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Case Report

Biologics to the Rescue in Case of Stevens–Johnson Syndrome/Toxic Epidermal Necrolysis

Sharmila Patil[1], Manjyot Gautam[1], Fiza Mohd Rafiq Choudhary[1], Anmol Vivek Israni[1], Akanksha Keshav Ghodke[1]

[1]Department of Dermatology Leprosy Venerology, D. Y. Patil Medical College and Hospital, Navi Mumbai, Maharashtra, India.

***Corresponding author:**
Akanksha Keshav Ghodke, Department of Dermatology Leprosy Venerology, D. Y. Patil Medical College and Hospital, Navi Mumbai, Maharashtra, India.

akankshaghodke@yahoo.com

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ABSTRACT

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are serious adverse drug reactions, triggered by medications, infections, malignancies and idiopathic causes. Clinically, they manifest as widespread, painful erythematous macules and target-like lesions, often accompanied by full-thickness or localised epidermal necrosis. Our patient, a 33-year-old male, presented with oral ulcers and painful red lesions starting from the face and progressing to involve trunk and upper extremities 5 days after administration of intravenous diclofenac for severe headache. Additional symptoms included ulceration over lips and buccal mucosa. He was diagnosed clinically as a case of SJS-TEN overlap with Severity of illness score for toxic epidermal necrolysis (SCORTEN) of 3 and was given intravenous corticosteroids. Here, we report a case of SJS-TEN overlap with corticosteroids-induced acute psychosis, treated successfully with etanercept monotherapy.

Keywords: Etanercept, Stevens–Johnson syndrome-toxic epidermal necrolysis, Biologics

INTRODUCTION

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe cutaneous adverse reactions, with mortality rates ranging from 1% to 3% for SJS and 30% to 50% for TEN.[1] SJS and TEN are characterized by skin detachment of <10% and >30% body surface area respectively. Involvement of oral, genital and ocular mucosa with a prodrome of flu like illness can be seen.[2] Overlapping SJS-TEN is defined by 10–30% skin involvement.[3] The female-to-male ratio for SJS/TEN is 1.5:1. Patients' ages vary from 3 to 78 years, with most falling between 21 and 40 years, showing a female predominance.[4] Increasing age, severe comorbidities and larger areas of skin detachment are associated with a poorer prognosis. The SCORTEN severity score is a tool used to predict mortality in cases of TEN.[5]

Clinically, SJS/TEN presents with painful blisters, violaceous macules and atypical target-like lesions, involving both skin and mucous membranes. Symptoms usually arise 4–28 days after starting the causative drug, often following a prodromal phase. Most cases show mucosal involvement, especially in the eyes, oral cavity and genital areas, accompanied by systemic complications such as secondary skin infections, pneumonia, hepatitis and sepsis.

The exact pathophysiology of SJS/TEN remains unclear, but research indicates a role for immune complex-mediated hypersensitivity or types III and IV hypersensitivity reactions. Drug antigen-specific CD8+ T cells, activated within the epidermis, release cytolytic peptides such as granulysin, granzyme B and perforin, with granulysin being a primary mediator of keratinocyte death.

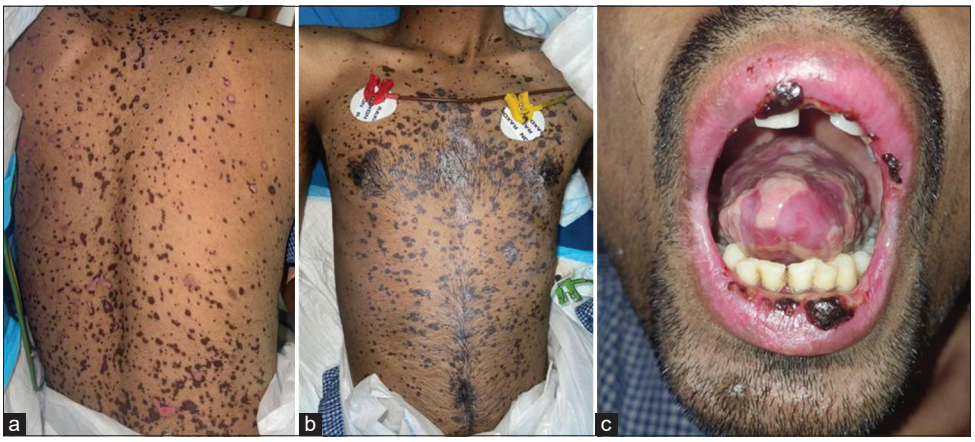

Figure 1: Pre-treatment photograph showing multiple well-defined hyperpigmented to violaceous macules with erosions and crusting seen over the (a) back, (b) chest and abdomen, (c) oral mucosa and lips.

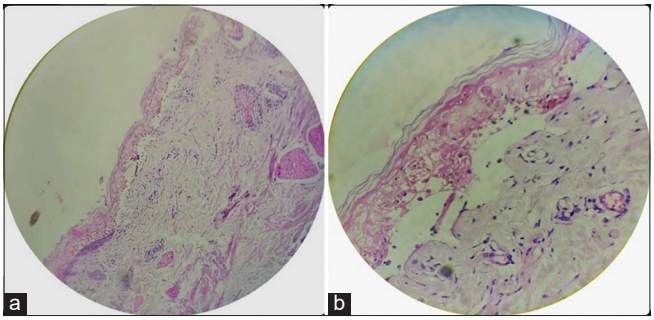

Figure 2: (a and b) Histopathology showing necrotic and apoptotic keratinocyte in the stratum spinosum and stratum basale in the epidermis with subepidermal blister with melanin in the cavity of the blister [Haematoxylin and Eosin] (a) 10X, (b) 40X.

Elevated serum levels of granulysin and IL-15 are associated with greater disease severity and increased mortality.[6] In addition, elevated levels of tumour necrosis factor alpha (TNF-α) have been noted in TEN. These findings suggest that TNF-α inhibitors, such as etanercept and infliximab, may help mitigate the progression of SJS/TEN by reducing TNF-α levels.

CASE REPORT

A 33-year-old male presented to the casualty with painful raw lesions on the mouth, chest, abdomen and back. Two days before the onset of lesions, he received injection diclofenac for a headache, after which he developed red painful lesions on the lips that spread to the face, neck, abdomen, bilateral upper limbs and groin. He also experienced fever, burning sensation, difficulty eating hot/spicy food, redness, watery discharge from both eyes and photophobia. After which, he went to a doctor and was given injection hydrocortisone (100 mg TDS) for 4 days but he showed no improvement. Later, he presented to us, and on examination, the patient was conscious but non-cooperative, disoriented in time, place and person and vitally stable with no systemic involvement. There were no known drug allergies or co-morbidities. There was no history of drug abuse, alcohol intake or known mental disorders.

On cutaneous examination, dusky-red erythematous and purpuric macules were observed, along with multiple well-defined erythematous to hyperpigmented plaques with crusting and areas of epidermal detachment on the chest, abdomen, back, groin and bilateral upper limbs [Figure 1a and b]. Haemorrhagic crusts were noted on the lips and oral mucosa, with bleeding and ulceration [Figure 1c]. Erythematous erosions with crusting were visible on the upper eyelids, accompanied by eyelash matting. Palms and soles exhibited erythematous to violaceous papules forming plaques, with positive pseudo Nikolsky sign on trunk lesions. Erythematous erosions with slough were found on the scrotum.

Laboratory findings showed a normal white blood cell count, elevated serum creatinine level and C-reactive protein levels and deranged serum electrolytes (Na-132, cl -108), and urine routine microscopy showed proteinuria and haematuria. Normal blood sugar levels, blood culture and sensitivity showed methicillin-resistant coagulase-negative staphylococcus and chest X-ray was normal and magnetic resonance imaging (MRI) of the brain was normal.

Skin biopsy showed necrotic and apoptotic keratinocyte in the stratum spinosum and stratum basale in the epidermis, subepidermal blister with melanin in the cavity of the blister [Figure 2]. Superficial dermis, peri appendageal and perivascular region showed sparse lymphocytic infiltrate [Figure 2a and b]. Thus a diagnosis of SJS TEN overlap was made with a SCORTEN of 3.

The patient was admitted to the intensive care unit and was treated by discontinuing the offending drug and starting injectable steroids (injection hydrocortisone 100 mg TDS for 3 days), antibiotics (piperacillin + tazobactam), painkillers (tramadol) and antihistamines (pheniramine

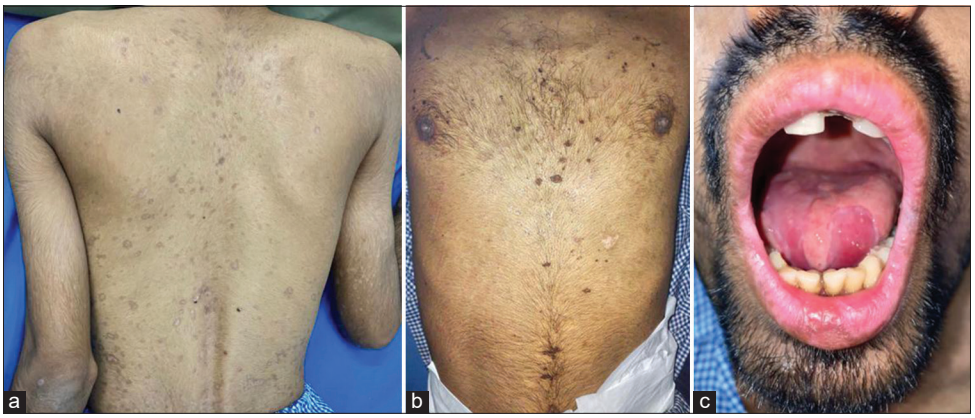

Figure 3: Post-treatment photograph after 6 days of 2nd dose of etanercept shows healed erosions, re-epithelisation of the lesions on (a) back, (b) chest and (c) oral mucosa.

maleate). Topical treatments included emollient (liquid paraffin), antibiotics (fusidic acid), anaesthetic agents (choline salicylate, lidocaine) and steroids (triamcinolone acetonide). Eye care consisted of antibiotics (moxifloxacin), lubricating agents (carboxymethyl cellulose) and steroid eye drops (prednisolone). Supportive care included hydration, nutrition and wound care.

On the 3rd day, the patient became disoriented and speech was incoherent. After ruling out organic causes (MRI brain was normal), a diagnosis of steroid induced psychosis was made. To mitigate this, steroid-sparing agents were considered, opting against cyclosporine due to abnormal creatinine levels. Therefore, the patient received injection etanercept 25 mg subcutaneously on days 1 and 3.

Two-day post-treatment initiation, cutaneous lesions stabilised, with reduction in adherent crusts and erosions over the tongue and buccal mucosa. Healthy granulation tissue and re-epithelisation was seen after 6 days of 2nd dose [Figure 3].

DISCUSSION

SJS/TEN is a severe disease with no established standard treatment. In 85% of SJS/TEN cases, the responsible drug is identified alongside SCORTEN assessment.[7] Supportive care includes restoring and protecting the skin barrier, ensuring airway protection, managing infections and maintaining fluid and nutritional balance, as patients are in a highly catabolic state.[7] Although systemic corticosteroids were once considered a treatment for SJS/TEN, their efficacy remains debated.[1]

Treatment options include intravenous immunoglobulin, which may be combined with corticosteroids. Cyclosporine A, a calcineurin inhibitor, works by inhibiting the activation of CD4+ and CD8+ T cells, reducing the production of cytotoxic proteins such as granzyme B, granulysin and perforin which are central to keratinocyte apoptosis in SJS/TEN. TNF-α upregulates inducible nitric oxide synthase in keratinocytes through granulysin expression, which leads to nitric oxide buildup and FasL-mediated cell death, and this cell-mediated cytotoxic reaction triggers widespread keratinocyte apoptosis, causing extensive skin damage.[8] Thus, TNF-α inhibitors can be used as part of the treatment.

CONCLUSION

SJS and TEN are dermatologic emergencies with high morbidity and mortality rates. TNF-α plays a significant role in cytotoxic protein production, especially granulysin which further exacerbates keratinocyte cell death. Therefore, TNF-α inhibitors such as etanercept show promise in the treatment of SJS/TEN by speeding up skin healing, shortening re-epithelisation time and reducing complications and side effects during hospitalisation. Etanercept can be given as a single dose or two subcutaneous doses but should be started promptly after the disease begins. It is advisable to avoid combining it with other immunosuppressive agents to prevent excessive immunosuppression.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

REFERENCES

1. Chong I, Chao A. Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis and Treatment with a Biologic: A Case Report. Perm J 2017;21:16-60.
2. Pathania V, Kothari R, Tripathy D, Sengupta P, Vashisht D, Shankar P. Single dose Etanercept Monotherapy for Treating Stevens-Johnson Syndrome. Indian J Drugs Dermatol 2021;7:91.
3. Kurnia IY. The Role of Tumor Necrosis Factor-Alpha (TNF-α) Inhibitor in Steven Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TEN) Management: A Systematic Review. Intisari Sains Medis 2022;13:436-42.
4. Patel TK, Barvaliya MJ, Sharma D, Tripathi C. A Systematic Review of the Drug-induced Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Indian Population. Indian J Dermatol Venereol Leprol 2013;79:389-98.
5. Dobry AS, Himed S, Waters M, Kaffenberger BH. Scoring Assessments in Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. Front Med (Lausanne) 2022;9:883121.
6. Mukherjee EM, Phillips EJ. Where to Place Etanercept and Combination Treatment for Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis? Ann Allergy Asthma Immunol 2022;129:269-70.
7. Chang HC, Wang TJ, Lin MH, Chen TJ. A Review of the Systemic Treatment of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. Biomedicines 2022;10:2105.
8. Dreyer SD, Torres J, Stoddard M, Leavitt E, Sutton A, Aleshin M, *et al*. Efficacy of Etanercept in the Treatment of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. Cutis 2021;107:E22-8.

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