# The multidisciplinary approach to the management toxic epidermal necrolysis syndrome (TENS) – a case report

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**Abstract**

Toxic epidermal necrolysis syndrome (TENS) is a severe idiosyncratic reaction, most commonly triggered by medications, and characterized by fever and mucocutaneous lesions leading to necrosis and sloughing of the epidermis. A case of TENS in a sixteen year old boy following polypharmacy is presented. Complete haematological and biochemical tests were carried out and management was symptomatic. This report shows the multidisciplinary approach to the management and highlights the role of the dental surgeon in the management. It concludes that multidisciplinary approach to healthcare provision will be of benefit to the recipients and suggests that awareness be created on drug use and pharmacovigilance.

**Key words. Toxic Epidermal Necrolysis syndrome management**

## Introduction

Adverse Drug Events (ADEs) result from interactions between a pharmacologic agent and the human immune system. These types of reactions constitute only a small subset of all adverse drug reactions. Allergic reactions to medications represent a specific class of drug hypersensitivity reactions mediated by IgE. Immune-mediated drug reactions may be discussed generally in the Gell and Coombs classification system, a widely accepted conceptual framework for understanding complex immune reactions[1]. However, some reactions involve additional, poorly understood mechanisms that are not easily classified. Identifiable risk factors for drug hypersensitivity reactions include age, female gender, concurrent illnesses, and previous hypersensitivity to related drugs[2]. ADEs constitute an important public health problem whose dimensions have been imprecisely defined and contribute an estimated 3.1% to 6.2% of hospitals admission studied[3].

**Gell and Coombs classification of drug hypersensitivity reactions(4).**

| Immune reaction | Mechanism | Clinical manifestations | Timing of reactions |
|---|---|---|---|
| **Type I (IgE-mediated)** | Drug-IgE complex binding to mast cells with release of histamine, inflammatory mediators | Urticaria, angioedema, bronchospasm, pruritus, vomiting, diarrhea, anaphylaxis | Minutes to hours after drug exposure |
| **Type II** (Cytotoxic) | Specific IgG or IgM antibodies directed at drug-hapten coated cells | Hemolytic anemia, neutropenia, thrombocytopenia | Variable |
| **Type III (Immune reaction)** | Tissue deposition of drug-antibody complexes with complement activation and inflammation | Serum sickness, fever, rash, arthralgias, lymphadenopathy, urticaria, glomerulonephritis, vasculitis. | 1 to 3 weeks after drug exposure |
| **Type IV (Delayed, cell-mediated)** | MHC presentation of drug molecules to T cells with cytokine and inflammatory mediator release | Allergic contact dermatitis, maculopapular drug rash. | 2 to 7 days after cutaneous drug exposure |

In diagnosing a cutaneous eruption resulting from an adverse drug reaction it is important to decide whether the eruption is primarily due to the drug, or to an interaction between the disease and the drug. Cutaneous reactions frequently occur when patients are receiving a number of drugs, and thus etiological relationship may be difficult to assess. Some cutaneous drug reactions may be dose-dependent or due to exacerbation of underlying disease. Treatment is largely supportive and includes discontinuation of the causative agents, symptomatic treatment including management of epithelial and mucosal ulcerations as well as patient education[2].

The predisposing factors of ADEs include: female gender, adult, HIV infection, and concomitant viral infection, previous hypersensitivity to chemically-related drug, asthma, renal insufficiency, liver disease, polypharmacy and alcoholism[5-7].

This paper presents unusual and a rare case of adverse drug reactions in the form of TENS seen in a young, immunocompetent male with no previous history of hypersensitivity, the patient neither smoke cigarette nor alcohol. The medical management of the condition was described and dental surgeon's role in the management of the case is also highlighted.

**Case Report**

A sixteen year old student presented at the emergency unit of a private health facility in Egor Local Government Area of Edo State, with a history of generalised itching, blood-stained, bullous eruptions all over the body and oral ulceration as well as inability to feed. These occurred sputum immediately following treatment for malaria using multiple unknown pharmacological. He was taken to another chemist who gave some unidentified injections before coming to the hospital accompanied by the mother and some relatives.

On examination, the patient was weak, pale and appeared dehydrated with pus discharging from the mouth and the eyes. Extra-orally, the lips complete but ulcerated, crusted and incompetent, with marked fetor oris. An intra-oral examination revealed generalized mucosal erosion with desquamation of the gingivae. The temperature on presentation was 39.0$^{o}$C, pulse 102 min-1 and respiratory rate 24 min-1. Laboratory examination showed a packed cell volume of 0.49, Creatinine 0.7mg% and Urea 44.0mg%.

Marked fetor oris, pain, inability to eat and bleeding per oral necessitated the dental surgeons' invitation. A working diagnosis of toxic epidermal necrolysis syndrome (TENS) following adverse drug reaction was made and treatment, following withdrawal of 'the causative drugs' was largely supportive and symptomatic as well as patient and parents education.

The patient was rehydrated with fluids (500mls of 0.90% w/v of NaCl (Normal saline), alternated with intravenous 500mls of 5% dextrose in normal saline) every four hours on days one and two, then every eight hours from day three to seven.

He was also on intravascular hydrocortisone sodium succinate 200 mg stat, then 100mg every eight hours for five days and Intravascular chlorpheniramine maleate 2 mg eight hourly for five days;

parenteral tramadol 100mg eight hourly, the 50mg eight hourly for the following two days, followed by oral doses of ibuprofen 200mg eight hourly over a four day period for relief of pain and;

Intravenous amoxicillin, 500mg and metronidazole, 500mg were employed throughout the period.

(Warm saline mouth bathe, lignocaine anaesthetic spray pro re nata and tetracycline mouth rises three hourly) were also prescribed.

The patient's condition improved with the disappearance the numerous ulcerations and he was able to feed and take his medications per oral on the fifth day after admission. His recovery was assessed as satisfactory by the various teams that were invited to manage and he was discharged on the third week, after a fine scaling and root planning.

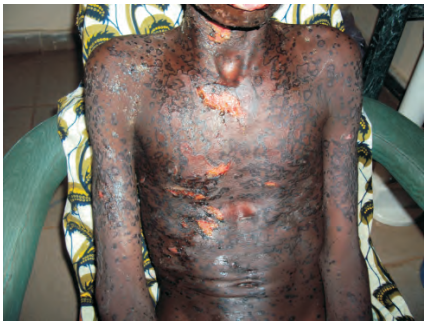

**Figure 1. Photograph of the patient three days post admission***
*Earlier pictures are not available because patient and parents declined consent until day three.

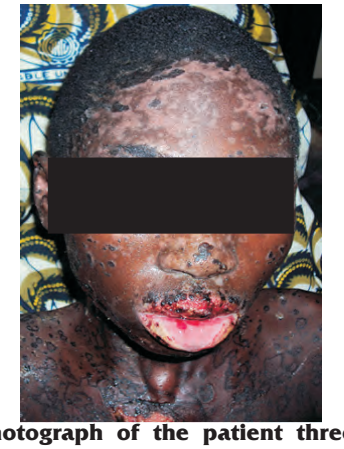

**Figure 2. Photograph of the patient three days post admission**

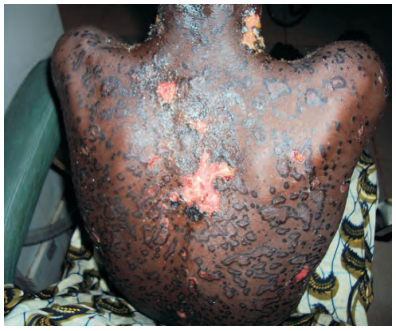

**Figure 3. Photograph of the patient three days post admission**

**Figure 4. Photograph of the patient 8 days post admission**

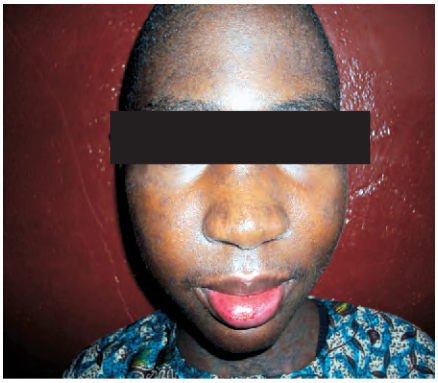

**Figure 5. Photograph of the patient 8 days post admission**

## Discussion

Erythema multiforme (ER), Stevens-Johnson syndrome (AJS) and toxic epidermal necrolysis syndrome (TENS) are conditions characterized by blisters (bullous reactions); they have traditionally been regarded as related disorders, with occasionally overlapping signs and symptoms. Similar disorders include necrosis of keratinocytes, leading to blisters and epidermal detachment. Recent evidence suggests that ER should be separated from SJS and TENS: ER is usually not caused by drugs, while SJS and TENS in general are adverse drug reactions[9].

ER is an acute disease characterized by symmetrically distributed papular lesions affecting mainly the extremities, often with mucosal erosions. The typical lesion is target-shaped: it is concentrically organized with three different-coloured zones, often with a blister in the centre, and it is clearly demarcated from the surrounding skin. There may be general symptoms such as fever and malaise. SJS (formerly also called erythema multiforme of major type) shows widespread skin lesions, which may either be target shaped or consist of erythematous macules with epidermal detachment, together with severe mucosal erosions. Erosions of the skin do not exceed 10%of body surface area. The general symptoms are more marked than in EM.

TENS is characterized by widespread erythematous areas with epithelial necrosis and epidermal detachment (> 10 per cent of body surface area), leaving bare dermis. Initially there are often also small erythematous or purpuric lesions with or without blisters. Extensive mucosal erosion is frequent. General symptoms, usually severe, include high fever, malaise and painful skin. TENS is a rare, potentially life-threatening medical emergency characterized by wide-spread epidermal sloughing of skin accompanied by mucus membrane involvement. In the majority of the cases, there is a history of recent drug ingestion. Further supporting the notion of a drug- provoked reaction is the fact that readministration of the suspect drug can cause a recurrence of TENS. Antibiotics; such as sulphonamides and penicillins, NSAIDS; particularly of oxicam-types, and anticonvulsant medications; particularly phenobarbital, phenytoin, carbamazepine and valproic acid are the most common drugs identified in cases of TENS[9-14].

The pathophysiologic process results from an outpouring of cytokines and matrixmetalloproteinases (MMPs) which have a destructive effect on the extracellular matrix and may play a part in the epidermal/dermal cleavage seen with this disease and serious ADEs have been estimated to account for 3.1% to 6.2% of hospitals admissions and mortality rate averages 30% of cases[15].

The case presented is described as unusual because polypharmacy is the only similarity between the case and usual presentation which include: female gender, adult, HIV infection, and concomitant viral infection, previous hypersensitivity to chemically-related drug, asthma, renal insufficiency, liver disease, polypharmacy and alcoholism[6-8]. 'Healthy' status of the patient is thought to be largely responsible for the smooth recovery of the patient following the supportive interventions of the various managing teams.

This paper concludes that multidisciplinary approach to healthcare provision will benefit patients of ADEs optimally and suggests that awareness should be created on drug use and pharmacovigilance, particularly at the grassroots.

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