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Toxic Epidermal Necrolysis: A Clinical Case Report with Emphasis on Diagnosis, Management, and Prognostic Implications

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ABSTRACT

Toxic epidermal necrolysis (TEN) is a rare, life-threatening dermatologic emergency characterized by extensive keratinocyte apoptosis, resulting in widespread epidermal detachment and mucosal involvement. Its pathogenesis is primarily linked to an immune-mediated response triggered by certain medications. This report presents a case of a 33-year-old female who developed TEN following administration of an antibiotic regimen. The patient exhibited progressive skin detachment affecting over 30% of the body surface area, with concurrent ocular and oral mucosal involvement. Despite initial delays in diagnosis, aggressive management with fluid resuscitation, prompt drug discontinuation, and systemic immunosuppressants led to stabilization and eventual recovery. This case highlights the importance of early recognition, the need for a multidisciplinary approach, and the challenges in managing complications such as secondary infections and multi-organ dysfunction. Additionally, we discuss the diagnostic criteria, therapeutic options, and the role of emerging therapies, providing a comprehensive overview for clinicians facing similar cases.

KEYWORDS: Toxic epidermal necrolysis, Stevens-Johnson syndrome, keratinocyte apoptosis, dermatologic emergency, mucosal involvement, drug-induced hypersensitivity, immunosuppressive therapy, multidisciplinary management.

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INTRODUCTION

Toxic epidermal necrolysis (TEN) is an acute and severe mucocutaneous reaction, first described by Alan Lyell in 1956, that shares pathophysiological similarities with Stevens-Johnson syndrome (SJS). Together, SJS and TEN form a disease continuum distinguished by the extent of skin detachment, with TEN involving more than 30% of the total body surface area (TBSA). This rare entity has an incidence of 0.4 to 1.9 cases per million people annually and carries a mortality rate ranging from 25% to 35%, making early diagnosis and management critical. The majority of TEN cases are drug-induced, with anticonvulsants, sulfonamides, and antibiotics being the most common culprits. The condition is characterized by widespread keratinocyte necrosis mediated through an aberrant immune response involving cytotoxic CD8+ T cells and the Fas-FasL pathway, leading to extensive epidermal detachment and mucosal erosions. Clinically, TEN presents with a prodrome of fever and malaise, followed by rapidly progressing erythematous macules, blisters, and full-thickness epidermal sloughing, resembling large-scale burns.1,2,3,4

Management of TEN requires an interdisciplinary approach, typically within an intensive care or specialized burn unit. Prompt withdrawal of the offending agent is the cornerstone of treatment, followed by supportive care aimed at maintaining fluid balance, electrolyte stability, and preventing secondary infections. Despite advancements in supportive therapies, immunomodulatory agents such as intravenous immunoglobulin (IVIG) and corticosteroids continue to be debated, with emerging evidence suggesting potential benefits of TNF-alpha inhibitors like etanercept. Given its high morbidity and mortality, understanding the prognostic factors is essential. The SCORTEN (Score of Toxic Epidermal Necrolysis) tool is widely used for risk stratification and prognostication.5,6,7,8

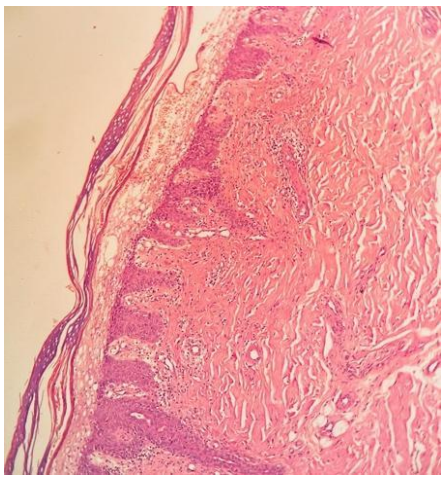
CASE PRESENTATION

Female patient, 33 years old, with a personal history of chronic kidney disease KDIGO G5 since 2009, initially treated with peritoneal dialysis, candidate for kidney transplantation, which was performed by living donor (mother), without apparent complications after the transplant, in treatment with unspecified steroid and Tacrolimus. Arterial hypertension diagnosed in 2022. In December 2022 the diagnosis of humoral rejection was made, for which management was started based on plasmatic replacement and new renal function replacement treatment was started based on hemodialysis. In March 2023, he presented a history of hospitalization for Mahurkar catheter infection for which treatment was given in his medical unit based on imipenem, amikacin and vancomycin for 17 days at unspecified doses.

Her current illness began on March 21, 2003 with fever of 39°, predominantly at night, which did not improve with the use of antipyretics, and was accompanied by an attack of the general condition. Diarrheic evacuations on fifteen occasions during the day, without mucus or blood, denies abdominal pain. She was admitted to the hospital where Gentamicin was administered at an unspecified dose and for an unspecified period of time. After starting this drug, she presented disseminated dermatosis, characterized by erythematous plaques, of different sizes, predominantly in the anterior and posterior thorax, as well as in the upper and lower extremities, with ill-defined borders, pruritic and burning, for which reason they decided to suspend Gentamicin and started a new antibiotic based on Amikacin.(Figure 1)

Figure 1. Skin with disseminated dermatosis.

On admission to the hospital unit, she continued with the dermatosis described above, with no other alterations. Laboratory tests showed only moderate normocitic normochromic anemia, negative viral panel and negative CMV antibodies. During her hospital stay she showed no improvement in dematologic lesions; disseminated dermatosis, characterized by areas of necrosis and violaceous erythema, which affected the whole body, pruritic and burning, with positive Nikolsky's sign (Figure 1).



New labs showed eosinophilia > 650 (7-17.4%), no elevation of transaminases or leukemoid reaction during the acute phase of the dermatosis, CRP: 86.8. Since there was no clinical improvement and she continued with diarrhea, cultures, coproparasitoscopy, anti-DNA antibodies, antimitochondrial antibodies, antinuclear antibodies, antimuscle smooth iGg antibodies were taken, all being negative. Due to the deterioration of the patient's condition, a telemedicine consultation was made to the Dermatology service, which referred dermatosis secondary to the use of antibiotics, for which a skin biopsy was suggested (Figure 2) Figure 2. Skin biopsy with presence of epidermal and subepidermal necrosis with detachment of the epidermis.

The patient continued with clinical deterioration, which led to her death. The biopsy report was compatible with epidermal necrolysis, but the result was obtained after her death.

DISCUSSION

The main cause of NET continues to be drug use. The main drugs that have been related are carbamazepine, phenytoin, phenobarbital, non-steroidal anti-inflammatory drugs (NSAIDs). Among those considered high risk; lamotrigine and nevirapine. Intermediate risk; macrolides. Low risk; sertraline and tramadol. It is important to consider some other causes, such as infections (e.g. herpes simplex virus, some Mycoplasma species, vaccines such as MMR, etc.)

When T lymphocytes are activated, CD8 tend to concentrate in the blisters and epidermis, CD4 infiltrate the dermis and TNF-α and interferon gamma (IF-γ) activate *Natural Killer* (NK) lymphocytes generating direct damage.

The characteristic clinical picture consists of three phases: prodromal period, necrolysis period and re-epithelialization period. The prodromal period is characterized by general symptoms, which usually last 48-72 hrs. The necrolysis period presents with confluent erythematous-purpuric macules on the trunk and face that usually extend to the rest of the body. The macules evolve to flaccid blisters that acquire a grayish color and are of serous or serohematic content, which usually rupture and leave bare areas. Nikolsky's sign and Asboe Hansen's sign are usually present. The re-epithelialization period lasts one to three weeks, residual hyperpigmentation, nail dystrophy and diffuse hair loss usually occur.

Histopathologic findings on skin biopsy are usually necrosis and separation of the epidermis, presence of necrotic keratinocytes, a pyknotic nucleus and denuded papillae.

There are two validated scales for predicting mortality in patients with severe pharmacoderma. The best known is the SCORTEN scale, which calculates the mortality rate based on seven variables . The second and recently validated one is the ABCD-10 scale, in which some extra variables were added to those present in the SCORTEN scale, which present an additional risk of mortality in patients with severe pharmacoderma.

CONCLUSION

Epidermal necrolysis is considered a dermatologic emergency. Management requires a multidisciplinary approach which focuses on general skin care, multiorgan support and pharmacological therapy aimed at limiting the immune and inflammatory response. It has been seen in different studies that patients have better survival when managed in the ICU. It is important to remove the causative drug at the time of diagnosis. On the other hand, resuscitation is a particularly important aspect, since the most frequent cause of hemodynamic instability and risk of shock is fluid loss. A meta-analysis was performed in 2021 which concluded that cyclosporine and the combination of gamma globulin with corticosteroid can reduce mortality in patients with toxic epidermal necrolysis. Surveillance of the acute picture is of vital importance due to the increased risk of mortality in the first year after diagnosis (50%). The management of TEN requires not only acute clinical acumen but also a deep understanding of its complex pathogenesis and individualized therapeutic strategies. This case contributes valuable insights into the challenges of managing TEN and advocates for a protocolized approach that integrates prompt drug withdrawal, intensive supportive measures, and, where appropriate, selective use of immunomodulatory therapies. Future research is warranted to elucidate optimal treatment algorithms and to explore novel therapies targeting specific immunopathological pathways, ultimately aiming to improve survival rates and quality of life for patients afflicted with this devastating condition.

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