Case Report: Severe Eye Complications from Stevens-Johnson Syndrome in a Human Immunodeficiency Virus–Infected Patient in Malawi

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Abstract. Stevens-Johnson syndrome (SJS) is a severe form of erythema multiforme that primarily affects skin and mucous membranes. In Malawi, manifestations of SJS may become more common in human immunodeficiency virus–infected patients receiving nevirapine-based antiretroviral therapy (ART) and/or cotrimoxazole preventative treatment. Approximately 500,000 patients have received these medications within the national ART program since 2004. Malawi has recently followed the World Health Organization guidelines to start ART earlier in the course of HIV infection because the CD4 cell threshold for starting ART has increased from 250 to 350 cells/μL. We describe a patient with severe ocular complications from SJS that developed soon after initiation of nevirapine-based ART and cotrimoxazole preventive treatment, which led to blindness. We draw attention to preventive measures that can potentially reduce permanent ocular damage from SJS.

INTRODUCTION

Stevens-Johnson syndrome (SJS) is a severe form of erythema multiforme, an acute inflammatory disease primarily affecting skin and mucous membranes. In Malawi, manifestations of SJS are commonly seen in human immunodeficiency virus (HIV)–infected patients receiving nevirapine-based antiretroviral therapy (ART) and/or cotrimoxazole preventative treatment. Approximately 500,000 patients have received these medications within the national ART program since 2004. Malawi has recently followed the World Health Organization guidelines to start ART earlier in the course of HIV infection because the CD4 cell threshold for starting ART has increased from 250 to 350 cells/μL. Patients with higher CD4 cell counts are at higher risk of nevirapine hypersensitivity, including patients with SJS. Ophthalmologists are familiar with SJS because 50% of patients have ocular complications, mainly involving eyelids, conjunctiva, and corneas, that can result in severe ocular damage. We describe a patient with SJS in whom severe ocular complications developed soon after initiation of nevirapine-based ART and cotrimoxazole preventive treatment, which eventually led to blindness.

CASE REPORT

A 25-year-old man came to our hospital because of rapidly progressing loss of visual acuity with a presenting vision of correct light projection in both eyes. He was HIV positive and was receiving treatment for tuberculosis. In August 2012, he began cotrimoxazole therapy one week before initiation of first-line ART with the standardized regimen for adults ( stavudine, lamivudine, and nevirapine). After two weeks, SJS/toxic epidermal necrolysis (TEN) developed in the patient. Foreign body sensation in both eyes was present from the outset. At admission approximately six weeks after onset of SJS, we diagnosed a severe lid margin inflammation with advanced symblephara, mild chemosis, and conjunctivitis and a rapidly progressive conjunctivialization of the cornea (Figures 1 and 2).

Full-size epithelial defects with advanced corneal thinning developed in the patient. Both anterior chambers were shallow, and appeared hazy because of severe intraocular inflammation. Iris, lens, and fundus were not accessible for examination by slit lamp. Over the course of two weeks, conjunctivitis progressed despite systemic antibiotics and local therapy with ofloxacin, povidone iodine, and atropine eye drops. He turned blind (no perception of light) within two weeks of admission, possibly from an incurable endophthalmitis of unknown origin.

DISCUSSION

Several drugs have been reported to trigger ocular complications from SJS/TEN in Africa. Saka and others reported that antibacterial sulfonamides (50.6%) were most common used in Togo, followed by nevirapine (23.6%), non-steroidal anti-inflammatory drugs (5.6%), and anti-epileptic medications (3.4%). In 89 patients, they described few ocular complications: blindness occurred in three patients and moderate dry eye syndrome occurred in one patient. A study in Benin of seven patients with SJS/TEN reported one patient with ocular complications caused by ART. The other six patients had SJS/TEN secondary to ingestion of sulfadoxine-pyrimethamine, but no eye complications. Stevens-Johnson syndrome and TEN do not appear to have a racial or geographic predilection. The incidence of SJS is believed to be 6 cases/1,000,000 population/year and that of TEN is 1–2 cases/1,000,000 population/year. In Malawi, severe cutaneous reactions to sulfadoxine-pyrimethamine and cotrimoxazole have been reported by Gimnig and others, who did not report any ocular complications.

In our experience, there is insufficient awareness of eye complications that can result from SJS/TEN among HIV-positive patients receiving ART in Malawi. Patients with SJS/TEN are often not reviewed by an ophthalmologist or an eye care specialist during the acute stage of the disease. Therefore, severe eye sequelae may not be recognized. This finding leads to insufficient care and treatment and a potential for severe ocular complications, including blindness. Many investigators have emphasized that consultation by an ophthalmologist is essential within the first days of acute SJS/TEN to avoid lid margin keratinization and tarsal scarring, together with lipid tear deficiency, which lead to blink related micro-trauma and subsequent corneal damage. Some investigators have suggested

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FIGURE 1. 1, Face of a Malawian patient with Stevens-Johnson syndrome (SJS) six weeks after onset. 2, Trunk of a Malawian patient with SJS six weeks after onset.

Photo 1 Face of Malawian patient with SJS - 6 weeks after onset; visual acuity: light perception in both eyes.

Photo 2 Trunk of Malawian patient with SJS – 6 weeks after onset.

FIGURE 2. 3, Overview of the eyes of a Malawian patient with Stevens-Johnson syndrome (SJS). 4 and 5, Slitlamp views of the right and left eye of a Malawian patient with SJS.

All photos 6 weeks after SJS onset.
that amniotic membrane transplantation (AMT) in the acute stage is essential to prevent sight-threatening complications.\textsuperscript{11–13} We expect to see an increase in the incidence of SJS/TEN as more patients with higher CD4 cell counts start ART, following changes in the CD4 cell threshold in the Malawi and World Health Organization ART guidelines. Patients with higher CD4 cell counts are at higher risk of nevirapine hypersensitivity syndromes, including SJS.\textsuperscript{3} It is important that ART providers in Malawi and other countries in the region who use nevirapine-based first-line ART are aware of the severe eye complications associated with SJS/TEN, so that they can refer patients in a timely fashion or start appropriate preventive and therapeutic measures if referral is not possible.

Providers of ART in rural settings should know how to treat acute eye complications with topical lubricants, topical steroid eyedrops, and lysis of developing symblephara by using a sterile glass rod. Vitamin A ointment may be used for corneal re-keratinization. The benefit of peeling pseudomembranes is unproven. Keratitis must be treated early with antibiotics because it can easily develop into a corneal ulcer, as seen in our patient. Oral mucosal grafts are useful in more advanced cases such as severe corneal ulceration.

Steroid pulse therapy at disease onset could be of therapeutic importance in preventing ocular complications. Topical betamethasone also shows promise for preventing corneal epithelial stem cell loss in the limbal region and cicatricial changes.\textsuperscript{14} Satake and others reported that cultivated oral mucosal epithelial sheet transplantation (COMET) can offer a viable and safe alternative in the reconstruction of a stable ocular surface.\textsuperscript{15} Early intervention with AMT could have prevented the severe outcome in our patient. Although formal evidence is lacking, Gregory described the benefits of early AMT as the treatment of choice for acute SJS/TEN with severe ocular complications,\textsuperscript{12} but it has not yet been introduced in Malawi because of the need for technical expertise, risk of transmission of infections, and the requirement of storing material at \( -80^\circ\text{C} \), which are major challenges.

We report a patient from Malawi in whom blindness developed after SJS, which developed after initiation of nevirapine-based ART and cotrimoxazole preventive treatment. More awareness of the risk of severe eye complications in this setting may lead to earlier recognition and treatment of eye complications associated with SJS. Amniotic membrane transplantation could further improve outcomes, although a formal evidence base is lacking and operational challenges exist.

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