

## Case Report

# Amoxicillin induced toxic epidermal necrolysis (TEN): a case report

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**Received:** 17 February 2015

**Accepted:** 21 February 2015

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### ABSTRACT

Each year many patients are hospitalized due to adverse drug reactions. Adverse reactions are the recognized hazards of drug therapy and they can occur with any class of drugs and many studies revealed that the incidence is more in case of antibiotics. Amoxicillin is a broad spectrum, bactericidal, beta lactam antibiotic, commonly used to combat various infections. Penicillin group of drugs are known to cause cutaneous drug eruptions especially in pediatric population. Most of the time, these eruptions are mild in nature, however, sometimes they represent the early manifestation of rare, severe drug-induced cutaneous reactions, such as Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Toxic Epidermal Necrolysis (TEN) is a rare, life threatening dermatological disorder that is usually induced by medications. Seventy percent of the cases of TEN are drug induced, most commonly implicated drugs being anticonvulsants, antibiotics and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). Here, we report a case of toxic epidermal necrolysis induced by amoxicillin in a 16 year old female patient. Rigorous treatment with systemic corticosteroids and immunoglobulins helped in recovery of the patient. The case is being reported to emphasize the need for efficient pharmacovigilance in order to motivate adverse drug reaction reporting so as to gather more and more data regarding adverse drug reactions. Through this report, we also seek the support of everyone concerned to detect and, if possible, prevent adverse reactions to drugs.

**Keywords:** TEN, Amoxicillin, Pharmacovigilance, Adverse drug reactions

### INTRODUCTION

Toxic Epidermal Necrolysis (TEN) and Stevens Johnson Syndrome (SJS) are considered to be two ends of a spectrum of severe epidermolytic adverse cutaneous drug reactions that predominantly involve the skin and mucous membranes, differing only by their extent of skin detachment.

SJS is considered a minor form of TEN characterized by less than 10% total body surface area (TBSA) of skin detachment, and an average reported mortality of 1-5%, whereas TEN is characterized by more than 30% skin detachment, and an average reported mortality 25-35%.<sup>1</sup>

Both conditions are characterized by keratinocyte apoptosis and cleavage of the epidermis from the dermis resulting in exposure of large areas of dermis akin to superficial and partial thickness burn injuries.

TEN was originally described by Debre et al. in 1939 in French as *l'erythrodermie bulleuses avec epidermolyse*.<sup>2</sup>

In 1956, Alan Lyell described four patients with an eruption resembling scalding of the skin which he called toxic epidermal necrolysis or TEN.<sup>3</sup> So it is now recognized as TEN Lyell's syndrome.

Worldwide, the average annual incidence of TEN is 0.4-1.3 cases per million population.<sup>4</sup>

TEN can be induced by drugs or infection, immunization, environment chemicals, radiation or can be idiopathic.<sup>5</sup>

## CASE REPORT

### History

A 16 year old female patient presented with history of throat pain to a local doctor for which she was prescribed capsule amoxicillin 500 mg bd  $\times$  3 days and tablet paracetamol 500 mg bd  $\times$  3 days.

After consumption of the first dose of medication, patient developed painful bleeding oral ulcers with which, she then presented to Dhiraj hospital on the same day.

Two days later, patient developed bilateral painful skin lesions which were unruptured and filled with fluid. These lesions first appeared over both the fore arms and then gradually progressed to involve face, trunk, extremities, eyes, genitals and arms.

Patient complained of burning sensation all over the lesions developed associated with nausea, headache, burning micturition and constipation.

### Findings on examination

#### General Examination

The general condition of the patient was fair, patient was conscious, oriented, with all her vital signs in normal range. Bilateral upper limb edema was present. Patient had increased salivation, redness of eyes, photophobia, difficulty in opening eyes, inability to take foods or talk, discharge of pus from oral cavity.

#### Systemic examination

No significant abnormalities were detected.

#### Local examination

Ill defined, multiple, erythematous macular lesions with darker hemorrhagic centres were present on the face, chest, abdomen, back, upper and lower limbs.

Vesicular lesions involving the mucosal areas were present on the tongue, buccal mucosa, eyes and genitalia which were associated with local bleeding, purulent discharge and crusting.

‘Nikolsky’s sign’ was positive.

#### Laboratory findings

All the routine investigations were performed although.

Nothing was significant.

### Causality assessment

On causality assessment using Naranjo’s causality algorithm, association was probable for Amoxicillin.



**Figure 1: A 16 year old female patient with toxic epidermal necrolysis signs after amoxicillin administration.**

### Management

Both amoxicillin and paracetamol were withdrawn immediately.

Patient was treated aggressively with intravenous dexamethasone 8 mg/day  $\times$  5 days which was gradually tapered over a period of 15 days to 2 mg/day along with intravenous pheniramine maleate 50 mg bd  $\times$  5 days and thereafter SOS.

Intravenous immunoglobulin 15 gm/day was given from the 2<sup>nd</sup> day of admission  $\times$  3 consecutive days.

Injection ceftriaxone 1 gm bd  $\times$  3 days was administered followed by injection azithromycin 500 mg od  $\times$  5 days. This was followed by injection meropenam 1 gm tds  $\times$  15 days and injection linezolid 600 mg bd  $\times$  15 days.

Skin erosions, painful oral ulcers and ophthalmic lesions were treated symptomatically.

Supportive measures included IV fluids and correction of electrolyte imbalance.

Patient recovered from this fatal adverse reaction after rigorous treatment for 30 days.

She was discharged with the advice to continue topical antibiotics for skin lesions and to continue oral prednisolone in tapering doses.

On follow up visit, after a week the skin and eye lesions had completely healed and the patient was given an "alert card", mentioning various medications which were to be avoided.

## DISCUSSION

The cutaneous drug reactions are among the most commonly reported adverse drug reactions.

TEN is considered a severe form of the erythema multiforme spectrum.

Skin reactions in cephalosporin drug allergy are approximated to occur between 1% to 3 % of patients.

Drug exposure and a resulting hypersensitivity reaction is the cause of the very large majority of cases of TEN.

To date, the pathogenesis of TEN is still not fully understood.

Originally, it was hypothesized that the major factor involved was CD8+ cytotoxic T cells, although more recently it is believed that Fatty Acid Synthetase (FAS) and FAS Ligand (FASL) are more responsible for keratinocyte death.

TEN is most commonly characterized by skin changes (scattered 2-ring target-like lesions with a dark-red center and lighter red halo and red macules with central blistering that can coalesce to larger areas of denuded skin), hemorrhagic mucositis (mouth, eyes, genitals, and respiratory tract), and systemic symptoms (fever, malaise, and possible internal organ involvement).

The most commonly reported drugs for inducing TEN when used over a short period of time are trimethoprim-sulfamethoxazole, sulfonamide antibiotics, aminopenicilins, cephalosporins, quinolones, carbamazepine, phenytoin, phenobarbital, valproic acid, oxycams, allopurinol and corticosteroids.<sup>2</sup>

As a consequence of the discovery of the anti-Fas potential of pooled human intravenous immunoglobulins (IVIG) *in vitro*, IVIG have been tested for the treatment of TEN, and their effect reported in different noncontrolled studies. To date, only one study out of 12 non controlled studies confirm the known excellent tolerability and a low toxic potential of IVIG when used with appropriate precaution in patients with potential risk factors.<sup>3</sup>

Our patient showed improvement with high dose of IVIG and did not experience any adverse event related to IVIG.

As sepsis is the most dreadful complication, higher antibiotics are commonly administered to TEN patients.

Currently, no treatment modality has been established as a standard for these patients.

Due to rarity of these disorders, there are no randomized controlled trials of pharmacological agents in the treatment of TEN.

However, there are case reports of successful treatment with IVIG, systemic corticosteroids, plasmapheresis, cyclosporine, cyclophosphamide, anti Tumour Necrosis Factor- $\alpha$  (TNF- $\alpha$ ) and hemodialysis<sup>6</sup> but with limited data to be recommended as first line treatment.

## CONCLUSION

Indices TEN is a complex pathology, although the incidence is relatively low, it is important to identify patients at risk to avoid delaying therapy.

Despite continued research efforts and an enhanced understanding of the likely mechanism involved, no specific treatment has demonstrated significant enough improvement to truly affect the associated morbidity and mortality in TEN patients.

Since amoxicillin is a broad spectrum bactericidal antimicrobial agent and most common drug used in microbial infections, which is a common problem in a developing country like India where poverty and poor hygienic conditions is the leading cause of infections, occurrence of such events has to be managed carefully.

Our patient could be salvaged with timely appropriate treatment but it is good to remember that "prevention is always better than cure".

Reporting of such events is utmost necessary, efficient pharmacovigilance holds key in this regard.

Avoiding offending drugs in family members of the victim because of genetic susceptibilities to TEN/SJS could also be emphasized.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

## REFERENCES

1. French LE. Toxic epidermal necrolysis and Stevenson Johnson syndrome: our current understanding. *Allergol Int.* 2006;55:9-16.

2. Debre R, Lemy M, Lamotte M. L'erythrodermie bulleuses avec epidermolyse. *Bull Soc Pediatr (Paris)*. 1939;37:231-8.
3. Lyell A. Toxic epidermal necrolysis: an eruption resembling scalding of the skin. *Br J Dermatol*. 1956;68:355-61.
4. Abood GJ, Nickoloff BJ, Gamelli RL. Treatment strategies in toxic epidermal necrolysis syndrome: where are we at? *J Burn Care Res*. 2008 Jan-Feb;29(1):269-76.
5. Nagy N, McGrath JA. Blistering skin diseases: a bridge between dermatopathology and molecular biology. *Histopathology*. 2010 Jan;56(1):91-9.
6. Mukasa Y, Craven N. Management of toxic epidermal necrolysis and related syndromes. *Postgrad Med J*. 2008;84:60-5.

DOI: 10.5455/2320-6012.ijrms20150442

**Cite this article as:** Patel JB, Agrawal P, Soitawala S, Sattigeri BM. Amoxicillin induced toxic epidermal necrolysis (TEN): a case report. *Int J Res Med Sci* 2015;3:1011-4.