal damage) or a scleral contact lens. In patients with severe corneal damage, scleral contact lenses (pioneered by Perry Rosenthal, MD) not only provide vision correction but also protect the cornea by encapsulating it in a fluid reservoir. In cases with even more severe corneal damage, a keratoprosthesis may be necessary.

Finally, limbal stem cell allografts—using grafts supplied by an eye bank or a relative—can be used to replace limbal stem cells, although the long-term survival of these grafts is often poor.

Kimberly C. Sippel, MD, is assistant professor of ophthalmology at the Weill Cornell Medical College of New York-Presbyterian Hospital, New York, NY. Refractive EyeCare senior editor Kay Downer assisted in the preparation of this manuscript.