SkinSerious: Disseminated intravascular coagulation complicating Stevens-Johnson syndrome and toxic epidermal necrolysis

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The American Academy of Dermatology's SkinSerious campaign highlights how dermatologists treat serious diseases. Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) top the list.

Despite debate about the nosology of SJS and TEN, the disorders are classified by the extent of detached skin surface area: SJS (<10%), SJS/TEN overlap (10%-30%), and TEN (>30%). Both are rare, but SJS is 3 times more common than TEN. The vast majority of cases are drug induced, although infections (mycoplasma, cytomegalovirus, dengue) and vaccinations may be etiologic. The pathophysiology of SJS/TEN involves $CD8^+$ cytotoxic lymphocytes, the Fas-Fas ligand (FasL) pathway of apoptosis, granulysin, nitrous oxide, and the tumor necrosis factor alpha/death receptor pathway.[1]

A retrospective review of 71 cases of SJS and TEN (21 pediatric and 50 adult patients) reported a 35.3% mortality for TEN and 6.5% for adults with only SJS. Survival was 100% in pediatric patients with SJS. Two of the adults with SJS died, presumably because of complications of disseminated intravascular coagulopathy (DIC). None with SJS-TEN overlap died of their disease. The authors suggest that averaging the mortality rates of TEN and SJS is not advised because SJS is mainly a mucocutaneous disorder with good prognosis versus TEN associated with systemic toxicity of multiple organs.[2]

The complications of SJS/TEN are legion—multidisciplinary management of fluid and electrolyte abnormalities; pain; thermodysregulation; and ocular, pulmonary, gastrointestinal, and renal dysregulation is mandatory. Survivors may contend with life-altering cicatricial sequelae.

Abbreviations used:

DIC:	disseminated intravascular coagulopathy
SJS:	Stevens-Johnson syndrome
TEN:	toxic epidermal necrolysis

DIC, associated with infection, cancer, or trauma, is characterized by the systemic activation of blood coagulation, which generates intravascular fibrin, causing thrombosis of small- and medium-sized vessels, with resultant organ dysfunction. In this issue of the *Journal of the American Academy of Dermatology*, Chen et al[3] investigated the risk and outcomes of DIC in patients with SJS/TEN by analyzing 150 patients with SJS/TEN (75 with SJS, 22 with overlapping SJS/TEN, and 53 with TEN) and their complete DIC profiles (platelet count, prothrombin time, activated partial thromboplastin time, D-dimer, fibrinogen, and fibrin degradation products). DIC was diagnosed in 32 patients (21.3%), primarily those with TEN. DIC was significantly associated with systemic complications (gastrointestinal bleeding, respiratory failure, renal failure, liver failure, infection, and bacteremia). Among patients with SJS/TEN, DIC was associated with a greater than 10-fold increase in mortality (78.1% vs 7%).[3] In a retrospective review of 396 patients with SJS/TEN,

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5 (1.3%) developed DIC, with 4 dying of the disease.[4]

The cornerstone of SJS/TEN management is discontinuation of the offending drug or treatment of the inciting infection, combined with exquisite supportive care. Ongoing controversy regarding therapeutic intervention continues. Tsai et al,[5] in a network meta-analysis of 67 studies encompassing 2079 patients, found that combination therapy with corticosteroids and intravenous immunoglobulin may reduce mortality risks in patients with SJS/TEN overlap and TEN. Cyclosporine and etanercept are considered promising therapies, but more studies are required to provide clearer evidence.[5] No matter what therapeutic approach is taken, clinicians must be vigilant for the earliest signs of DIC in patients with SJS/TEN and treat these patients aggressively in the hope of decreasing mortality. Seriously.

Conflicts of interest

None disclosed.

REFERENCES

1. Oakley AM, Krishnamurthy K. Stevens-Johnson syndrome. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2020.
2. Nowsheen S, Lehman JS, El-Azhary RA. Differences between Stevens-Johnson syndrome versus toxic epidermal necrolysis. *Int J Dermatol*. 2021;60(1):53-59.
3. Chen CB, Hsu TH, Chung-Yee Hui R, et al, Taiwan Severe Cutaneous Adverse Reaction Consortium. Disseminated intravascular coagulation in Stevens-Johnson syndrome and toxic epidermal necrolysis. *J Am Acad Dermatol*. 2021;84. https://doi.org/10.1016/j.jaad.2020.08.065.
4. El-Azhary RA, Nowsheen S, Gibson LE, DiCaudo DJ. Disseminated intravascular coagulopathy: a complication of Stevens-Johnson syndrome/toxic epidermal necrolysis. *Int J Dermatol*. 2021;60:185-189.
5. Tsai TY, Huang IH, Chao YC, et al. Treating toxic epidermal necrolysis with systemic immunomodulating therapies: a systematic review and network meta-analysis. *J Am Acad Dermatol*. 2021;84(2):390-397.