

Amoxicillin induced toxic epidermal necrolysis: a case report**Tittu George Zachariah^{1*}, K.N. Sathyanarayana Rao¹, Tonita Mariola Noronha², Swathi Acharya¹, Pooja M¹, Noble J¹**¹Department of Pharmacology, K.S. Hegde Medical Academy, Mangalore, India²Department of Dermatology, Justice K.S. Hegde Charitable Hospital, Mangalore, India**Received:** 05 April 2016**Revised:** 08 April 2016**Accepted:** 10 May 2016***Correspondence to:**Dr. Tittu George Zachariah,
Email: tittu327@gmail.com**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.**ABSTRACT**

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 paediatric 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 12 year old male patient. Treatment with strong antibiotics, immunosuppressant and other supportive measures 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 every-one concerned, to detect and, if possible, prevent adverse reactions to drugs.

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

Amoxicillin, an acid stable, semi-synthetic drug belongs to a class of antibiotics called the penicillins (β -lactam antibiotics). It is shown to be effective against a number of infections caused by wide range of gram-positive and gram-negative bacteria.¹ Amoxicillin is used as an effective therapy for sinusitis, otitis media, acute exacerbations of chronic bronchitis, epiglottitis, urinary tract infections, meningitis and salmonella infections. Adverse reactions include hypersensitivity reactions: angioedema, anaphylaxis, serum sickness: mild fever, rash, leukopenia to severe arthralgia, purpura, lymphadenopathy, splenomegaly, mental changes, generalised edema, albuminuria and haematuria.

Cutaneous adverse reactions like skin rashes, urticaria, itching, fixed drug eruption, angioedema are the common ones among the various adverse drug reactions (ADR).^{2,3} In this wide spectrum of cutaneous reactions, Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but serious form of ADRs affecting patient's life.²

Clinically, SJS and TEN are characterized by polymorphic lesions like erythematous macules, papules, and plaque, vesicles, and bullae predilected to distal extremities with Nikolsky's sign positive. "Target" lesion with bull's eye appearance is characteristic of SJS and TEN. Oral, genital, and conjunctival mucosa is often involved in the form of erosion or ulceration.⁴ The basic difference between SJS and TEN is the percentage of

body surface area (BSA) involved: <10% in SJS; >30% in TEN; 10 to 30% in SJS-TEN overlap.^{3,4}

SJS and TEN are immune-mediated reactions, due to various etiological factors like drugs, infections, malignancy, and radiation therapy.³ The drugs commonly implicated as the cause of SJS/TEN are anticonvulsants, sulfonamides, non-steroidal anti-inflammatory drugs and antibiotics.⁵⁻⁷

Incidence of SJS and TEN is 0.05 to 2 persons per million populations per year.^{8,9}

CASE REPORT

History

A 12 year old male patient presented with history of high grade intermittent fever and burning micturition to a local doctor for whom he was prescribed tablet Moxitor CV 625 mg (amoxicillin and clavulanic acid) twice daily and tablet paracetamol 500 mg thrice daily. After consumption of the medication, patient developed rashes all over the body associated with itching and fever, for which he consulted at K.S. Hegde hospital. Later patient developed fluid filled lesions all over the body and oral lesions associated with fever. These lesions first appeared on abdomen and then spread to limbs to face and then gradually progressed to involve oral mucosa, eyes and genitals.



Figure 1: Onset of presentation (diagnosis: amoxicillin induced toxic epidermal necrolysis).

General examination

The general condition of the patient was fair, patient was conscious, oriented, with all his 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 food and talk, discharge of pus from oral cavity.

Systemic examination

No significant abnormalities were detected.

Local examination

- Multiple flaccid bullae present over chest, abdomen, back, bilateral arms, thighs and legs.
- "Nikolsky's sign" was positive (chest).
- Erythematous plaques with central dusky hue present over bilateral forearms.
- Multiple papulo vesicles present over bilateral forearms, hands and legs.
- Hyper pigmented macules present over bilateral thighs and legs.
- Erosions and haemorrhagic crusting present over lower and upper lip.
- Whitish plaques present on tongue and buccal mucosa.
- Purulent discharge present over bilateral legs, mouth.
- Erosions present over bilateral upper eyelids.
- Periorbital edema was present.
- Erosions present over glans penis.

Investigations

All the routine investigations were performed and nothing was significant except mild hypokalemia (sodium: 132).



Figure 2: After treatment.

Management

- Both Moxitor CV and paracetamol were withdrawn immediately.
- Patient was treated with antibiotics like azithromycin and linezolid along with cyclosporine,

I.V methylprednisolone and fresh frozen plasma transfusion.

- Skin erosions, painful oral ulcers and ophthalmic lesions were treated symptomatically.
- Supportive measures included I.V fluids and correction of electrolyte imbalance.

DISCUSSION

Cutaneous drug reactions are the most commonly reported adverse drug reactions. TEN though rare, is considered as a severe form of erythema multiform spectrum.¹⁰ It is important to recognize the clinical characteristics of the mucocutaneous eruption at early stage due to the high mortality rate, which ranges from 16 to 25% .¹¹⁻¹⁴ The most frequent cause of this conditions is medication.^{15,16} Drug exposure and a resulting hypersensitivity reaction is the cause of the very large majority of cases of TEN. Till 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 form larger areas of denuded skin), haemorrhagic mucositis (mouth, eyes, genitals, and respiratory tract) and systemic symptoms (fever, malaise, and possible internal organ involvement). Certain genetic factors are associated with increased risk of TEN. For example, certain HLA-types such as, HLA-B*1502, HLA-A*3101 and HLA-B*5801 have been to be linked with TEN development when exposed to specific drugs.¹⁷⁻¹⁹ As sepsis is the most dreadful complication, drugs that are effective against multi drug resistant bacteria are commonly administered. 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 I.V immunoglobulins, systemic corticosteroids, plasmapheresis, cyclosporine, cyclophosphamide, anti-tumour Necrosis Factor- α (TNF- α) and hemodialysis but with limited data to be recommended as first line treatment.²⁰

CONCLUSION

TEN has 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. Reporting of such events is utmost necessary, efficient pharmacovigilance holds the key in this regard. Avoiding offending drugs in family members of the victim because of genetic susceptibilities to TEN/SJS could also be emphasized.

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