Case Report

A Rare Case of Phenytoin-Induced Toxic Epidermal Necrolysis

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ABSTRACT

Toxic Epidermal Necrolysis (TEN) is an uncommon and potentially fatal dermatological condition caused by medicines. Antiepileptic medicines such phenytoin, carbamazepine, and phenobarbital have been classified as high-risk for inducing TEN. After taking a daily dose of 100 mg of phenytoin for 8 days, a 25-year-old male with epilepsy, depression, and migraines developed TEN spanning more than 30% of his total surface area with mucosal involvement. Rigorous treatment of 18 days using systemic and topical antibiotics along with corticosteroids along with immunosuppressant agents helped in complete recovery. The disease is marked by skin lesions, bullous eruptions involving mucosal membranes, and systemic manifestations. We provide a case of phenytoin-induced TEN, with a brief description of the clinical aspects of the condition and the patient's therapy. According to the Naranjo adverse drug response causality evaluation, there is a "possible" causal relationship between the suspected drug and the adverse drug reaction, which is "moderately" severe.

Keywords: Adverse Drug Reaction (ADR); Phenytoin; Toxic Epidermal Necrolysis; Anticonvulsants.

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INTRODUCTION

Toxic epidermal necrolysis (TEN) is a rare, potential life-threatening dermatological condition that is usually induced by a reaction to medications[1]. It is characterized by dermoepidermal detachment. 95% of the patients with TEN have the history of medication use. It is a drug-induced reaction and the most common causative agents include sulfonamides, barbiturates, pyrazolones, and antiepileptic[2].

Antiepileptic drugs shows adverse reactions such as Stevens-Johnson syndrome (SJS) and Toxic epidermal necrolysis (TEN). Most commonly prescribed antiepileptic agent is phenytoin which is known to cause adverse effects. An adverse drug reaction is defined as "any unpleasant or unexpected response to a medicine that occurs at a level regularly employed in man for prophylaxis, diagnosis, or treatment of diseases, or for adjustment of physiological function," according to the World Health Organization[3]. Steven Johnson Syndrome (SJS) and TEN affect 0.05 to 2 individuals per million on an annual basis[4]. SJS is linked to a 1-5 percent mortality rate, which rises to 25-35 percent in the event of TEN. Adverse medication reactions were reported to be responsible for roughly 0.3 to 7% of mortality among hospitalized patients (ADR)[3].SJS refers to cases where epidermal detachment affects less than 10% of the body surface area (BSA); TEN refers to cases where the detachment affects more than 30% of the BSA; and SJS-TEN overlap refers to cases where the detachment affects between 10% and 30% of the BSA. Phenytoin is implicated in 13.37 percent of drug-induced SJS-TEN cases[3]. Duration for phenytoin induced cutaneous rashes develops between 2 to 8 weeks after initiation of treatment and may progress despite discontinuation of the drug. Termination of the causative drug and supportive care are the cornerstone of management of TEN[4]. Various immunomodulatory treatments for SJS and TEN have been proposed, such as glucocorticoids, intravenous immunoglobulin (IVIG) and cyclosporine[2].

CASE REPORT

A 25-year-old male patient was taken to the hospital with redness in his eyes for two days and itchy skin lesions all over his body for one day. He was unable to swallow due to ulceration and blood discharge from the lips since one day. Patient was known case of depression, migraine and seizures. He was on tablet imipramine 75 mg since four years and tablet phenytoin 100 mg since one week. By cutaneous examination: patient was found to be with multiple, well defined, hyper pigment papules of varying sizes with violaceous hue over the scalp, face, chest, back and extremities. Few bullae over the back and abdomen, few lesions over the palms were noted (figure 2). Ulceration and crusting of lower lip (figure 1), erosions over the forehead and back were noted. His physical examination revealed a temperature of 100° F, a heart rate of 133 bpm, and a systolic blood pressure of 130 mmHg. His blood tests revealed a white blood cell count (WBC) of 7530/l, hemoglobin 14.4 g/dl, serum sodium 126mEq/L,

serum potassium 4.7 mEq/L, and serum chloride 93 mEq/L. A diagnosis of phenytoin induced toxic epidermal necrolysis was made. For further treatment, the patient was admitted to the Intensive Care Unit (ICU). Treated with intravenous Injection decadran 2 mg, injection pantoprazole 40mg and injection paracetmol immediately along with this he was prescribed chlorhexidine mouthwash, mucopine gel, and Tess cs (Choline Salicylate (9 percent w/v)) oral gel, as well as tablet fluconazole 150 mg. Due to overall body lesions he was advised for banana leaf dressing. The above mentioned treatment was followed for 5 days. As patient had developed red conjunctiva, scaly lesions over eye lids and whitish discoloration of eye lid margins, edematous lid margins so referred to ophthalmologist then he advised medication Zoxan eye ointment and carboxyl methyl cellulose eye drops. The patient was referred to a neurophysician for a history of seizures, he suggested that the pill phenytoin be substituted with injections levipil 500 mg and injection midazolam 5 mg. Then patient referred to ENT surgeon he evaluated and found nasal cavities narrowing due to extensive crusts and prescribed nasoclear nasal drops. Seizure control was achieved by midazolam and levipil, skin ointment and eye drops were used for the topical treatment of skin and eye infections respectively. Overall treatment was continued for about 20 days.

The patient responded favourably to the treatment and recovered (Figure 3 & 4) from this fatal adverse reaction after rigorous treatment for 20 days. He was discharged from the hospital with the advice to continue tablet levipil 500 mg, tablet pantoprazole 40 mg, chlorhexidine mouth wash, carboxyl methyl cellulose eye drops, tablet fluconazole 150 mg and tablet cyclosporine100 mg. On follow-up visit, after a week the skin and eye lesions had completely healed and he had no fresh complaints. The patient was handed a "warning card" that listed many medications that should be avoided. The association between phenytoin and TEN was evaluated using World Health Organization (WHO). Uppsala Monitoring Centre (UMC) causality assessment criteria, Naranjo's Probability Scale and Modified Hartwig and Siegel Severity Scale. According to WHO-UMC scale the reaction was of 'probable' nature. Naranjo's Scale revealed a score of 8, also signifying a probable association. According to Modified Hartwig and Siegel Severity Scale, the ADR was placed at level 5, wherein the patient required intensive medical care.

Figure 1: Ulceration and crusting of lower lip

Figure 2: Spreading bullae all over the body.

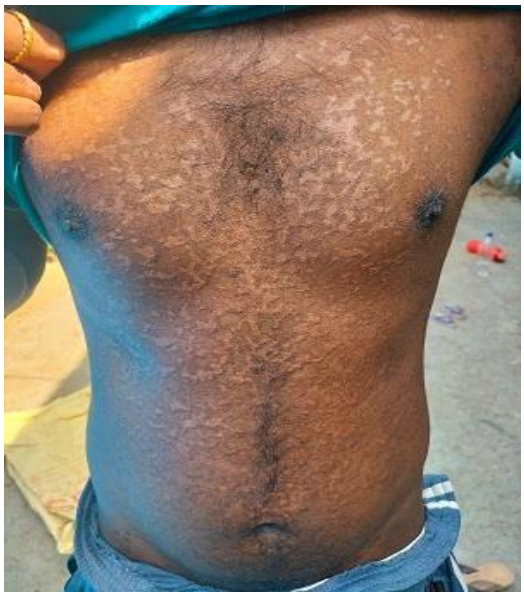

Figure 3 & 4: Improvements in the lesions of skin and oral mucosa after treatment

DISCUSSION

TEN is a severe and life-threatening mucocutaneous reaction caused by some drugs, such as phenytoin. It is characterized by rapidly developing extensive erythema, necrosis, and detachment of the epidermis and mucous membranes that result in severe complications[6]. In current case patient developed redness of eyes discomfort on swallowing first and cutaneous eruption like itchy skin lesions by following day after phenytoin intake. Cutaneous involvement typically starts to affect the trunk, face, palms and soles[5]. More than 90% of the cases include mucocutaneous involvement of buccal, genital and ocular mucosa[6]. These mucocutaneous involvement where also observed in our case. In current case suspected causative drug phenytoin was immediately withdrawn and patient was managed symptomatically with supportive care and early initiation of moderate to high dose of corticosteroids (Injection deccadran 2 mg) for 8 to 10 days and immunosuppressant (tablet cyclosporine 100 mg) for 10 to 15 days.

The current instance received an 8 on the Naranjo causality assessment, suggesting that there is a chance that the ADR was caused by phenytoin, and the Hartwig severity assessment classified the ADR as level 5, indicating a moderately severe reaction needing intensive care hospitalization.

CONCLUSION

TEN is a life-threatening condition linked to the use of anticonvulsants such as phenytoin, which can run in families. Proper communication with the patient regarding use of medications is most important in such life threating condition. According to the paper, phenytoin consumption should be closely monitored in the population for the incidence of TEN type ADR, and patients should be taught about anticonvulsant side effects and cross reactivity with molecules of similar structure.

Abbreviations

TEN: Toxic epidermal necrolysis, SJS: Stevens-Johnson syndrome, ADR: Adverse drug reaction, BSA: Body surface area, IVIG: Intravenous immunoglobulin, WHO: World health organization, WBC: White blood cells, ICU: Intensive care unit, UMC: Uppsala Monitoring Centre, ENT: Ear Nose Throat.

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