

Toxic Epidermal Necrolysis: Treatment of Two Cases with Intravenous Immunoglobulin

Charles Yarbrough* and Lacey Vence

Marshall University, Huntington, West Virginia, USA

*Corresponding author: Yarbrough C, Marshall University, Huntington, West Virginia, USA, Tel: +304-529-0900; E-mail: yarbroughc@marshall.edu

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Abstract

Toxic epidermal necrolysis (TEN) is a severe allergic reaction, often to drugs, with an approximate 30-40% mortality. Discontinuation of the offending drug and burn unit supportive care are agreed upon as initial therapy. However, use of Intravenous Immunoglobulin (IVIG) has been shown effective but controversial.

We report 2 cases of TEN treated with IVIG for 5 days and burn unit intensive care therapy. One case had early adjunctive systemic corticosteroid therapy; the other case had no systemic steroids. Both cases demonstrated a severity of illness score for TEN (SCORTEN) at day 1 of 35.3% and day 3 of 58.3%.

Previous reports base their opinion regarding IVIG effectiveness on studies that do not uniformly specify these treatment details or wherein IVIG treatment protocol was for less than 5 days. Inclusion of this data and use of this treatment protocol may demonstrate significantly improved outcomes in TEN patients treated with IVIG.

Keywords: Toxic epidermal necrolysis; Intravenous immunoglobulin; Severe allergic reaction

Introduction

TEN is a severe allergic reaction most often caused by sulfonamide antibiotics, anticonvulsants, nonsteroidal anti-inflammatory drugs, and nevirapine [1,4]. The eruption is of rapid onset becoming generalized in 3-5 days. Patients are initially febrile and lesions are very painful. Early lesions are macular with dusky erythema, progressing to vesiculobullous areas, which show a positive Nikolsky sign. Mucous membranes are commonly involved.

SCORTEN	% Mortality
0-1	3.2
2	12.1
3	35.3
4	58.3
5 or 7	90

Table 1: SCORTEN estimates.

Bastuji-Garin et al. have made the most accepted classification of TEN, however they include bullous erythema multiforme (BEM) as one of their categories [5,6]. Today it is felt that BEM is a different disease [7], with characteristically localized acral targetoid lesions in a younger and healthier population with a much milder clinical course than TEN. Stevens - Johnson syndrome (SJS), also an allergic bullous

eruption, is the early and clinically less severe member of the "SJS/TEN" classification system. Note, all members of the SJS/TEN group share the common histopathologic finding of epidermal detachment or sloughing:

1. SJS- <10% skin involvement
2. SJS/TEN overlap- 10-30% skin involvement
3. TEN- >30% skin involvement

SCORTEN is a mathematical model used to estimate disease severity and mortality in SJS/TEN. This was developed in 20002 and uses the following parameters:

1. Age >40 years
2. Heart rate >120 beats/min
3. Presence of cancer
4. Epidermal detachment >10% on day one
5. Blood urea nitrogen >28mg/dL (10mmol/L)
6. Glucose >252mg/dL (14 mmol/L)
7. Bicarbonate <20 mEq/L

One point is given for each parameter, with mortality reaching 90% with 5 or more points (Table 1) [8]. Hyponatremia has been recently proposed as an additional risk factor in TEN [1]. SCORTEN has been shown to accurately predict mortality in TEN [2,5].

There is general agreement that therapy of TEN begins with discontinuation of the offending drug, and early supportive burn unit treatment. In question is the use of systemic steroids as monotherapy or in conjunction with other systemic therapy, versus therapy with just IVIG. Also, the dosing of IVIG and duration of therapy are not firmly established.

Day	1	2	3	4	5	6	7	8	9	10	12	29
	Admission									Burn ICU		Discharge
Therapy		IVIG 1gm/kg					IVIG1 gm/kg	IVIG 0.7 gm/kg	IVIG 0.7 gm/kg	IVIG 0.57 gm/kg		
		Solumedrol 125mg IV	Significant improvement			New lesions	Wide-spread lesions			Impressive improvement		
						Intubate				Extubate		
Rash	35%		>60%									<5%
SCORTEN	3 (35%)		4 (58%)									

Table 2: Case 1 medical history.

Case Report

Case 1

58 year old female had a 13 hour history of pruritic erythematous eruption involving her back, arms, legs, and neck. Patient had recently been taking ibuprofen as her only new medication and had no known allergies. SCORTEN of 3 on day 1=35.3% mortality (age 58 years, pulse 136, epidermal sloughing>10%). Patient initially had focal areas of sloughing, which within 3-5 days were widespread, involving>60%. On admission a macular painful erythematous eruption developed without blisters or sloughing. Initial therapy included IV solumedrol 125 mg (only dose given) and IVIG 88 gms (1 g/kg), both given the second hospital day (Table 2).

A gap of four days without IVIG was followed by four consecutive days of IVIG (Table 2). After the first dose of IVIG a significant improvement in appearance of lesions was obvious. However, 4 days after the first dose of IVIG new macular erythematous and bullous lesions began appearing with large areas of sloughing. IVIG was restarted four days after the first infusion and continued daily for a total of 5 days IVIG (Table 2).

Day	1	2	3	4	5	6	15	31
	Admission		Burn ICU					Discharge
Therapy		IVIG 1 gm/kg	IVIG 1 gm/kg	IVIG 1 gm/kg	IVIG 1 gm/kg	IVIG 1 gm/kg		
			Intubate				Extubate	
Rash	50%		64%					<5%
SCORTEN	3 (35%)		4 (58%)					

Table 3: Case 2 medical history.

The patient was readmitted to the hospital 15 days after starting Vancomycin/Rifampin with bullous and painful erythematous eruption with 50% skin involvement. Skin biopsy and clinical findings were compatible with TEN, and patient was treated with IVIG 1 g/kg for 5 consecutive days (Table 3).

Unfortunately, the patient was not transferred to the burn unit until her 9th hospital day, which was the day of her 4th IVIG infusion. At that time, she had 70% surface skin areas involved with sloughing and/or exfoliation. Many areas were showing less erythema and early re-epithelialization.

On the 10th hospital day the patient received her 5th and final dose of IVIG, and “impressive improvement” of the skin lesions was noted.

Case 2

73 years old male developed a surgical wound infection 34 days post spinal surgery with cerebrospinal fluid culture positive for methicillin resistant staphylococcus aureus and subsequent treatment with IV Vancomycin/Rifampin. On day 7 after starting antibiotics oral blisters were observed and a painful eruption of the back near the incision was noted. Diagnosis of this eruption was Herpes Zoster, and the patient was started on Valacyclovir. The patient was discharged on Vancomycin/Rifampin and Valacyclovir. Five days post hospital discharge the patient was seen in the emergency room with bilateral lower back which was still felt to be Herpes Zoster. The patient was sent home on same medications.

Discussion

These two cases demonstrate the effectiveness of IVIG in TEN. The first case treated with 5 doses of IVIG over a 9 day period; the second case with 5 days IVIG therapy over a 5 day period. Case one also was given one dose of intravenous solumedrol initially. Case one serendipitously shows the improvement of lesions with just one dose

of IVIG, only to be followed by severe recurrent disease. Although just one case, it shows that if IVIG is briefly given, outcomes may be significantly influenced; and if restarted for a total of 5 days therapy, TEN is arrested. The second case supports daily monotherapy with IVIG at 1 g/kg for 5 consecutive days, and both show the effectiveness of infusion of IVIG for 5 total days. Future IVIG treatment protocols may involve early 1g/kg/day dosing for the first 2-3 days with taper at 3-5 days, as shown in Case 1.

Both cases document critical data for drawing conclusions regarding therapeutic effectiveness of IVIG: namely timing of beginning IVIG, total DAILY dose, number of days treated, timing of burn unit admission (not general intensive care unit), in addition to support for SCORTEN.

Only through publication of cases or a prospective study using similar therapy protocols documenting outcomes can a consensus be achieved regarding effectiveness of TEN treatments with IVIG.

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