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A decade of burn unit experience with Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis: Clinical pathological diagnosis and risk factor awareness

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ABSTRACT

Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN) is a rare and often fatal spectrum of mucocutaneous diseases usually attributable to severe adverse drug reactions. Burn units are referral centers for patients at the most extreme end of the disease continuum. Our burn center admits a much higher percentage of TEN (>30% BSA) cases than reported in most prior reviews. The purpose of this study was to analyze the diagnostic and prognostic value of variables collected on referred SJS/TEN patients. We retrospectively analyzed 94 patients admitted to our unit with a presumptive SJS/TEN diagnosis made in most cases by the referring center. Most of the diagnoses were clinical. Fifty of the 94 patients underwent biopsy when the clinical diagnosis was questionable. Of the 50 patients who underwent biopsy, 18 (36%) received an alternative diagnosis. Analysis was therefore limited to 76 patients, i.e. 44 patients felt to have firm clinical diagnoses plus 32 patients with diagnoses confirmed by biopsy. Mean age was 54.3 years (17–93) and overall gender ratio was 43 F vs. 33 M (56.6% vs. 43.4%). Mean LOS was 15.2 days (1–48) and overall mortality was 23.7% (18/76). Univariate analysis revealed percent body surface area (%BSA) did not show statistically significant association with mortality. Histopathological correlation for diagnosis is not standardized across institutions worldwide. Due to challenges in the diagnosis of SJS/TEN and the high incidence of error in clinical diagnosis, it is recommended that all patients with presumed SJS/TEN receive skin biopsies with H&E and direct immunofluorescence. We propose a diagnostic approach in order to address this need. Lack of association between %BSA and mortality suggests that all biopsy-proven SJS/TEN cases belong in specialty centers due to the unstable nature of the disease and risk for rapid progression.

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1. Introduction

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are conditions of mucocutaneous necrosis that are classified based on body surface area of involvement (% BSA). SJS is characterized by <10% BSA affected, SJS-TEN Overlap is between 10 and 30% BSA, and TEN is >30% BSA [1]. The incidence of SJS/TEN is approximately 1.9 per million per year [2]. SJS is more prevalent than TEN by as much as 3 to 1 [3] and the overall mortality rate ranges from 10% for SJS to over 30% for TEN [4]. Medications are the most common causes, with allopurinol, sulfonamides, anticonvulsants, and nonsteroidal anti-inflammatory drugs being the most common offenders [5,6].

In this study we examined the diagnosis of SJS/TEN patients and risk factors for mortality. Patients often present with a prodrome of fever and malaise followed by erythema, macules, targetoid lesions, bullae, desquamation, mucosal inflammation, and/or positive Nikolsky sign [7,8]. Characteristic histopathology reveals keratinocyte necrosis and varying degrees of dermal-epidermal separation [3]. Universal diagnostic criteria for SJS/TEN do not exist. At times the clinical features of other skin diseases may closely resemble SJS/TEN, but in these cases a skin biopsy will usually establish the alternative diagnosis [9] (Fig. 1).

Of note, erythema multiforme (EM) is a mucocutaneous disease indistinguishable on biopsy but classified as a separate disease clinically [24,25]. Patients with EM develop raised lesions symmetrically on distal extremities, whereas SJS/TEN lesions are more often flat or purpuric with trunk and/or widespread distribution [26]. EM is almost always due to *Herpes simplex virus* and *Mycoplasma pneumonia* instead of drugs, thus knowing the causative agent lends credence to each diagnosis [27,28]. Rarely, drug reactions may lead to EM and infections can cause SJS/TEN, however the diagnosis is still made according to clinical presentation [25,27].

Our burn center manages a very high percentage of TEN cases, allowing us to analyze a novel population set in comparison to the less severe and more common SJS end of the spectrum. The SCORTEN severity-of-illness scoring system was utilized retrospectively to predict mortality [29]. The present study seeks to retrospectively analyze the diagnostic and prognostic value of clinical and histopathological factors collected from SJS/TEN patients.

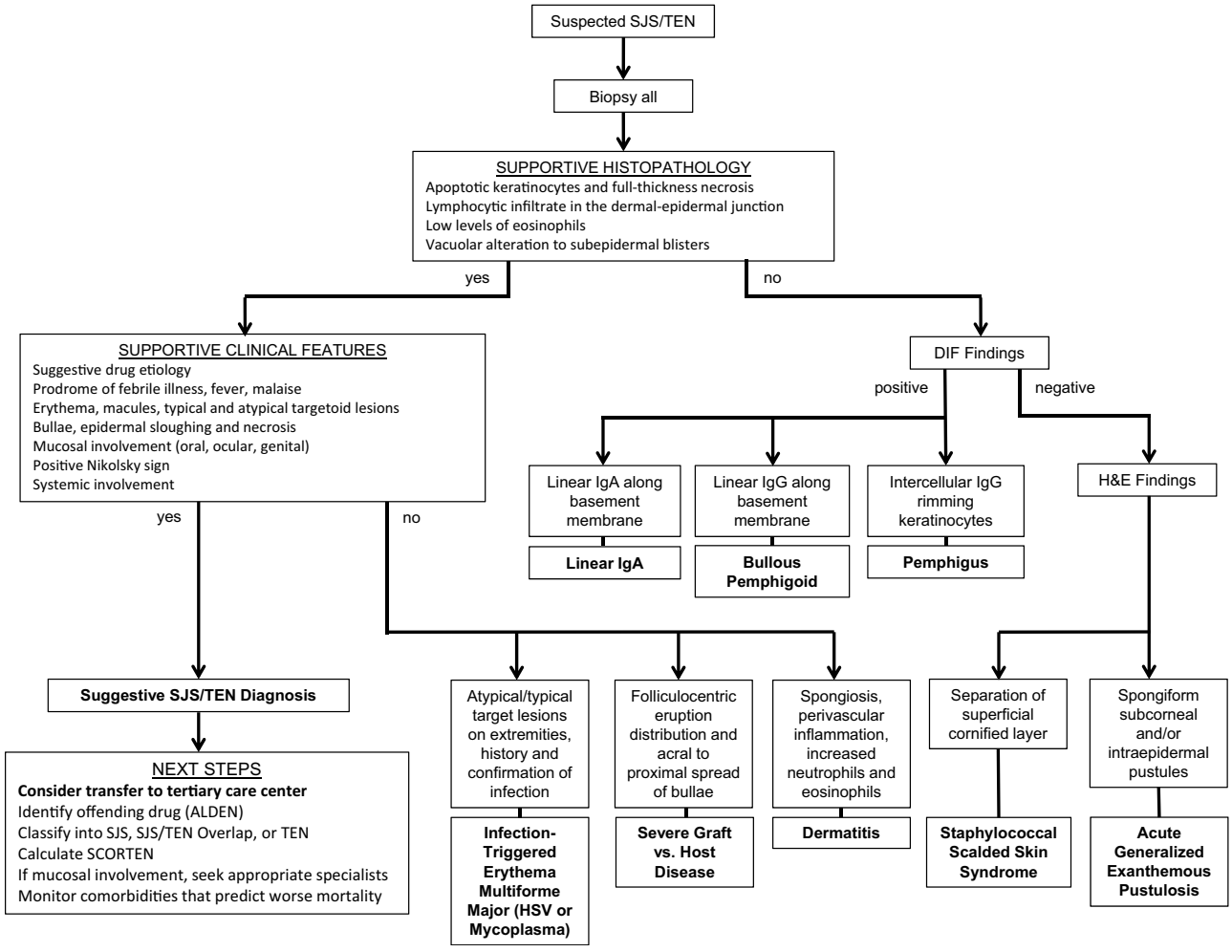

Fig. 1 – Proposed diagnostic approach to Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis. ALDEN: algorithm of drug causality for epidermal necrolysis; DIF: direct immunofluorescence; HSV: herpes simplex virus; SCORTEN: severity-of-illness score for toxic epidermal necrolysis; SJS: Stevens-Johnson syndrome; TEN: toxic epidermal necrolysis.