Clinical Outcomes of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis Based on Hospital Admission Type

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PRACTICE **POINTS**

- Early identification and diagnosis of Stevens-Johnson syndrome and toxic epidermal necrolysis are essential to improving patient outcomes.
- Patients transferred from outside hospitals often present with more severe disease due to delays in diagnosis and initiation of appropriate treatment.
- Inpatient dermatology consultation plays a vital role in accurately diagnosing and managing life-threatening dermatologic conditions.
- Establishing timely interhospital transfer protocols may help expedite access to specialized treatment and improve patient outcomes.

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) require prompt hospital admission with access to inpatient dermatologic care. Delayed admission of 5 days or more has been associated with increases in overall mortality, bacteremia, intensive care unit (ICU) admission, and length of stay. In this study, we analyzed the association between admission pathway and clinical outcomes of patients with SJS/TEN. A single-center retrospective chart review was performed at Atrium Health Wake Forest Baptist Medical Center (AHWFBMC)(Winston-Salem, North Carolina), to assess demographics, comorbidities, outside hospital transfer status, complications during admission, inpatient length of stay in days, interventions received, and site of admission: directly from AHWFBMC emergency department or transferred from an outside hospital.

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare, life-threatening conditions that involve widespread necrosis of the skin and mucous membranes.[1] Guidelines for SJS and TEN recommend management in hospitals with access to inpatient dermatology to provide immediate interventions that are necessary for achieving optimal patient outcomes.[2] A delay in admission of 5 days or more after onset of symptoms has been associated with increases in overall mortality, bacteremia, intensive care unit (ICU) admission, and length of stay.[3] Patients who are not directly admitted to specialized facilities and require transfer from other hospitals may experience delays in receiving critical interventions, further increasing the risk for mortality and complications. In this study, we analyzed the clinical outcomes of patients with SJS/TEN in relation to their admission pathway.

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The eTable is available in the Appendix online at https://www.mdedge.com/cutis.

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Methods

A single-center retrospective chart review was performed at Atrium Health Wake Forest Baptist Medical Center (AHWFBMC) in Winston-Salem, North Carolina. Participants were identified using i2b2, an informatics tool compliant with the Health Insurance Portability and Accountability Act for integrating biology and the bedside. Inclusion criteria were having a diagnosis of SJS (*International Classification of Diseases, Tenth Revision*, code L51.1; *International Classification of Diseases, Ninth Revision*, code 695.13), TEN (*International Classification of Diseases, Tenth Revision*, code L51.2; *International Classification of Diseases, Ninth Revision*, code 695.15) or Lyell syndrome from January 2012 to December 2024. Patients with erythema multiforme or bullous drug eruption were excluded, as these conditions initially were misdiagnosed as SJS or TEN. Patients with only a reported history of prior SJS or TEN also were excluded.

The following clinical outcomes were assessed: demographics, comorbidities, age at disease onset, outside hospital transfer status, complications during admission, inpatient length of stay in days, age of mortality (if applicable), culprit medications, interventions received, Severity-of-Illness Score for Toxic Epidermal Necrolysis (SCORTEN) upon admission, site of admission (eg, floor bed, ICU, medical ICU, burn unit), and length of disease process prior to hospital admission. Patients then were categorized as either direct or transfer admissions based on the initial point of care and admission process. Direct admissions included patients who presented to the AHWFBMC emergency department and were subsequently admitted. Transfer patients included patients who initially presented to an outside hospital and were transferred to AHWFBMC. Data regarding the wait time for Physician Access Line requests and the time elapsed from the initial transfer call to arrival at the tertiary hospital also were collected—this is a method that outside hospitals can use to contact physicians at the tertiary hospital for a possible transfer. Statistical analysis was performed using unpaired *t* tests and χ^2 tests as necessary using GraphPad By Dotmatics Prism.

Results

A total of 112 patients were included in the analysis; of these, 71 had a diagnosis with biopsy confirmation of SJS, SJS/TEN overlap, or TEN (Table 1). Forty-one patients were excluded due to having a diagnosis of erythema multiforme or bullous drug eruption or a reported history of prior SJS or TEN without hospitalization. All biopsies were performed at AHWFBMC. Of the 71 confirmed patients with SJS/TEN, 54 (76%) were female with a mean age of 44 years. The majority of patients identified as Black (35 [49%]) or White (27 [38%]), along with Asian (7 [10%]) and other (2 [3%]). The most common comorbidity was cardiovascular disease in 42 (59%) patients, followed by type 2 diabetes in 36 (51%) patients. Among these 71 patients with SJS/TEN, 29 (41%) were directly admitted to the tertiary hospital, while 42 (59%) were transferred from outside hospitals.

Of the 71 confirmed patients with SJS/TEN, sulfonamides were identified as the most common inciting drug in 25 (41%) patients, followed by β-lactam antibiotics in 16 (23%) patients (Table 2). This is consistent with previous literature of sulfamethoxazole with trimethoprim as the primary causative drug for SJS and TEN in the United States.[1]

Clinical Outcomes—Of the 71 patients, there were 23 (32%) cases of SJS, 29 (41%) cases of SJS/TEN overlap, and 19 (27%) cases of TEN (eTable). The initial and maximum affected body surface area (BSA) was higher in transfer admissions, with a mean maximum BSA of 38.55% in the transfer group compared to 19.14% in the direct admissions. The mean SCORTEN (range, 0-5) was 1.6 overall, with a higher mean score of 1.92 in the transfer group compared to 1.07 in the direct admissions.

TABLE 1. Demographics of Study Population

Characteristic	Direct admissions (n=29)	Transfer admissions (n=42)
Mean age, y	42	46
Female, n (%)	21 (72.41)	33 (78.57)
Ethnicity, n (%)		
White	12 (41.38)	15 (35.71)
Black	12 (41.38)	23 (54.76)
Asian	4 (13.79)	3 (7.14)
Other	1 (3.45)	1 (2.38)
Comorbidities, n (%)		
Cardiovascular disease	19 (65.52)	23 (54.76)
Type 2 diabetes	15 (51.72)	21 (50)
Pulmonary disease	4 (13.79)	10 (23.81)
Renal disease	3 (10.34)	7 (16.67)
Malignancy	3 (10.34)	3 (7.14)
HIV	3 (10.34)	2 (4.76)
Autoimmune disease	6 (20.69)	12 (28.57)
Psychiatric disorder	9 (31.03)	14 (33.33)

Transfer patients had a longer mean stay at the tertiary hospital (13.71 d) compared to direct admissions (7.17 d). The mean time from symptom onset until tertiary hospital admission was 8.5 days; transfer and direct admission patients had similar mean time from symptom onset of 9.02 days and 7.86 days, respectively. Although the duration of cutaneous symptoms from onset until tertiary hospital admission was similar (P=.283) between direct admissions (7.86 d) and transfer patients (9.02 d), the transfer group presented with greater disease severity at the time of admission. Transfer patients had a higher mean maximum BSA involvement (38.55% vs 19.14% [P=.005]), elevated SCORTEN (1.92 vs 1.07 [P=.029]), and longer mean hospital stays (13.71 d vs 7.17 d [P<.0001]) compared to direct admissions.

Despite the absence of mortality in both groups, transfer patients showed a higher number of ICU admissions (19 vs 5 [P=.014]) and burn unit admissions (9 vs 2 [P=.096]), bacteremia (16 vs 4 [P=.025]), acute kidney injury (13 vs 10 [P=.755]), acute respiratory failure (12 vs 5 [P=.272]), and transaminitis (8 vs 3 [P=.319]).

Outside Hospital Treatments—All outside hospitals provided supportive care with intravenous fluids and acetaminophen; however, further care provided at outside hospitals varied (Table 3), with transfer patients most frequently being treated with diphenhydramine (69% [29/42]), antimicrobial medications (57% [24/42]), steroids (40%), and epinephrine (10% [4/42]). Some patients may have received more than one of these treatments. Based on outside hospital treatments, the primary care teams' main clinical concerns were allergic reactions and infection, as 33 (79%) patients received diphenhydramine (29 [89%]) or epinephrine (4 [12%]) and 24 (52%) received antimicrobial medications. Of the 42 transfer patients, 24 (57%) received or continued these medications before transfer; the medications were promptly discontinued upon tertiary hospital admission.

Once the outside hospitals contacted the tertiary hospital for a referral, the mean length of time between the transfer request and Physician Access Line call was 17.13 minutes (Table 4). Following the transfer request, the mean length of time for arrival at the tertiary hospital was 6.22 hours. The mean length of stay at the outside hospital prior to the patient being transferred was 3.84 days.

TABLE 2. Inciting Drugs Identified as the Causative Agent of SJS and TEN

Inciting drug, n (%)	Direct admissions (n=29)	Transfer admissions (n=42)
Allopurinol	6 (20.69)	8 (19.05)
Anticonvulsants	4 (13.79)	6 (14.29)
β-lactam antibiotics	5 (17.24)	11 (26.19)
Dapsone	0 (0.00)	1 (2.38)
NSAIDs	2 (6.90)	1 (2.38)
Pembrolizumab	1 (3.45)	0 (0.00)
Sulfonamides	11 (37.93)	14 (33.33)

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis.

Comment

This retrospective study examined 71 patients with biopsy-confirmed SJS, SJS/TEN overlap, or TEN to evaluate differences in clinical outcomes between direct and transfer admissions. Transfer patients had a higher mean maximum affected BSA (38.55% vs 19.14% [P=.005]) and elevated SCORTEN (1.92 vs 1.07 [P=.029]); a higher number of transfer patients were admitted to the ICU (19 vs 5 [P=.014]) and burn unit (9 vs 2 [P=.096]), and this group also demonstrated longer hospitalization stays (13.71 vs 7.17 [P<.0001]). There were more complications among transfer patients, including bacteremia (16 vs 4 [P=.025]), which is consistent with findings from the existing literature.[3]

Once the decision for transfer of the patients included in our study was initiated and accepted, there was a prompt response and transfer of care; the mean length of time for Physician Access Line request was 17.13 minutes, and the mean transfer time to arrive at the tertiary hospital was 6.22 hours; however, patients spent an average of 3.84 days at outside hospitals, reflecting that transfer calls frequently were initiated due to urgent clinical decline of the patient rather than as an early intervention strategy. The management at outside hospitals often included the continuation of antimicrobial medications, which were discontinued upon transfer to AHWFBMC. Causative agents were either previously prescribed for a new medical condition or initiated for the management of suspected infections at outside hospitals. This may reflect the difficulty in correctly diagnosing SJS/TEN and initiating appropriate management at hospital facilities without an inpatient dermatologist.

The presence of inpatient dermatologists can improve the diagnostic accuracy and treatment of various conditions.[4,5] Dermatology consultations added or changed 77% of treatment plans for 271 hospitalized patients.[4] The impact of this intervention is reflected by the success of early dermatology consultations in reducing the length of hospitalization and use of inappropriate treatments in the care of skin diseases.[6-8]

Access to dermatologic care has been an identified need in inpatient hospitals that may limit the ability of hospitals to promptly treat serious conditions such as SJS/TEN.[9] From an inpatient dermatology study from 2013 through 2019, 98.2% of 782 inpatient dermatologists

TABLE 3. Treatments Received by Transfer Patients Prior to Tertiary Hospital Admission

Outside hospital interventions	Patients, n (%)
Diphenhydramine	29 (69%)
Antimicrobial medications	24 (57%)
Steroids	17 (40%)
Epinephrine	4 (10%)

TABLE 4. Timing Metrics for Physician Access Line Transfers

Metric	Time
Mean wait time for Physician Access Line request, min (SD)	17.13 (8.06)
Mean time between Physician Access Line request and arrival to tertiary hospital, h (SD)	6.22 (3.73)
Mean length of stay at outside hospital before transfer to tertiary hospital, d (SD)	3.84 (2.46)

reside in metropolitan areas, limiting the availability of care for rural patients; this study also found a decreasing number of facilities with inpatient dermatologists.[10]

The limitations of our study include a small sample size of 71 patients, which restricted the generalizability of our results. Our study also was based at a single tertiary center, which thereby limited the findings to this geographic area. It also was difficult to match patients by their demographic and comorbid conditions. The retrospective study design depended on the accuracy and completeness of medical records, which can introduce information bias. Future studies should compare the clinical outcomes of SJS/TEN based on burn unit and ICU admissions.

Conclusion

Prompt identification of SJS/TEN and rapid transfer to hospitals with inpatient dermatology are essential to optimize patient outcomes. Developing and validating SJS/TEN diagnosis and transfer protocols across multiple institutions may be helpful.

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APPENDIX

eTABLE. Clinical Characteristics of Patients Based on Direct vs Transfer Hospital Admissions

	Direct admissions (n=29)	Transfer admissions (n=42)	*P* value
Diagnosis, n (%)			
SJS	13 (44.83)	10 (23.81)	
SJS/TEN overlap	10 (34.48)	19 (45.24)	
TEN	6 (20.69)	13 (30.95)	
Mean BSA affected, % (SD)			
Initial BSA affected	11.5 (14.43)	21.82 (17.05)	
Maximum BSA affected	19.14 (15.49)	38.55 (28.60)	.005
Mean SCORTEN (SD)	1.07 (0.75)	1.92 (1.11)	.029
Area of involvement, n (%)[a]			
Oral	26 (89.66)	38 (90.48)	
Pharynx	6 (20.69)	13 (30.95)	
Ocular	11 (37.93)	26 (61.90)	
Genital	8 (27.59)	13 (30.95)	
Complications, n (%)			.471
Bacteremia	4 (13.79)	16 (38.10)	.025
ICU admission	5 (17.24)	19 (45.24)	.014
Burn unit admission	2 (6.90)	9 (21.43)	.096
Acute kidney injury	10 (34.48)	13 (30.95)	.755
Acute respiratory failure	5 (17.24)	12 (28.57)	.272
Transaminitis	3 (10.34)	8 (19.05)	.319
Mortality, n (%)	0 (0.0)	0 (0.0)	
Mean duration from cutaneous symptom onset to tertiary hospital admission, d (SD)	7.86 (4.24)	9.02 (4.73)	.283
Mean duration of hospitalization at tertiary hospital, d (SD)	7.17 (3.59)	13.71 (7.36)	<.0001

Abbreviations: BSA, body surface area; ICU, intensive care unit; SCORTEN, Severity-of-Illness Score for Toxic Epidermal Necrolysis; SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis.

[a]Patients may have had more than one affected area.