Acute Management of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis to Minimize Ocular Sequelae

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Although relatively rare, Stevens-Johnson syndrome (SJS) and its more severe variant, toxic epidermal necrolysis (TEN), exhibit significant levels of mortality and morbidity relative to all other severe drug-induced blistering disorders. At the acute stage, the management algorithm for SJS/TEN involves exclusion of infectious agents, identification and prompt withdrawal of the suspected drug, and institution of treatment tailored individually according to the cause, type, and stage of the complications. Because the primary objective is to save the patient’s life, the majority of medical attention is devoted to acute treatment of widespread skin blisters and failing vital organs. Thus, consulting ophthalmologists have not held an active role in instituting effective measures to ameliorate the condition of SJS/TEN despite potentially blinding complications.

In addition to SJS/TEN’s detrimental effects on the skin, an overwhelming majority of suffering patients also develop ocular surface inflammation and ulceration at an acute stage. For some SJS/TEN patients, ocular morbidity and visual loss can be caused during hospitalization by limbic stem cell deficiency following large corneal epithelial defects affecting the limbus. However, a significant number of patients still retain clear corneas and normal vision upon discharge, but gradually develop corneal blindness at the chronic stage because of cicatricial complications of the conjunctiva, fornix, tarsus, or lid margin after prolonged ulceration and inflammation of the ocular surface.

There are various methods of management of SJS/TEN at the acute stage. Some believe that T-cell–mediated immunologic responses are the cause of SJS/TEN and have consequently administered high-dose glucocorticoids, cyclophosphamide, or cyclosporine as a means of arresting the progression of skin lesions. However, these drugs are of unproven benefit at the acute stage. Nevertheless, at the acute stage it is feasible to differentiate EM clinically from SJS/TEN simply based on the type of skin lesions and their predominant body distribution, as proposed by Bastuji-Garin and associates in 1993. In doing so, EM differs from SJS/TEN with respect to clinical course, prognosis, cause, and treatment. Indeed, subsequent clinical characterization, clinicopathologic correlation, and a large international case-control epidemiologic survey have substantiated that EM, defined by typical targets or raised atypical targets with primary acral (ie, extremities) distribution, is benign and self-limited, may...
The presence of a severe adverse cutaneous reaction to a drug may lead to a variety of clinical manifestations, from mild skin rashes to life-threatening conditions such as toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS). These conditions are characterized by extensive epidermal necrosis and inflammation, leading to widespread skin detachment and potentially ocular involvement.

In contrast to TEN, SJS is less extensive and characterized by predominant epidermal necrosis with minimal inflammatory infiltrate. The second issue lies in whether there is a better strategy that one may deploy to abort disease progression by specifically targeting the pathogenic basis that leads to skin blisters and relentless ocular surface inflammation. In contrast to EM, where there is more inflammatory (lichenoid) infiltrate, SJS/TEM is pathologically characterized by predominantly epidermal necrosis with minimal inflammatory infiltrate in the dermal stroma, in which macrophages and dendritic cells show strong immunoreactivity for tumor necrosis factor (TNF-α)-expression. Besides scant amounts of cytotoxic CD4+ T cells in the dermis and CD8+ T cells in the epidermis that might secrete perforin and granzyme B to invoke cell lysis, TNF-α and the CD95 (Fas) receptor-ligand system have been implicated as prime mediators leading to keratinocyte apoptosis and consequentially to necrosis. Therefore, besides intravenous infusion of human immunoglobulins, which is presumed to block the Fas receptor, another attractive and novel therapy may be transplantation of cryopreserved amniotic membrane as a biological bandage over the entire ocular surface. This surgical procedure, when performed within 2 weeks from the onset of ocular involvement, rapidly suppresses inflammation and promotes epithelialization at the acute stage. As a result, it prevents cicatricial complications at the chronic stage. Such clinical efficacies are supported by experimental studies exhibiting amniotic membrane's anti-inflammatory action that is manifest by rapid elimination of polymorphonuclear neutrophils, mononuclear inflammatory cells, or macrophages via facilitation of cellular apoptosis. They are also supported by downregulation of T-helper cytokines secreted by activated lymphocytes and downregulation of several pro-inflammatory cytokines such as TNF-α secreted by activated macrophages.

Further clinical studies with a larger sample size are warranted to help determine the pros and cons of these new therapies that can be delivered at the acute stage. In addition to research into the underlying destructive pathogenic mechanism, explaining how rapid diffuse necrosis (apoptosis) develops in the epidermis and mucosal epithelia, these new therapies will undoubtedly propel ophthalmologists into an active and integral role for the acute management of SJS/TEN to halt potentially blinding sequelae of this most devastating ocular surface disease.

**REFERENCES**


