Burn Center Care of Patients with Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

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KEYWORDS

• Toxic epidermal necrolysis • Stevens-Johnson syndrome • Burn center • Exfoliative conditions

KEY POINTS

- Although patients with Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are now routinely referred to burn centers for definitive care, not all cases of SJS or even SJS-TEN overlap automatically warrant burn center admission. However, the more extensive the degree of exfoliation (especially in TEN), the greater is the need for and benefit from providing care in a burn center setting.
- Diagnosis of SJS and TEN relies on careful documentation of systemic, cutaneous, and mucosal features obtained from a detailed history and physical examination, combined with histologic confirmation by biopsy.
- The treatment bundle in the burn center should include cessation of the causative medication; careful airway assessment and protection, if indicated; directed (rather than routine) fluid replacement for hypovolemia; early enteral nutrition; wound coverage with skin substitutes; urgent ophthalmologic consultation; careful surveillance for infection; avoidance of prophylactic antibiotics; and consideration of a pharmacologic intervention to attempt to halt the disease process.
- Pharmacologic interventions to halt the disease process have not been examined through large high-quality studies and consensus on use of these agents is lacking.

INTRODUCTION

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe, potentially life-threatening, adverse cutaneous reactions that most commonly are precipitated by the use of a medication. Although these conditions are rare, with only 1.5 to 1.9 cases occurring per million of the population per year, the associated mortality ranges between 9% for SJS to 30% to 50% for TEN.[1] An important feature of these conditions is varying degrees of detachment of the epidermis, which results in wounds that are analogous to superficial partial thickness burns. Consequently, patients with SJS and TEN are frequently referred to specialized burn units for their care, primarily to optimize wound and dressing management but also to garner all of the other beneficial aspects of multidisciplinary care that modern burn treatment facilities can offer for patients with large cutaneous wounds. Not surprisingly, a multicenter review of TEN found that delayed referral of patients with TEN to a burn center was associated with significantly lower odds of survival.[2] This article reviews all aspects of SJS and TEN but

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primarily focuses on the important principles of management of patients with these conditions.

NOMENCLATURE AND CLASSIFICATION

SJS and TEN likely represent different degrees of severity of the same disease process.[3] In both conditions, there must be a skin rash that features epidermal detachment as well as erosion of mucosal membranes (mucositis) at 2 or more locations. In SJS, epidermal detachment is limited to less than 10% of the total body surface area (TBSA) whereas in TEN, epidermal loss occurs over greater than 30% of the TBSA. When the epidermal detachment involves 10% to 30% of the TBSA, the condition is referred to as SJS-TEN overlap. In SJS, SJS-TEN overlap, and TEN, the rash features spots but not typical target lesions, although flat atypical target lesions can be seen. The spectrum of SJS-TEN should be distinguished from another distinct condition, erythema multiforme major, which occurs following infection with herpes simplex virus or *Mycoplasma pneumoniae*, and which features oral mucositis, a rash consisting of typical target lesions, as well as raised atypical target lesions but minimal to no epidermal detachment. A final entity, TEN without spots, features diffuse erythema but no spots or target lesions and epidermal detachment involving greater than 10% of the TBSA. These points of classification are summarized in **Table 1**.[4]

CAUSES OF STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS

Although approximately 75% of cases of SJS-TEN result from the use of a drug, it is recognized that viral illnesses, influenza-like illnesses, and *M pneumoniae* infections may also be causative.[5] A recent case-control study[6] identified that drugs with the highest risk of inducing SJS-TEN included allopurinol, anti-infective sulfonamides (eg, cotrimoxazole), phenytoin, carbamazepine, phenobarbital, lamotrigine (an antiepileptic drug), nevirapine (an anti–human immunodeficiency virus [HIV] drug), and oxicam-type nonsteroidal anti-inflammatory drugs (NSAIDs) (eg, meloxicam). The latency period between initiation of these high-risk drugs and onset of the cutaneous reaction ranged between 4 and 28 days. Commonly prescribed drugs that carry a moderate risk of inducing SJS-TEN included cephalosporins, macrolide and quinolone antibiotics, tetracycline, and acetic acid–type NSAIDs (eg, diclofenac). Frequently prescribed drugs that had no increased risk of causing SJS-TEN included valproic acid (in contrast to most of the other antiepileptics), angiotensin converting enzyme (ACE)-inhibitors, beta blockers, calcium channel blockers, diuretics and oral hypoglycemic drugs that carry a sulfonamide structure, and propionic type NSAIDs (eg, ibuprofen). Although these drugs do not seem to carry a higher risk of causing SJS-TEN, they have been implicated in individual cases of SJS-TEN and, in general, have a much longer latency period than the high-risk drugs (eg, >30 weeks in the case of valproic acid). Unfortunately, there are no reliable in vivo or in vitro tests to identify drug causality in SJS-TEN, although the lymphocyte transformation test and granulysin expression test have been explored.[7,8] Two essential principles to remember with respect to medication use and causes of SJS-TEN are

- All medications should be considered as potential suspects, including intermittently used drugs such as vitamins and analgesics,

Table 1
Classification of exfoliative skin reactions

	Erythema Multiforme Major	SJS	SJS-TEN Overlap	TEN	TEN Without Spots
Mucositis	Oral mucositis	≥2 sites	≥2 sites	≥2 sites	≥2 sites
Spots	No	Yes	Yes	Yes	No
Atypical target lesions	Yes, raised	Yes, flat	Yes, flat	Yes, flat	No
Typical target lesions	Yes	No	No	No	No
Epidermal detachment	Negligible	<10% TBSA	10%–30% TBSA	>30% TBSA	>10% TBSA
Mortality	None	10%	—	30%–50%	—

Adapted from Bastuji-Garin S, Rzany B, Stern RS, et al. Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. Arch Dermatol 1993;129:92–6.